EQUITY RESEARCH

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RBC 2016 Biotech Roadmap: Key themes, top catalysts, and best ideas

Top ideas: BIIB, CELG, VRTX, REGN, BMRN, PRTA, ACOR, SANN, SRPT, ITCI and more

Inside this 270+ page report, we lay out 2016 key themes, catalysts and events, key questions, and thoughts, opinions, and models for over 50+ biotech stocks under RBC coverage. *We are hosting a conference call with a separate, detailed 250pg+ slide deck with even more information on Monday (Dec 21st) at 10:00am ET (contact RBC sales for dial-in and slides).*

After five years of a historically bullish outlook and consistent 30%+ returns for the NBI in each of the last three years (vs S&P500 2012-2014 CAGR of +20%), we expect much less outperformance in 2016 for the biotech sector than prior years. We believe the sector could trade in a more modest 15-20% trading band and importantly – investors will have to be much better stock pickers to find winners than in prior years where most stocks simply went up with a tidal wave of investor capital pouring into the space in 2013-2015.

We are fundamentally positive on secular innovation and transformative technology developments that continue to define biotech, thus supporting why there will be select winners in 2016 – but based on our views and conversations with portfolio managers, our outlook for stock performance of the overall sector is more tempered due to: 1) less generalist moneyflow likely to come in 2016 vs prior years, 2) election year jitters and political rhetoric that will likely keep more investors more on the sidelines in 2016 (fund managers believe HC not as attractive during election year with HC on agenda), and 3) much less robust earnings upside to consensus models for the large caps that will keep momentum/growth players more interested in other levered cyclical plays in the market (e.g. AMGN, BIIB, CELG, GILD on track in '15 to report 5-10%+ higher annual EPS results than original guidance at the start of those years and we don't see that much upside EPS in 2016). Of the four "mega caps" in biotech, we see less big data readouts for the large caps in 2016 except BIIB.

Top larger-cap longs are BIIB, VRTX, BMRN, CELG, REGN: 1) Buy BIIB as investors come back to this name in 2016 because it's the most catalyst-rich stock we see for 2016, with the most upside vs downside potential (Alzheimer's, LINGO, SMN-Rx). **2) Buy VRTX** for strong Orkambi launch, strong likelihood of reaching high profitability ("parabolic earnings trajectory"), and two new next-generation correctors in Phase II as a "triple pill," which Street will focus on in 2016 because it could add $1B-$2B more down the road. **3) Buy BMRN** for confidence in dwarfism, Batten's Phase I/II data/ filing to FDA, gene therapy hemophilia call option, and Phase III Peg-Pal results, as well as takeout optionality. **4) Buy CELG** for large portfolio of big pipeline drugs and partnerships reading out, for longer Revlimid "tail" with PD-1 combos, Phase III NHL data (REMARC), and for potential patent settlement for 2024-2025+. **5) Buy REGN** for continued growth and market expansion of Eylea, especially in DME, and emergence as a stand-alone biopharma with its own propietary pipeline that could increase top-line growth (driven by blockbuster launches), drive profitability, and set it up as a potential take out candidate.

Top smid caps for 2016-2017: PRTA, FGEN, AXON, ACOR, SANN, SRPT, MDVN, PBYI, DVAX, ITCI, CRIS, AERI, MDCO, SGEN.

Price target and rating changes inside: ABUS (OP) PT lowered to $12 from $20, ICPT (OP) PT lowered to $300 from $490, CELG (OP) '16 EPS reduced to $5.65 vs consensus $5.68 INFI (OP) PT lowered to $12 from $15, and ARQL (upgrade to OP) PT raised to $5 from $4. *Please see inside report for details.*

Priced as of prior trading day's market close, EST (unless otherwise noted).
All values in USD unless otherwise noted.
For Required Conflicts Disclosures, see Page 276.

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Biotech for 2016: We're fundamentally positive but more tempered on stock performance this year

After five years of a historically bullish outlook and consistent 30%+ returns for the NBI in each of the last three years (vs S&P500 2012-2014 CAGR of +20%), **we expect much less outperformance in 2016 for the biotech sector than prior years.** We believe the sector could trade in a more modest 15-20% trading band and importantly – investors will have to be much better stock pickers to find winners than in prior years where there was a significant tidal wave of capital pouring into the space in 2013-2015.

We are fundamentally positive on secular innovation and transformative technology developments that continue to define biotech, thus supporting why there will be select winners in 2016 – but based on our views and conversations with portfolio managers, our outlook for the stock performance of the overall sector is just more tempered due to 1) less generalist moneyflow likely to come in 2016 vs prior years, 2) election year jitters and political rhetoric that will likely keep more investors on the sidelines in 2016, 3) much less robust earnings upside to consensus models for the large caps that will keep momentum/growth players more interested in other levered cyclical plays in the S&P500 (e.g. AMGN, BIIB, CELG, GILD on track to report 10-15% higher annual EPS results than original guidance at the start of those years and we don't see 10-15% upside earnings in 2016). Of the four "mega caps" in biotech we see less big data readouts for the large caps in 2016 except BIIB. If an Alzheimer's drug is positive in 2016+ (LLY/BIIB), this could really heat up the biopharma enthusiasm level across the board.

Top large-cap longs are BIIB, VRTX, BMRN, CELG, REGN: 1) Buy BIIB as it's the most catalyst-rich stock we see for 2016 with the most upside vs downside potential (Alzheimer's, LINGO, SMN-Rx). **2) Buy VRTX** for strong Orkambi launch, strong likelihood of reaching profitability ("parabolic"), and two new next-generation correctors in Phase II as a "triple pill," which could add $1B-$2B more down the road. **3) Buy BMRN** for continued confidence in dwarfism, Batten's Phase I/II data/ filing to FDA, gene therapy hemophilia call option, and Phase III Peg-Pal results, as well as takeout optionality. **4) Buy CELG** for large portfolio of big pipeline drugs and partnerships reading out, for longer Revlimid "tail" with PD-1 combos, Phase III NHL data (REMARC), and for potential patent settlement for 2024-2025+. **5) Buy REGN** for continued growth and market expansion of Eylea, especially in DME; Praluent's trajectory to achieve blockbuster status; REGN2222 differentiating and getting approved for RSV; increased top-line growth and profitability (driven by blockbuster launches); and emergence as a stand-alone biopharma with its own propietary pipeline that could increase top-line growth, drive profitability, and set it up as a potential take out candidate.

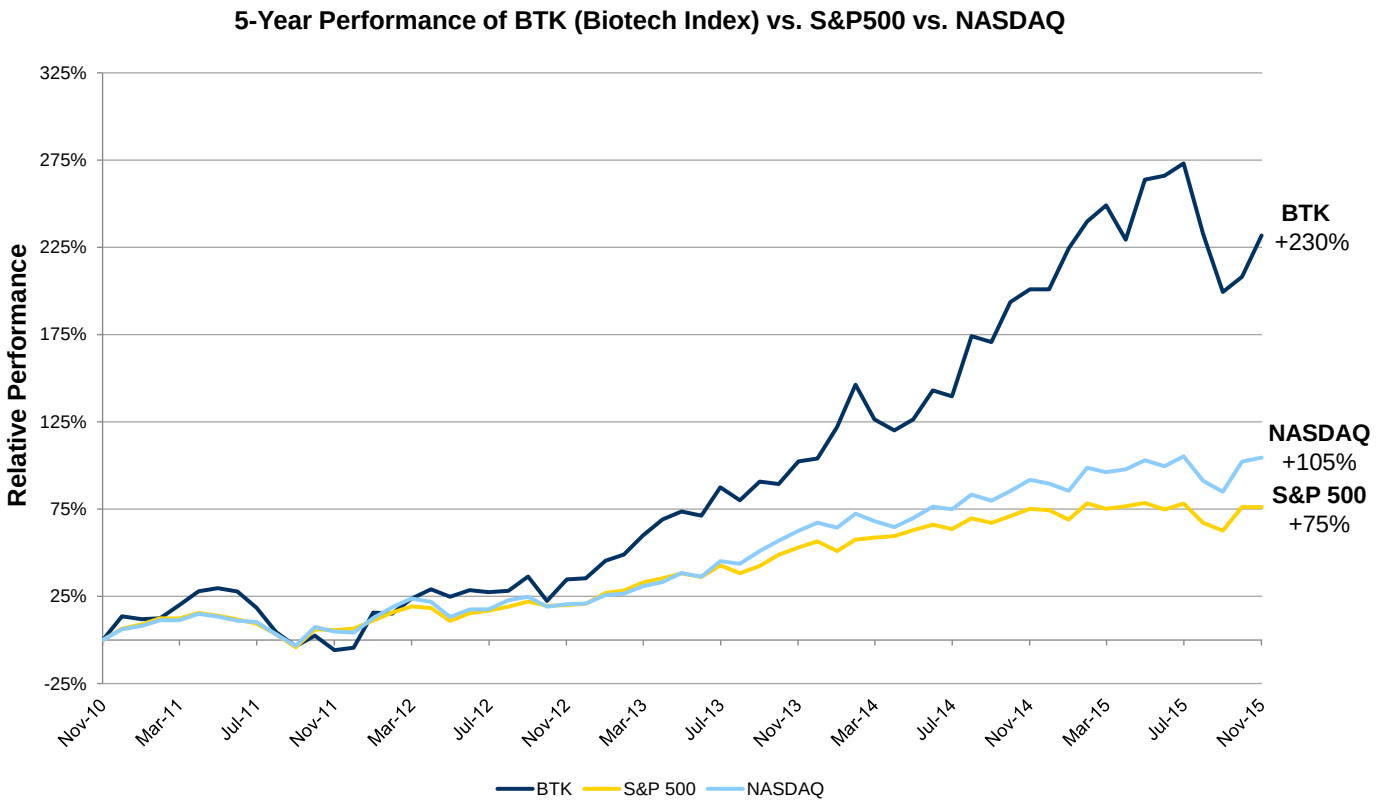
Top smid caps for 2016-2017

(Yee) 1) PRTA should continue to climb higher for Phase I Parkinson's data of PRX002 in H1:16, and Phase I/II amyloidosis data of NEOD001 (including expansion cohort) in mid'16 and pivotal Phase IIb data YE:17+**; 2) FGEN** – off-the-radar smid cap but big upside potential for oral anemia drug roxadustat (Phase III data, regulatory filing in China, partnered with big pharma AZN/Astellas) and for diamond-in-the-rough fibrosis drug FG-3019; **3) AXON** – under-appreciation of new 2nd drug in-licensed for dementia and similar to $3.5B ACAD program not in the stock yet; Phase III Alzheimer's data in 2017 will be a binary catalyst, but we also like AXON for Phase II results in Lewy Body Dementia, and potential for in-licensing more neuro assets. **4) ACOR**– we predict a lot more IP settlements will be coming and the Street will have to realize no generics likely until 2027, which implies 25%+ upside potential to stock; Phase III Civitas Parkinson's data finally coming YE:16 and we predict positive and stock could go up another 10%+.

(Simeonidis) 1) SANN is the only company in the DMD space with a positive Phase III study. FDA and EMA filings for DMD are expected in 1Q16. If approved, idebenone could generate $873MM in peak 2025 US/EU sales in DMD. **2) SRPT** FDA AdCom panel for eteplirsen is now confirmed for January 22, with the PDUFA a month later (February 26). The new SRPT management team has worked closely with FDA and we believe that SRPT has shown probably just enough evidence with its latest dystrophin data to get the nod**. 3) MDVN** – The key question and driver for growth has been and will continue to be "how quickly and how far can XTANDI penetrate the urology segment"? We continue to believe that the move into the early urology segments will be difficult, and this is what investors will be looking for in the next couple of quarters of sales. **4) PBYI** is expected to submit the neratinib NDA in 1Q16, followed by the MAA. While there are some questions about approvability (notably, diarrhea issues), including some that believe that there could be a RTF letter, most investors believe the drug will get a positive decision by YE16/early 17. **5) DVAX** binary event coming up in 1Q16 with Phase III Hep B data; almost everyone expects positive data, so anything other than that would be a major disappointment; assuming positive data, discussion shifts to size of market opportunity, commercial strategy and launch

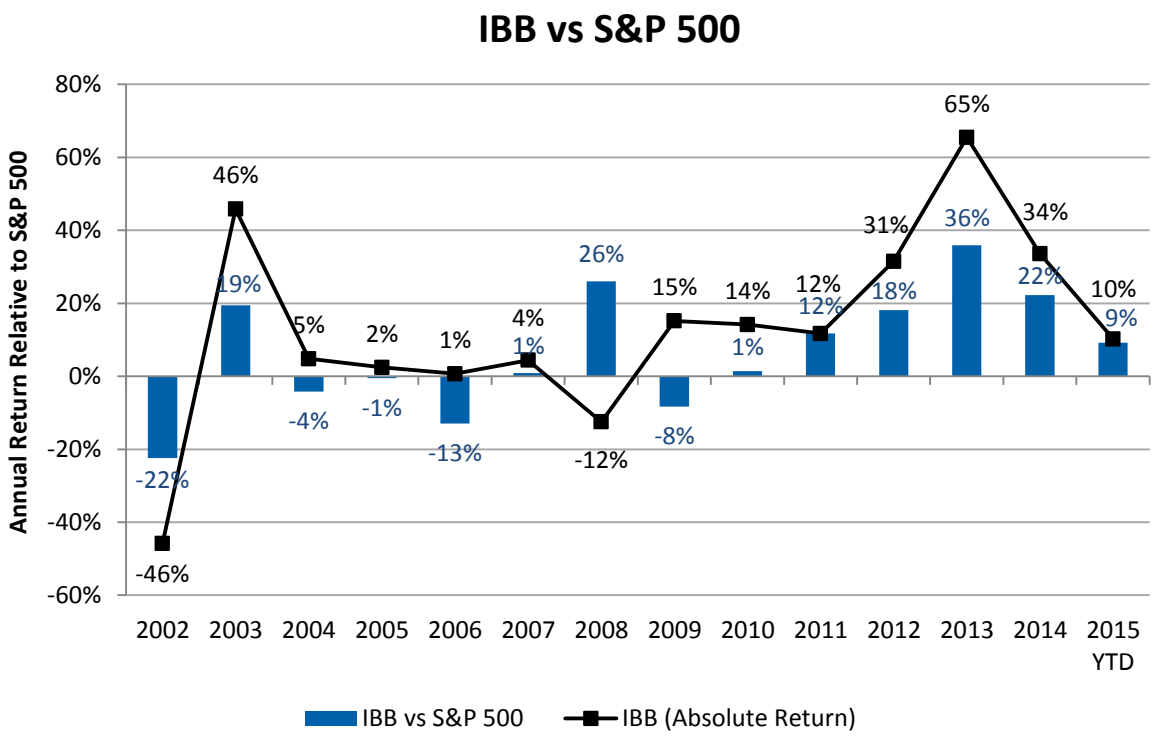
(Butt) 1) ITCI should trend higher due to ITI-007 Phase III data in schizophrenia by 2H:16 and Phase III data in bipolar depression in 2H:16/2017. **2) CRIS** for growth in Erivedge prescriptions, anti-PD-L1 and IRAK4 kinase inhibitor Phase I data in 2016, and pipeline expansion with more oral checkpoint inhibitors added**. 3) AERI** has significant upside due to Phase III data for Roclatan in 2016, potential partnerships for Rhopressa and Roclatan, and potential approvals and launches in 2017/2018 in the US. **4) MDCO** catalysts include ALN-PCSsc Phase II start in 2016, MDCO-216 Phase II data in 2016, and Carbavance Phase III data in 2016/2017. **5)** SGEN is an attractive long-term investment with several catalysts over the next couple of years, including results from Phase III studies in HL, Phase II DLBCL updates for Adcetris and SGN-CD19, Phase I/II AML updates for SGN-CD33A and SGN-CD19A, and potential licensing of technology by additional partners.

Exhibit 1: Biotech has had an impressive run over the past half-decade



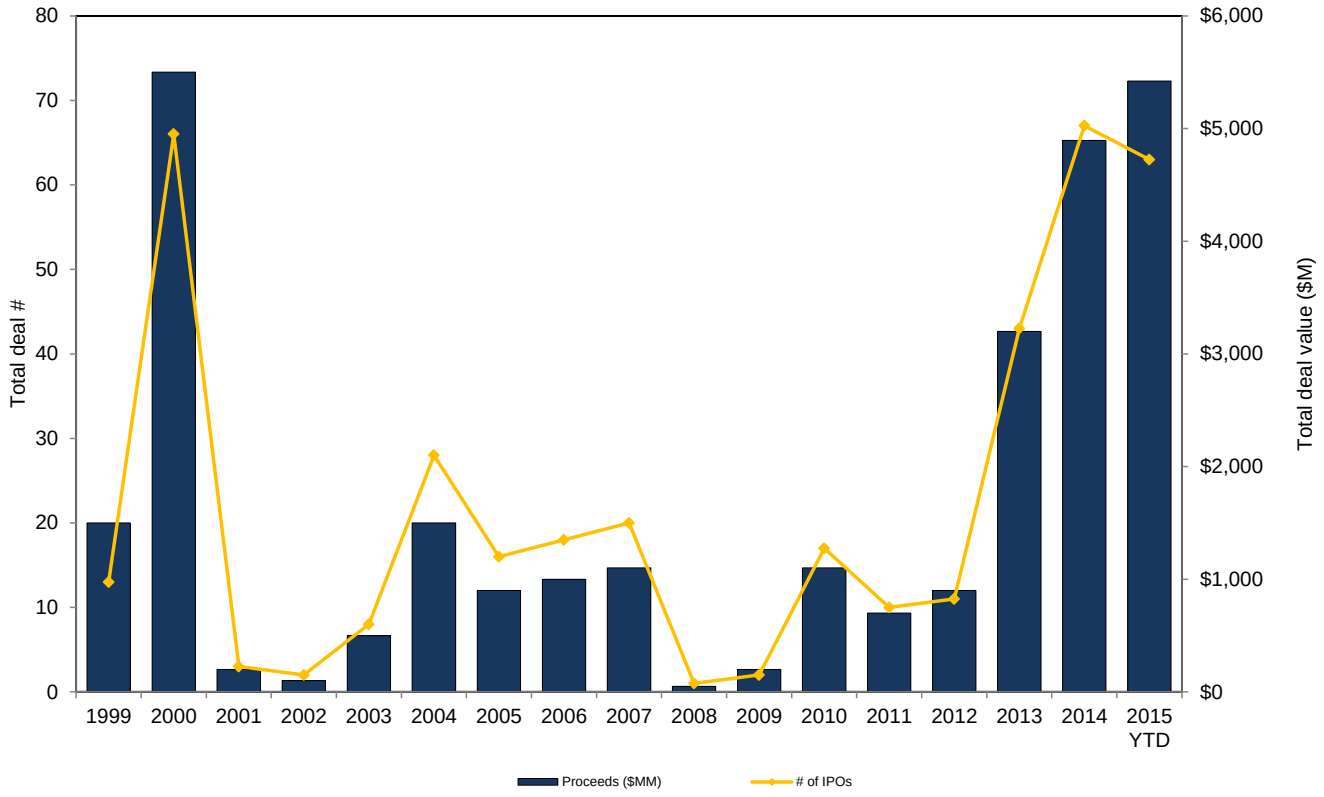
Source: FactSet, RBC Capital Markets

Exhibit 2: IBB's relative performance by year



Source: FactSet

Exhibit 3: 2015 ended up being just like 2000: Number of IPOs and dollars raised (1999-2015)



Source: www.sec.gov, NASDAQ, RBC Capital Markets

Exhibit 4: Recent mega biopharmaceutical M&A deals valued at approximately 4x estimated peak sales

Date Announced	Acquiror	Target	Primary Asset	Primary Indication	Disease Category	Lead Stage	M&A Transaction Details							Target on Conference Call	PR on Target's Website
							Deal Value ($B)	LTM sales ($M)	Peak Sales Est ($M)	Deal value/ LTM sales	Deal value/ Peak sales	Cash / Stock*	Termination Fees		
Jan-12	**Amgen**	**Micromet**	Blinatumomab	ALL	Cancer	Phase II	**$1.2**	-	$300	-	**4.0 x**	All Cash	$40M	No Call Held	N/A
Nov-12	**Gilead**	**Pharmasset**	Sovaldi	Hepatitis C	Infectious disease	Phase II	**$11.0**	-	$4,000	-	**2.8 x**	All Cash	$332M	No	N/A
Aug-13	**Amgen**	**Onyx**	Kyprolis	Multiple myeloma	Cancer	Marketed	**$9.9**	$512	$2,000	19.4 x	**5.0 x**	All Cash	303M	No	Yes
Nov-13	**Shire**	**ViroPharma**	Cinryze	Hereditary angioedema	Orphan disease	Marketed	**$3.9**	$400	$1,000	9.7 x	**3.9 x**	All Cash	$327M	Yes	N/A
Jan-14	**Forest**	**Aptalis**	Canasa	Ulcerative colitis	Gastrointestinal	Marketed	**$2.9**	$688	-	4.2 x	**-**	All Cash	-	No	Yes
Feb-14	**Mallinckrodt**	**Cadence**	Ofirmev	Mild to moderate pain	Pain management	Marketed	**$1.3**	-	-	-	**-**	All Cash	$20M	No	N/A
Feb-14	**Actavis**	**Forest**	Namenda Linzess	Alzheimer's IBS-C	Neurologic Gastrointestinal	Marketed	**$25.0**	-	-	-	**-**	$7B Cash $17B Stock	$2050M	Yes	Yes
Apr-14	**Mallinckrodt**	**Questcor**	H.P. Acthar Gel	Acute MS exacerbations	Autoimmune	Marketed	**$5.6**	$760	$1,500	7.4 x	**3.7 x**	$1.8B Cash $3.4B Stock	$326M	Yes	N/A
Jun-14	**Merck**	**Idenix**	IDX21437	Hepatitis C	Infectious disease	Phase I/II	**$3.5**	-	$1,500	-	**2.3 x**	All Cash	$116M	No Call Held	N/A
Aug-14	**Roche**	**InterMune**	Pirfenidone	Idiopathic pulmonary Fibrosis	Orphan disease	NDA review (US) Marketed (EU)	**$8.3**	-	$1,600	-	**5.2 x**	All Cash	$266M	No	N/A
Oct-14	**Endo**	**Auxilium**	Xiaflex	Dupuytren's contracture, Peyronie's disease	Urology	Marketed	**$2.3**	$400	$800	5.8 x	**2.9 x**	$914M Cash $950M Stock	$220M	Yes	Yes
Dec-14	**Otsuka**	**Avanir**	Nuedexta	Pseudobulbar affect	Neurologic	Marketed	**$3.5**	$110	$500	31.8 x	**7.0 x**	All Cash	$90M	No Call Held	Yes
Dec-14	**Merck**	**Cubist**	Cubicin	S. aureus bacteremia, cSSSI	Infectious disease	Marketed	**$7.9**	$1,370	$2,000	5.8 x	**4.0 x**	All Cash	$250M	No	No
Jan-15	**Shire**	**NPS Pharmaceuticals**	Gattex Natpara	Short bowel syndrome Hypoparathyroidism	Orphan	Marketed BLA review	**$5.2**	$100	$900	52.0 x	**5.8 x**	All Cash	$156M	Yes	No
Mar-15	**AbbVie**	**Pharmacyclics**	Imbruvica	CLL, MCL, WM	Cancer	Marketed	**$21.0**	$730	$4,000	28.8 x	**5.3 x**	$11.7B Cash $8.4B Stock	$680M	No	No
Mar-15	**Horizon Pharma**	**Hyperion Therapeutics**	Ravicti Buphenyl	Urea cycle disorder	Metabolic	Marketed	**$1.1**	$110	$250	10.0 x	**4.4 x**	All Cash	$110M	No	N/A
Mar-15	**Teva**	**Auspex**	SD-809	Chorea associated w/ Huntington's disease	Neurologic	NDA ready	**$3.2**	-	$700	-	**4.6 x**	All Cash	$104M	Yes	Yes
May-15	**Alexion**	**Synageva**	Kanuma	LAL Deficiency	Orphan	BLA review (US) MAA review	**$8.4**	-	$1,500	-	**5.6 x**	$4.3B Cash $4.5B Stock	$325M	No	No
Jul-15	**Celgene**	**Receptos**	Ozanimod	Multiple sclerosis, Ulcerative colitis	Neurologic Gastrointestinal	Phase III	**$7.2**	-	$5,000	-	**1.4 x**	All Cash	$630M	No	No
Nov-15	**Shire**	**Dyax**	DX-2930	Hereditary angioedema	Orphan disease	Phase III	**$5.9**	-	$1,000	-	**5.9 x**	All Cash	$460M	Yes	Yes
Nov-15	**AstraZeneca**	**ZS Pharma**	ZS-9	Hyperkalaemia	Cardiovascular Metabolic	BLA review (US) MAA review	**$2.7**	-	$750	-	**3.6 x**	All Cash	$86M	No	No
						Average	***$6.7***	*$518*	*$1,628*	*17.5 x*	***4.3 x***				
						Min	$1.1	$100	$250	4.2 x	1.4 x				
						Max	$25.0	$1,370	$5,000	52.0 x	7.0 x				

* Stock and cash mix amounts are estimated based on initial announcement data

Source: FactSet and company reports

Source: FactSet, company reports, RBC Capital Markets

Exhibit 5: 2016's most important catalysts and anticipated price movements for stocks within our coverage

1. **BMRN: DMD FDA PDUFA early January 2016 (Jan '16) ~10-20% move**
2. **GILD: MRK elbasivir/grazoprevir Hep C PDUFA date Jan 28, 2016 (Jan '16) ~5% move**
3. **CELG: Potential settlement with ACT on Revlimid litigation (H1:16) ~10% move**
4. **BIIB: Eisai Alzheimer's Abeta BAN2401 Phase I/II data (spring '16) -5-10% to +20% move**
5. **ICPT: FDA AdCom vote on PBC on April 7, 2016 (Apr '16) ~10% move**
6. **BMRN: Phase 1/2 results of BMN-190 in Batten's disease and gene therapy hemophilia data (April '16) ~5%-10% move**
7. **ICPT: OCA approval for PBC with PDUFA date May 29, 2016 (May '16) ~5-10% move**
8. **PRTA: Phase I/II expansion cohort data for NEOD001 in cardiac/renal amyloidosis (Q2:16) ~10% move**
9. **VRTX: Phase I safety data on VX-152 / VX-440 (mid '16) ~5% move**
10. **BIIB: Phase II (SYNERGY) MS data for anti-LINGO (mid '16) -10% to +20% potential upside**
11. **ESPR: Phase II study of '1002 in combination with high-dose statins (mid '16) 10-30% move**
12. **AMGN/ ESPR: MRK's CETP CV outcomes for hypercholesterolemia (Q3:16) ~3-5% move for AMGN, 10-20% move for ESPR**
13. **CELG: Phase III maintenance readout (REMARC) of elderly patients with DLBCL and treated with R-CHOP (Q3:16) ~5% move**
14. **AMGN: Phase III (FOURIER) CV outcomes data and IVUS data (H2:16) ~ 5% move**
15. **VRTX: VX-661 Phase III "hetero" futility interim analysis of 150 patients for CF (H2:16) ~ 5% move**
16. **VRTX: VX-152, VX-440 potential Phase II efficacy data in hetero CF (YE:16) ~10-20% move**
17. **BIIB: ISIS SMN-Rx data (YE:16) -5% vs. +20% potential upside**
18. **GILD: Phase II simtuzumab HVPG cirrhosis data in portal hypertension (YE:16) ~5% move**
19. **BIIB: LLY solanezumab Phase III Alzheimer's data (EXPEDITION-3) (YE:16) -10% to +30% move**
20. **ACOR: Civitas CVT-101 Phase III Parkinson's data (YE:16) ~10% to 20% move**

Source: Company reports, RBC Capital Markets estimates

Exhibit 6: Top SMID-cap biotech "themes" for 2016

1. **Gene Therapy**
   - BLUE, ONCE, AAVL, SGMO, PRQR, QURE, BMRN, CLDN, AGTC, RGNX, VYGR

2. **CAR-T**
   - KITE, JUNO, NVS, BLCM, BLUE, CLLS, CYAD, ZIOP
   - More data at ASCO and ASH 2016 and potential broader indications in oncology

3. **T-Cell and Immunotherapy**
   - ADRO, ATRA, ADAP, NK
   - INCY, MGNX, FPRX, ADXS, NLNK, DVAX, NKTR, TSRO, SGEN, ABBV (PCYC), etc.

4. **Hepatitis B**
   - ABUS (formerly TKMR), ARWR, GBIM, ASMB, JNJ (Novira), Replicor, Spring Bank Pharmaceuticals and other private companies entering the clinic in 2015
   - Moving into Phase I/II trials, getting closer to some proof of concept

5. **RNAi (siRNA/miRNA), antisense**
   - ALNY, ISIS, ARWR, ABUS, RGLS, WaVe, etc.

6. **RNA and Gene Editing**
   - Moderna Therapeutics, Editas Medicine, CRISPR Therapeutics, Intellia Therapeutics

Source: Company reports, RBC Capital Markets estimates

Exhibit 7: Historical Medicare and Medicaid exposure to large caps

Company	2014 US Product Revenue (M)	% of US Rev into Govt. Channels	Amount into US Govt Channels (M)	2014 WW Revenue (M)	US Govt as % of WW Revs
GILD	$18,182	35%	$6,364	$24,890	26%
AMGN	$15,396	50%	$7,698	$20,063	38%
BIIB	$5,567	30%	$1,670	$9,703	17%
CELG	$4,483	40-50%	$1,793 - $2,241	$7,670	23% - 29%

Note: Total revenue includes non-product revenue (i.e. revenue from "unconsolidated joint businesses" and "other").
Source: Company reports, RBC Capital Markets estimates

Exhibit 8: Upcoming FDA/EMA regulatory events

Ticker	Drug	Application	Indication	Timing	Details
ATLN	selexipag	NDA	PAH	Dec 22, 2015	PDUFA decision date
ATLN	selexipag	MAA	PAH	Dec 22, 2015	Potential EU approval
BMY	Opdivo (nivolumab)	sBLA	previously treated NSQ NSCLC	Jan 2 ,2016	PDUFA decision date
BMRN	drisapersen (Kyndrisa)	NDA	DMD	Early Jan 2016	PDUFA decision date
AMGN	Kyprolis	sNDA	relapsed multiple myeloma	Jan 22, 2016	PDUFA decision date
SRPT	eteplirsen	NDA	DMD	Jan 22, 2016	FDA Advisory Panel
MRK	Opdivo + Yervoy	sBLA	previously untreated advanced melanoma	Jan 23, 2016	PDUFA decision date
AMGN	Kyprolis	sDNA	relapsed multiple myeloma (ENDEAVOR trial)	Jan 22, 2016	PDUFA decision date
MRK	Grazoprevir/ Elbasvir	NDA	hepatitis C virus	Jan 28, 2016	PDUFA decision date
CELG	Revlimid	Legal	Myeloma	Jan 2016	Natco expert discovery begins
AMGN	Enbrel	Legal	Autoimmune diseases	Feb 22, 2016	Estimated IPR institution decision (Bass)
SRPT	eteplirsen	NDA	DMD	Feb 26, 2016	PDUFA decision date
GILD	Harvoni	sNDA	Post-transplant patients, decompensated cirrhosis	Feb, 2016	estimated PDUFA
GILD	R/F/TAF	NDA	HIV	Mar 1, 2016	PDUFA decision date
RHHBY	alectinib (Alecensa)	NDA	ALK-positive, locally advanced or metastatic NSCLC	Mar 4, 2016	PDUFA decision date (granted priority review)
REGN	Alirocumab	Legal	LDL-C lowering	Mar 7, 2016	AMGN vs REGN/ SNY: Update on litigation
ICPT	OCA	NDA	PBC (Primary Biliary Cholangitis)	April 7, 2016	AdCom panel date
GILD	F/TAF	NDA	HIV-1 infection	April 7, 2016	PDUFA decision date
CELG	Revlimid	NDA	non-del 5q low risk/ INT-1 transfusion MDS	April 2016	est. PDUFA date
ACAD	Pimavanserin	NDA	Parkinson's disease Psychosis	May 1, 2016	PDUFA decision date
ICPT	OCA	NDA	PBC	May 29, 2016	PDUFA date (priority review granted Aug 31, 2015)
CELG	Revlimid	legal	IP litigation	H1:16	Potential settlement with ACT on Revlimid
AMGN	Evolocumab	NDA	LDL-C lowering	H1:16	Expected Japan Approval
ICPT	OCA	MAA	PBC	mid '16	potential EMA approval
AMGN	etelcalcetide (AMG 416)	NDA	Secondary hyperparathyroidism in pts with CKD	Aug 24, 2016	PDUFA decision date
Sandoz	biosimilar Neulasta	BLA	Decrease incidence of infection due to neutropenia	Sep 2016	est PDUFA date
JNJ	Stelara (ustekinumab)	BLA	Adult patients with moderate-to-severe Crohn's	Sep 2016	est PDUFA date
BMRN	drisapersen (Kyndrisa)	MAA	DMD	Q3:16	potential EMA approval by 3Q:16
AMGN	biosimilar Humira	BLA	Plaque Psoriasis and Rheumatoid Arthritis	Nov 2016	Estimated PDUFA for ABP 501
AMGN	biosimilar Humira	MAA	Plaque Psoriasis and Rheumatoid Arthritis	Dec 2016	Estimated EMA approval for ABP 501
CLVS	Rociletinib	NDA	Advanced EGFR-Mutant NSCLC	H2:16	est PDUFA decision date (granted priority review)
INFI	IPI-145	NDA/MAA	double-refractory iNHL	YE:16	Submit global regulatory filings
UTHR	Remodulin	NDA	PAH	YE:16	Potential approval of implantable pump
REGN	Alirocumab	sBLA	LDL-C lowering	2016	Once monthly dose

**highlighted in blue indicate events of high interest*

Source: Company reports, RBC Capital Markets estimates

Exhibit 9: Upcoming key clinical trial data (part 1)

Ticker	Trial	Drug	Indication	Stage	Timing	Comments
ABUS		TKM-PLK1	GI-NET, ACC	Phase IIa	YE:15	Potential Phase IIa data
ABUS		TKM-PLK1	HCC	Phase IIa	YE:15	Dose escalation HCC expansion cohort data
GLPG/ABBV		GLPG1837 (Potentiator)	Cystic fibrosis	Phase II	YE:15	Initiate Phase II study in Class III mutation patients
BIIB		STX-100	IPF	Phase II	YE:15/ early '16	Phase II double-blind MAD of STX-100
FGEN	(Study 069)	FG-3019	Pancreatic Cancer	Phase II	Jan '16	Prelim. Data: FG+abraxane+gemcitabine at ASCO GI Meeting
BIIB		MT-1303	IBD	Phase III	early 2016	Initiate Phase III studies in IBD
BMRN		PEG-PAL	PKU	Phase III	Mar/Apr '16	Top-line results from pivotal Phase 3 trial
ELY/AZN		AZD3293	Alzheimer's	Phase II/III	Q1:16	Phase II interim analysis on BACE inhibitor
GLPG/ABBV		Filgotinib	Crohn's Disease	Phase II	Q1:16	Topline data following 20 weeks of treatment
GLPG		GLPG1205	Ulcerative colitis	Phase IIa	Q1:16	Topline data in Q1:16
BCRX	OPuS-2	avoralstat	HAE	Phase III	Q1:16	Phase III data of 1st-gen 3x daily pill
BMRN		BMN 190	NCL-2 (Batten's)	Phase I/II	Q1:16	Phase 1/2 results in Batten disease
GILD		GS-9620	HBV	Phase II	Q1:16	Potential top-line data in virally supressed patients
BIIB/Eisai		BAN2401	Alzheimer's	Phase II	Spring '16	Topline results for BACE inhibitor
BIIB/Eisai		E2609	Alzheimer's	Phase II	Spring '16	Topline result of safety stage
CLVS	TIGER-1	Rociletinib (CO-1686)	FL NSCLC	Phase II/III	June '16	Initial data potentially at ASCO
ARIA	ALTA	Brigatinib	ALK+ Xalkori failures	Phase II	June '16	Results from pivotal Phase II trial
MRK		MK8931	Alzheimer's	Phase III	mid 2016	BACE inhibitor data
ARWR		ARC-AAT	AATD	Phase I	mid 2016	Data in AATD (alpha-1 antitrypsin deficiency) patients
BIIB	SYNERGY	BIIB-033	RRMS	Phase II	mid 2016	MS data on LINGO
BIIB		BIIB-054	Parkinson's	Phase I	mid 2016	Phase I SAD results of BIIB-054
PRTA		NEOD001	Amyloidosis	Phase I/II	mid 2016	Full data including expansion cohort
ACOR		CVT-301	Parkinson's	Phase III	mid 2016	Potential results from Phase III
ACAD		pimavanserin	Alzheimer's Psychosis	Phase II	mid 2016	Topline results from Phase II
PRQR	PQ-010-002	QR-010	Cystic fibrosis (F508del)	Phase I	mid 2016	Topline results
PRQR	PQ-010-001	QR-010	Cystic fibrosis (F508del)	Phase 1b/2	mid 2016	Topline results
CELG	NSCL-003	Abraxane/carboplatin	NSCLC	Phase III	mid 2016	Top-line data (first-line stage IIIB / IV squamous
ESPR	ETC1002-035	ECT-1002	Hypercholesterolemia	Phase II	mid 2016	Potential Phase II data on '1002/high-dose statin combo
GILD		GS-9620	HIV	Phase I	H1:16	Topline data from Phase I study in HIV cure
AMGN		Romosozumab	postmenopausal osteopo	Phase III	H1:16	Phase III data
ABUS		TKM-HBV	HBV	Phase II	H1:16	Potential Phase II interim results (multi-dosing trial)
ACOR		Ampyra	Stroke	Phase I	H1:16	Phase I PK dose (three QD versions) data in humans
PRTA		PRX002	Parkinson's	Phase I	H1:16	Data from Phase I MAD portion of PRX002 in PD patients

Source: Company reports, RBC Capital Markets estimates

Exhibit 10: Upcoming key clinical trial data (part 2)

Ticker	Trial	Drug	Indication	Stage	Timing	Comments
GILD		Simtuzumab	IPF	Phase II	H1:16	Topline data from IPF Phase 2 study
TBRA	CENTAUR	cenicriviroc (CVC)	NASH	Phase IIb	Q3:16	Top-line Phase IIb data from Tobira lead product
MRK	REVEAL	anacetrapib	hypercholesterolemia	Phase III	Q3:16	CV outcomes data
INFI	DYNAMO	IPI-145	iNHL	Phase II	Q3:16	Results from double-refractory iNHL
GILD		GS-4774	HBV	Phase II	Q3:16	Phase II topline data for treatment-naïve patients
CELG	REMARC	Revlimid	DLBCL	Phase III	Q3:16	Phase III maintenance readout for former R-CHOP patients
AMGN		Blincyto (blinatumomab)	R/R B-precursor ALL	Phase III	Q3:16	Phase III data
GILD		Simtuzumab	NASH	Phase II	Q4:16	Phase II futility analysis in NASH pts with advanced fibrosis
GILD		Idelalisib	CLL	Phase III	H2:16	Interim CLL frontline with bendamustine + rituximab
AXON		Nelotanserin	Dementia	Phase II	H2:16	Potential Phase II results for Lewy Body Dementia
ABUS		TKM-HBV	HBV	Phase II	H2:16	HBsAg reduction results from Phase II
GILD		GS-4997	PAH	Phase II	H2:16	Complete Phase II study in adults with PAH
FGEN		Roxadustat	Anemia	Phase III	H2:16	Data from two studies in dialysis and non-dialysis in China
REGN	ODYSEEY OLE	alirocumab	LDL-cholesterol	Phase III	H2:16	Phase III data
AMGN	IVUS	evolocumab	LDL-cholesterol	Phase III	H2:16	Data on vascular imaging in 960 patients
AMGN	FOURIER	evolocumab	LDL-cholesterol	Phase III	H2:16	Outcomes trial in 27,500 patients
CELG		Otezla	Psoriatic Arthritis	Phase III	H2:16	Data for untreated moderate-to-severe late stage patients
BIIB		BIIB-037	Alzheimer's	Phase Ib	H2:16	Potential titration dosing data from Phase Ib studies
VRTX		VX-661	Cystic Fibrosis	Phase III	H2:16	"Hetero" futility analysis of 150 patients for CF
CELG	ABI-007-MBC-001	Revlimid	Triple N Breast Cancer	Phase II/III	YE:16	Data on First-line triple negative metastatic breast cancer
ARIA	OPTIC	Iclusig	Refractory CP-CML	Phase II	YE:16	Preliminary data of three doses
REGN	ODYSSEY CHOICE II	alirocumab	LDL-cholesterol	Phase III	YE:16	Phase III data
VRTX		VX-152, VX-440	Cystic Fibrosis	Phase II	YE:16	Phase II data in hetero CF
DYAX		DX-2930	HAE	Phase III	YE:16	Potential pivotal data from Phase III study of DX-2930
BCRX		BCX7353	HAE	Phase II	YE:16	Phase II data for once daily oral pill
BITI		SYN120	Parkinson's Dimentia	Phase Iia	YE:16	Potential Phase IIa data for SYN120 in PDD
LLY	EXPEDITION-3	solanezumab	Alzheimer's	Phase III	YE:16/ early '17	Top-line data and press release
BIIB	ENDEAR/CHERISH	SMN-Rx	SMA	Phase III	YE:16/ early '17	Phase III data
CELG	AUGMENT	Revlimid/Rituximab	R/R FL	Phase III	YE:16/ early '17	Phase III top-line data
BIIB/PRGO	ASCEND	Tysabri	SPMS	Phase III	2016	Phase III data presentation
ACOR		Ampyra	Post-stroke	Phase III	2016	Potential interim look in post-stroke walking deficit
AMGN		AMG-334	Chronic migraine	Phase IIb	2016	Phase IIb results for AMG-334 in chronic migraine
MDCO/ALNY		ALN-PSCsc	LDL-cholesterol	Phase II	2016	Phase II data
ACOR		rHIgM22	Acute RMS	Phase I	2016	Potential results from Phase I trial in acute relapse MS
INFI	DUO	IPI-145	CLL	Phase III	2016	Results from trial of IPI-145 vs Ofa in R/R CLL

**highlighted in blue indicates events of high interest*

Source: Company reports, RBC Capital Markets estimates

Exhibit 11: Biopharma IPOs since 2012

Announced Date	Issuer Ticker	Issuer Name	IPO Size (M)	Offer Price	Last Close	Offer To Date
09/04/2012	ICPT	Intercept Pharmaceuticals Inc	$86	$15	$156.08	941%
11/08/2013	RARE	Ultragenyx Pharmaceutical Inc	$139	$21	$109.87	423%
05/19/2014	KITE	Kite Pharma Inc	$147	$17	$63.03	271%
03/19/2014	ALDR	Alder Biopharmaceuticals Inc	$80	$10	$36.25	263%
05/14/2013	BLUE	Bluebird Bio Inc	$116	$17	$61.45	261%
07/26/2013	FPRX	Five Prime Therapeutics Inc	$72	$13	$44.72	244%
04/12/2013	PTLA	Portola Pharmaceuticals Inc	$140	$15	$49.52	242%
06/17/2014	SAGE	Sage Therapeutics Inc	$104	$18	$60.95	239%
06/10/2013	AGIO	Agios Pharmaceuticals Inc	$119	$18	$56.45	214%
01/30/2014	ITCI	Intra-Cellular Therapies, Inc.	$124	$18	$53.91	208%
08/07/2013	XLRN	Acceleron Pharma Inc	$96	$15	$44.50	197%
10/05/2012	KBIO	KaloBios Pharmaceuticals Inc	$70	$8	$23.59	195%
10/11/2013	XNCR	Xencor Inc	$81	$6	$15.06	174%
06/30/2014	LOXO	Loxo Oncology Inc	$77	$13	$31.94	146%
10/24/2013	AERI	Aerie Pharmaceuticals, Inc.	$77	$10	$23.27	133%
04/29/2013	TBRA	Tobira Therapeutics Inc	$47	$4	$9.20	130%
05/27/2015	MCRB	Seres Therapeutics Inc	$154	$18	$41.09	128%
06/20/2014	ATRA	Atara Biotherapeutics Inc	$63	$11	$24.08	119%
05/16/2013	PTCT	PTC Therapeutics Inc	$144	$15	$32.50	117%
08/27/2014	DERM	Dermira Inc	$125	$16	$33.76	111%
06/05/2014	PFNX	Pfenex Inc	$50	$6	$11.87	98%
09/04/2013	MGNX	MacroGenics Inc	$92	$16	$31.43	96%
07/09/2013	XON	Intrexon Corp	$184	$16	$31.28	96%
12/30/2014	ONCE	Spark Therapeutics Inc	$185	$23	$44.13	92%
11/17/2014	JUNO	Juno Therapeutics Inc	$304	$24	$44.63	86%
07/11/2014	OTIC	Otonomy Inc	$115	$16	$29.33	83%
03/11/2015	KMPH	KemPharm Inc	$56	$11	$19.31	76%
03/11/2015	ADRO	Aduro Biotech Inc	$137	$17	$29.56	74%
08/28/2015	CTMX	CytomX Therapeutics Inc	$92	$12	$20.65	72%
09/25/2014	CHRS	Coherus Biosciences Inc	$92	$14	$22.41	66%
11/13/2014	FGEN	Fibrogen, Inc.	$168	$18	$29.15	62%
05/14/2013	ESPR	Esperion Therapeutics Inc	$81	$14	$22.58	61%
10/09/2015	VYGR	Voyager Therapeutics Inc	$81	$14	$21.44	53%
01/10/2014	AGTC	Applied Genetic Technologies C	$58	$12	$17.94	50%
01/08/2014	FLXN	Flexion Therapeutics Inc	$75	$13	$19.03	46%
01/13/2014	CNCE	Concert Pharmaceuticals Inc	$93	$14	$20.49	46%
09/16/2014	PRTO	Proteon Therapeutics Inc	$70	$10	$14.07	41%
05/19/2014	ARDX	Ardelyx Inc	$69	$14	$19.61	40%
11/08/2013	CARA	Cara Therapeutics Inc	$63	$11	$15.34	39%
03/23/2015	BPMC	Blueprint Medicines Corp	$169	$18	$25.03	39%
05/11/2012	OMED	OncoMed Pharmaceuticals Inc	$94	$17	$20.59	21%
05/11/2015	AXON	Axovant Sciences Ltd	$362	$15	$17.96	20%
07/29/2013	FMI	Foundation Medicine Inc	$122	$18	$20.90	16%
01/28/2014	AQXP	Aquinox Pharmaceuticals Inc	$53	$11	$12.63	15%
08/14/2015	EDGE	Edge Therapeutics Inc	$93	$11	$12.56	14%
04/18/2013	EPZM	Epizyme Inc	$89	$15	$16.60	11%
06/27/2014	AFMD	Affimed NV	$56	$7	$7.71	10%
05/15/2015	CYNA	Cynapsus Therapeutics Inc	$72	$14	$15.16	8%
10/24/2013	REPH	Recro Pharma Inc	$35	$8	$8.63	8%
08/24/2015	MIRN	Mirna Therapeutics Inc	$49	$7	$7.21	3%
11/18/2014	BLCM	Bellicum Pharmaceuticals Inc	$161	$19	$19.52	3%
10/13/2015	AXSM	Axsome Therapeutics Inc	$51	$9	$9.11	1%
03/29/2012	ADMA	ADMA Biologics Inc	$28	$9	$8.49	0%
10/20/2015	KURA	Kura Oncology Inc	$55	$8	$7.72	-4%
03/20/2013	PETX	Aratana Therapeutics Inc	$40	$6	$5.79	-4%
10/09/2015	WVE	WaVe Life Sciences Pte Ltd	$102	$16	$15.32	-4%
09/14/2015	DMTX	Dimension Therapeutics Inc	$73	$13	$12.14	-7%

Announced Date	Issuer Ticker	Issuer Name	IPO Size (M)	Offer Price	Last Close	Offer To Date
10/16/2013	EGLT	Egalet Corp	$58	$12	$11.13	-7%
03/03/2014	CORI	Corium International Inc	$52	$8	$7.19	-10%
06/09/2015	PIRS	Pieris Pharmaceuticals Inc	$28	$3	$2.39	-13%
06/18/2015	NBRV	Nabriva Therapeutics AG	$106	$10	$8.82	-14%
06/12/2015	DNAI	Pronai Therapeutics Inc	$158	$17	$14.58	-14%
09/10/2014	XENE	Xenon Pharmaceuticals Inc	$41	$9	$7.69	-15%
06/19/2014	INNL	Innocoll AG	$59	$9	$7.69	-15%
01/06/2014	ALDX	Aldeyra Therapeutics Inc	$12	$8	$6.75	-16%
10/04/2013	KPTI	Karyopharm Therapeutics Inc	$125	$16	$13.47	-16%
10/11/2013	VTL	Vital Therapies Inc	$62	$12	$10.07	-16%
05/13/2015	CATB	Catabasis Pharmaceuticals Inc	$69	$12	$9.99	-17%
08/17/2015	RGNX	REGENXBIO Inc	$159	$22	$17.80	-19%
10/04/2013	GLYC	GlycoMimetics Inc	$64	$8	$6.21	-22%
11/02/2015	MESO	Mesoblast Ltd	$68	$8	$6.20	-23%
06/12/2015	CERCU	Cerecor Inc	$26	$7	$5.03	-23%
08/12/2014	EYES	Second Sight Medical Products	$36	$9	$6.84	-24%
08/25/2014	CALA	Calithera Biosciences Inc	$80	$10	$7.50	-25%
05/18/2015	CYAD	Celyad SA	$80	$69	$50.40	-26%
02/14/2014	AKBA	Akebia Therapeutics Inc	$115	$17	$12.35	-27%
01/14/2013	ADHD	Alcobra Ltd	$25	$8	$5.81	-27%
04/06/2015	LIFE	aTyr Pharma Inc	$86	$14	$10.07	-28%
08/22/2013	ENZY	Enzymotec Ltd	$71	$14	$10.00	-29%
02/20/2015	CLLS	Cellectis SA	$228	$42	$27.78	-33%
08/08/2013	PULM	Pulmatrix Inc	$20	$7	$4.72	-35%
08/11/2014	TKAI	Tokai Pharmaceuticals Inc	$105	$15	$9.41	-37%
04/02/2012	STML	Stemline Therapeutics Inc	$38	$10	$6.27	-37%
08/28/2015	SBBP	Strongbridge Biopharma PLC	$25	$10	$6.11	-39%
05/13/2015	NVLS	Nivalis Therapeutics Inc	$89	$14	$8.47	-40%
08/14/2013	FATE	Fate Therapeutics Inc	$46	$6	$3.55	-41%
04/06/2015	ADAP	Adaptimmune Therapeutics Plc	$191	$17	$9.49	-44%
12/23/2013	GNCA	Genocea Biosciences Inc	$66	$12	$6.55	-45%
02/02/2015	XBIT	XBiotech Inc	$76	$19	$10.36	-45%
06/30/2014	AAVL	Avalanche Biotechnologies Inc	$117	$17	$9.23	-46%
09/20/2013	VCYT	Veracyte Inc	$65	$13	$7.04	-46%
03/10/2014	CERU	Cerulean Pharma Inc	$67	$7	$3.78	-46%
06/30/2014	EARS	Auris Medical Holding AG	$61	$6	$3.18	-47%
02/18/2014	VSAR	Versartis Inc	$145	$21	$10.66	-49%
06/22/2015	BNTC	Benitec Biopharma Ltd	$14	$9	$4.35	-53%
04/18/2014	ZFGN	Zafgen Inc	$110	$16	$7.15	-55%
07/29/2015	VTVT	vTv Therapeutics, Inc.	$117	$15	$6.51	-57%
02/17/2015	RKDA	Arcadia Biosciences Inc	$68	$8	$3.29	-59%
02/07/2014	ORPN	Bio Blast Pharma Ltd	$35	$11	$4.36	-60%
12/30/2014	HTGM	HTG Molecular Diagnostics Inc	$51	$14	$5.25	-63%
12/30/2013	EBIO	Eleven Biotherapeutics Inc	$58	$10	$2.83	-72%
10/07/2014	HSGX	Histogenics Corp	$65	$11	$2.97	-73%
05/24/2013	EVOK	Evoke Pharma Inc	$29	$12	$3.20	-73%
03/03/2015	OPGN	OpGen Inc	$17	$6	$1.53	-75%
07/01/2014	VKTX	Viking Therapeutics Inc	$28	$8	$2.02	-75%
12/30/2013	ARGS	Argos Therapeutics Inc	$50	$8	$1.85	-77%
10/11/2013	CLDN	Celladon Corp	$51	$8	$1.53	-81%
08/12/2013	BIND	BIND Therapeutics Inc	$76	$15	$2.59	-83%
09/23/2013	BIOC	Biocept Inc	$19	$10	$1.49	-85%
12/23/2013	NRX	NephroGenex Inc	$37	$12	$1.57	-87%
06/23/2014	MCUR	MacroCure Ltd	$54	$10	$1.20	-88%
07/01/2013	MBII	Marrone Bio Innovations Inc	$66	$12	$1.29	-89%
02/14/2012	ATOS	Atossa Genetics Inc	$4	$5	$0.35	-93%
06/14/2013	ONTX	Onconova Therapeutics Inc	$89	$15	$0.94	-94%

Source: FactSet, Bloomberg

Exhibit 12: Biotech IPO Lock-Up Calendar

Pricing Date	Issuer	Ticker	Proceeds ($mm)	Market Value ($mm)	IPO Price	Last Price	Return TD	Lock-up Expiration Date
11/20/15	Kitov Pharmaceuticals	**KTOV**	$13	$16	$12.00	$3.72	-69%	**5/18/16**
11/19/15	Axsome Therapeutics	**AXSM**	$51	$174	$9.00	$9.11	1%	**5/17/16**
11/12/15	Mesoblast	**MESO**	$60	$414	$8.00	$6.20	-23%	**5/10/16**
11/10/15	Voyager Therapeutics	**VYGR**	$70	$786	$14.00	$21.44	53%	**5/8/16**
11/10/15	WAVE Life Sciences	**WVE**	$102	$141	$16.00	$15.32	-4%	**5/8/16**
11/4/15	Kura Oncology	**KURA**	$50	$112	$8.00	$7.72	-3%	**5/2/16**
10/28/15	MyoKardia	**MYOK**	$54	$366	$10.00	$13.52	35%	**4/25/16**
10/22/15	Oasmia Pharmaceutical	**OASM**	$9	$126	$4.06	$3.59	-12%	**4/19/16**
10/21/15	Dimension Therapeutics	**DMTX**	$72	$302	$13.00	$12.14	-7%	**4/18/16**
10/15/15	Cerecor	**CERCU**	$26	$22	$6.50	$5.03	-23%	**4/12/16**
10/7/15	CytomX Therapeutics	**CTMX**	$80	$744	$12.00	$20.65	72%	**4/4/16**
10/6/15	Aclaris Therapeutics	**ACRS**	$55	$578	$11.00	$28.68	161%	**4/3/16**
10/2/15	NovoCure	**NVCR**	$165	$2,318	$22.00	$27.72	26%	**3/30/16**
9/30/15	Edge Therapeutics	**EDGE**	$80	$362	$11.00	$12.56	14%	**3/28/16**
9/30/15	Mirna Therapeutics	**MIRN**	$44	$74	$7.00	$7.21	3%	**3/28/16**
9/17/15	Nabriva Therapeutics	**NBRV**	$92	$94	$10.25	$8.82	-14%	**3/15/16**
9/16/15	Regenxbio	**RGNX**	$139	$451	$22.00	$17.80	-19%	**3/14/16**
8/18/15	Benitec Biopharma	**BNTC**	$14	$32	$9.21	$4.35	-53%	**2/14/16**
8/11/15	Global Blood Therapeutics	**GBT**	$120	$925	$20.00	$30.38	52%	**2/7/16**
8/5/15	Aimmune Therapeutics	**AIMT**	$160	$795	$16.00	$18.82	18%	**2/1/16**
8/4/15	Intec Pharma	**NTEC**	$30	$64	$6.00	$5.50	-8%	**1/31/16**
8/4/15	Zynerba Pharmaceuticals	**ZYNE**	$42	$112	$14.00	$12.22	-13%	**1/31/16**
7/30/15	EyeGate Pharmaceuticals	**EYEG**	$10	$20	$8.50	$2.56	-70%	**1/26/16**
7/29/15	vTv Therapeutics	**VTVT**	$117	$214	$15.00	$6.51	-57%	**1/25/16**
7/27/15	NantKwest	**NK**	$207	$1,271	$25.00	$15.67	-37%	**1/23/16**
7/23/15	Neos Therapeutics	**NEOS**	$72	$198	$15.00	$12.41	-17%	**1/19/16**
7/16/15	ProNAi Therapeutics	**DNAI**	$138	$438	$17.00	$14.58	-14%	**1/12/16**
7/16/15	Chiasma	**CHMA**	$102	$495	$16.00	$20.66	29%	**1/12/16**
6/30/15	Pieris Pharmaceuticals	**PIRS**	$25	$95	$2.75	$2.39	-13%	**12/27/15**
6/26/15	Seres Therapeutics	**MCRB**	$134	$1,605	$18.00	$41.09	128%	**12/23/15**
6/25/15	BioPharmX	**BPMX**	$10	$33	$2.75	$1.56	-43%	**12/22/15**
6/25/15	Catabasis Phamraceuticals	**CATB**	$60	$153	$12.00	$9.99	-17%	**12/22/15**

Source: Company reports, RBC Capital Markets estimates

Exhibit 13: RBC Biotech coverage universe (priced as of end of day ET 12/18/15)

Company	Ticker	Rating	Mkt Cap ($MM)	Price Target	Price ($)	Analyst
Gilead Sciences	GILD	Outperform	$146,424	$130	$101.60	Michael Yee
Amgen	AMGN	Outperform	$119,787	$190	$158.80	Michael Yee
Celgene Corp.	CELG	Outperform	$87,070	$150	$110.14	Michael Yee
Biogen Idec	BIIB	Outperform	$65,393	$450	$293.37	Michael Yee
Regeneron Pharmaceuticals	REGN	Outperform	$56,656	$676	$544.23	Adnan Butt
Vertex Pharmaceuticals	VRTX	Outperform	$28,628	$145	$116.51	Michael Yee
BioMarin Pharma	BMRN	Outperform	$16,841	$155	$104.44	Michael Yee
Medivation*	MDVN	Sector Perform	$7,169	$40	$43.79	Simos Simeonidis
United Therapeutics	UTHR	Sector Perform	$7,081	$175	$155.18	Michael Yee
Seattle Genetics	SGEN	Outperform	$5,812	$55	$41.67	Adnan Butt
Intercept Pharmaceuticals*	ICPT	Outperform	$3,798	$300	$156.08	Michael Yee
The Medicines Company	MDCO	Outperform	$2,749	$48	$39.58	Adnan Butt
Puma Biotechnology*	PBYI	Outperform	$2,367	$103	$72.97	Simos Simeonidis
Intra-Cellular Therapies*	ITCI	Outperform	$2,319	$74	$53.91	Adnan Butt
Prothena*	PRTA	Outperform	$2,229	$95	$71.03	Michael Yee
FibroGen*	FGEN	Outperform	$1,788	$38	$29.15	Michael Yee
Axovant Sciences*	AXON	Outperform	$1,781	$40	$17.96	Michael Yee
Acorda Therapeutics*	ACOR	Outperform	$1,757	$45	$40.72	Michael Yee
Sarepta Therapeutics*	SRPT	Outperform	$1,699	$62	$37.54	Simos Simeonidis
Ariad Pharmaceuticals*	ARIA	Sector Perform	$1,166	$8	$6.16	Michael Yee
ImmunoGen*	IMGN	Outperform	$1,179	$19	$13.55	Simos Simeonidis
PTC Therapeutics*	PTCT	Outperform	$1,114	$56	$32.50	Simos Simeonidis
Dynavax Technologies*	DVAX	Outperform	$1,041	$48	$27.08	Simos Simeonidis
Forward Pharma*	FWP	Outperform	$860	$45	$18.48	Michael Yee
Epizyme*	EPZM	Outperform	$692	$39	$16.60	Simos Simeonidis
MannKind Corporation*	MNKD	Underperform	$634	$1	$1.48	Adnan Butt
PDL BioPharma	PDLI	Sector Perform	$620	$6	$3.79	Adnan Butt
Aerie Pharmaceuticals*	AERI	Outperform	$614	$50	$23.27	Adnan Butt
Esperion Therapeutics*	ESPR	Outperform	$508	$40	$22.58	Michael Yee
Santhera Pharmaceuticals*	SANN-CH	Outperform	$504	$340.00**	$89.00	Simos Simeonidis
Arena Pharmaceuticals*	ARNA	Sector Perform	$461	$2	$1.90	Simos Simeonidis
Spectrum Pharmaceuticals*	SPPI	Outperform	$407	$12	$6.04	Adnan Butt
Infinity Pharmaceuticals*	INFI	Outperform	$395	$12	$8.03	Michael Yee
Curis*	CRIS	Outperform	$384	$7	$2.99	Adnan Butt
Arrowhead Research Corp.*	ARWR	Sector Perform	$356	$9	$5.98	Michael Yee
Xenoport Inc.	XNPT	Outperform	$353	$10	$5.59	Michael Yee
Ocular Therapeutix*	OCUL	Outperform	$260	$48	$10.50	Adnan Butt
Arbutus Biopharma*	ABUS	Outperform	$258	$12	$4.75	Michael Yee
Orexigen Therapeutics*	OREX	Outperform	$229	$5	$1.83	Simos Simeonidis
Synthetic Biologics*	SYN	Outperform	$225	$8	$2.48	Adnan Butt
Zafgen*	ZFGN	Sector Perform	$195	$7	$7.15	Simos Simeonidis
Endocyte*	ECYT	Outperform	$174	$10	$4.14	Adnan Butt
Biotie Therapies*	BITI	Outperform	$171	$35	$14.00	Simos Simeonidis
XOMA Corporation*	XOMA	Sector Perform	$162	$2	$1.36	Adnan Butt
ArQule*	ARQL	Outperform	$129	$5	$2.05	Adnan Butt
Marinus Pharmaceuticals*	MRNS	Outperform	$109	$14	$7.64	Simos Simeonidis
VIVUS*	VVUS	Outperform	$104	$4	$1.00	Simos Simeonidis
Nabriva Therapeutics*	NBRV	Outperform	$94	$22	$8.82	Adnan Butt
SCYNEXIS*	SCYX	Outperform	$86	$17	$6.19	Adnan Butt
SteadyMed*	STDY	Outperform	$37	$13	$2.71	Adnan Butt
Aptose Biosciences*	APTO	Outperform	$34	$19	$2.84	Adnan Butt

*Speculative risk rating assigned

***in CHF*

Source: FactSet, RBC Capital Markets estimates

Exhibit 14: Table of changes in price targets and estimates (discussed in this report)

Company	Scenario			Revenue Estimates (M)			EPS Estimates		
	Downside	Base	Upside	FY15	FY16	FY17	FY15	FY16	FY17
ABUS	$2	$12	$25	$17	$22	$29	($1.98)	($1.36)	($1.57)
prev.	$5	$20	$47						
ICPT	$50	$300	$420	$3	$18	$112	($8.38)	($17.64)	($19.35)
prev.	$107	$490	$598		$39	$122		($16.90)	($19.03)
CELG	$100	$150	$175	$9,278	$11,174	$13,239	$4.82	$5.65	$7.22
prev.							$4.88	$5.84	$7.48
INFI	$4	$12	$20	$109	$160	$278	($2.66)	($1.69)	($0.77)
prev.	$6	$15	$24						
PRTA	$18	$95	$125	$2	$26	$72	($2.66)	($2.47)	($1.93)
prev.									($1.95)
ARIA	$4	$8	$11	$117	$228	$264	($1.35)	($1.04)	($1.06)
prev.				$143	$196		($1.22)	($1.21)	($1.29)
ARQL*	$1	$5	$9	$11	$9	$14	($0.24)	($0.26)	($0.27)
prev.		$4	$8						

***Upgraded to Outperform from Sector Perform**

Source: RBC Capital Markets estimates

Company profiles – Large caps (Yee)

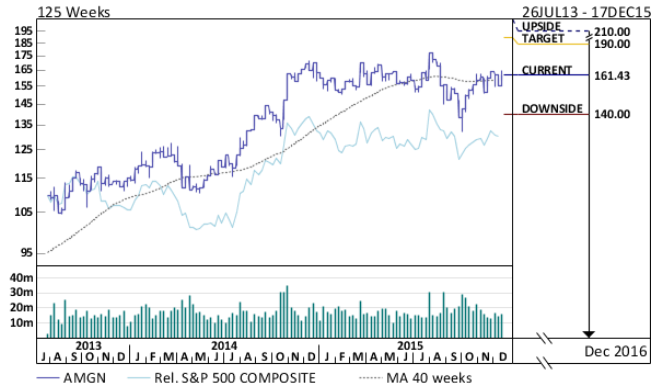
Amgen Inc. (AMGN)

Outperform

Price Target USD $190.00

Target/Upside/Downside Scenarios

Exhibit 15: Amgen Inc.



Source: RBC Capital Markets estimates

Target price/base case

Our base case of $190/share is based on applying a 17.6x multiple on our 2016 non-GAAP EPS. We believe this multiple is justified, as it is in the mid-range of peer large-cap biopharma companies with modestly slowing growth. We think the mid-range is reasonable given the improving prospects of its pipeline products despite slowing growth on its core products, which remain resilient with rapid declines unlikely in the near future.

Upside scenario

Our upside case of $210 is based on applying a higher 20x multiple on our 2016 non-GAAP EPS estimate. We believe this higher multiple can be attained if AMGN proves it can maintain steady and resilient growth on its top/bottom lines (e.g. if biosimilars don't take meaningful share) while increasing capital return in the form of dividends and executing on its pipeline candidates.

Downside scenario

Our downside scenario of $140 is based on applying a lower 13x multiple on our 2016 non-GAAP EPS estimate. This is at the low end of peer large-cap biopharma companies and we believe this could result from greater than expected biosimilar competition, and if AMGN fails to advance new products that can offset the potential decline in its existing core franchise. For example, major delays for PCSK9, failure of a major pipeline candidate, or increased biosimilar risk.

Investment summary

We view AMGN as a long-term positive based on several drivers that could continue to push the stock higher: 1) expectations are the lowest among its biotech peers; 2) PCSK9 just launched with outcomes data coming next year, and AMGN has several new yet under-appreciated mid/late-stage pipeline drugs (CGRP migraine drug, anti-sclerostin, etc.) reporting data in the next 12–18 months; 3) room for capital allocation improvement with growing dividend toward 2–3% and a re-instituted share buyback program; and 4) natural hedge against biosimilars from their own Humira, Herceptin, and Avastin type biosimilars launching in 2017.

Potential catalysts for the stock

Rapid launch of evolocumab (PCSK9): As a new mechanism and injectable route of administration in the blockbuster cholesterol lowering market, buyside expectations remain rather modest. However, with "outcomes" and imaging data coming H2:16, "floodgates" could open, suggesting $5-10B long-term peak potential versus cons $4-5B.

Multiple pipeline programs reading out over next 1-2 years: In addition to PCSK9 CV outcomes data, we expect 1. Phase III sclerostin (osteoporosis) data coming H1:16 = $1B potential; 2. Phase III CGR-P (migraine) data by 2017 = $1-3B+; 3. Phase I/II "I/O" immuno-oncology solid-tumor combo data AMG-820 (CSF1-R) + PD-1 (MRK) just started – data possible ASCO-16 (American Society of Clinical Oncology) or later (note FPRX has $1B market cap on this) - $1-2B+.

Risks to our investment thesis

Increased competition from new oral cholesterol lowering drugs: Competition for PCSK9s (AMGN's evolocumab) could come from an oral CETP inhibitor, such as anacetrapib from MRK. This could pose a meaningful competitive threat for AMGN's evolocumab and decrease its probability of becoming a blockbuster drug for the company.

Greater than expected competitive impact on AMGN's various core franchises: We believe competition to Neulasta and Neupogen pose potential threats, but we believe the base business is more durable than consensus. Biosimilar approval is not as quick as perceived, and the BPCIA could confer six additional months of protection against a biosimilar launch. However, inability of AMGN to meet sales estimates could erode investor confidence in resilience of the franchise and AMGN's ability to manage competitive threats. AMGN has many levers at its disposal (price increases, cost cuts, share buybacks).

2016 thoughts on AMGN

While the Street continues to talk about "biosimilar risk", and this is a naturally known long-term headwind, we believe the base business is more durable than consensus; biosimilars are not as easy as perceived (many delays recently), and there are four pipeline programs that are under-appreciated and will start to get more credit by the end of 2016. Importantly, we think the stock could grind higer post Spring as Phase III sclerostin data is coming H1:15 and Phase III CV Outcomes study finally reads out later Summer and very positive data could cause consensus to take up peak sales projections for PCSK-9 and drive a higher stock price from higher confidence in long-term sales for PCSK-9.

We believe 2016 guidance is conservative (was given on Q3 call) because they have been managing expenses much better than expected with new CFO over last year and this is an area of leverage (they may need to raise margin guidance longer-term).

Q4 earnings in January is likely to exceed consensus (typical strong seasonality and buy-up into Q1 price increases which then makes Q1 a little light). The Q4 R&D tax credit is likely to happen again and this is never in the guidance, which has boosted Q4 results for last few years…

More importantly and fundamental – we see **five pipeline programs** that we have positive views on that will matter over the next few years:

1. Phase III sclerostin (osteoporosis) data coming H1:16 = $1B potential
2. Phase III PCSK9 cholesterol "cv outcomes" data coming mid-16 = $5-10B long-term peak pot'l vs consensus $4-5B
3. Phase III CGR-P (migraine) data by 2017 = $1-3B+
4. Phase I/II "I/O" immuno-oncology solid-tumor combo data AMG-820 (CSF1-R) + PD-1 (MRK) just started – data possible ASCO-16 or later (note FPRX has $1B market cap on this) - $1-2B+
5. AMGN's own proprietary biosimilar program post 2017+ (9+ programs) not in consensus models

Bear case

- Neulasta biosimilars are coming from Apotex, Sandoz (filed now) and Coherus (completed bioequivalence study) and AMGN has said they expect biosimilars (but not before H2:16).
- Enbrel faces an IPR from the Bass Group on the key patent that extends protection out to 2026+ and consensus has no biosimilar erosion for this drug; possible decision on institution (review) by USPTO could be Feb 2016.
- PCSK9 outcomes have high expectations and expected to be positive – CV benefits below 15-20% would arguably be disappointing and may call into question consensus $4B+ in sales and market size of $10B with REGN/SNY.
- Additional pipeline programs cited have high competition and not clear yet how differentiated AMGN is on CGR-P migraine and I/O programs (they are not in the lead); osteoporosis is also a highly competitive primary care market.
- AMGN has their own biosimilar programs but we are not sure how this will play out – first one is Humira and confidence is waning on whether this will actually launch in 2018+ given ABBV commentary on IP and AMGN commentary around potential IP "respect".

Exhibit 16: Expected news flow for AMGN

Timing	Expected News Flow	Program
YE:15	Potential EMA approval of MAA for metastatic melanoma	T-Vec/MK-3475
Feb 22, 2016	Estimated IPR institution decision (Bass)	Legal
H1:16	Phase III readout from pivotal Phase III trials in postmenopausal osteoporosis (vs. placebo or alendronate)	Romosozumab (AMG 785)
Q3:16	Phase III results of blinatumomab in R/R B-precursor ALL	Blincyto (Blinatumomab)
Jul 10, 2016	PDUFA for sBLA for monthly single-dose admin	Repatha (evolocumab)
Aug 24, 2016	PDUFA for secondary hyperparathyroidism in patients with CKD	etelcalcetide (AMG 416)
Sep 2016	PDUFA for BLA for Sandoz's proposed biosimilar plegfilgrastism under 351k pathway	biosimilar plegfilgrastim
H2:16	Phase III CV outcomes data and Phase III CV imaging data	Repatha (evolocumab)
H2:16	Potential Phase III data for ABP 980 (biosimilar Herceptin)	Biosimilars
Nov 2016	Estimated PDUFA for ABP 501 (Humira) in Plaque Psoriasis and Rheumatoid Arthritis	Biosimilars
Dec 2016	Estimated EMA approval of ABP 501 (Humira) in Plaque Psoriasis and Rheumatoid Arthritis	Biosimilars
Dec 2016	Estimated EMA approval of Kyprolis in relapsed 2nd-line MM patients	Kyprolis (carfilzomib)
2016	Phase IIb results for AMG-334 in chronic migraine	AMG 334
2017 -2019	Launch Biosimilars Portfolio (Humira, Remicade, Avastin, Herceptin, Rituxan, Erbitux)	Biosimilars
H2:18	Phase III results of blinatumomab in Newly Diagnosed BCR-ABL(-) Adult ALL	Blincyto (Blinatumomab)

Source: Company reports and RBC Capital Markets estimates

Exhibit 17: Overview of patent status and sales for AMGN's key drugs

AMGN's Key Drugs Comparison (Geographic and Product Information)							
Drug	Type	United States			Europe		
		Patent Exp.	FY14 Revenue (M)	FY15E Revenue (M)[1]	Patent Exp.	FY14 Revenue (M)	FY15E Revenue (M)[1]
Enbrel	Biologic	2019 - 2029	$4,404	$4,974	Expired	$284	$269
Neulasta	Biologic	Expired	$3,649	$3,881	Expired	$947	$838
Epogen	Biologic	Expired	$2,031	$1,964	Expired	-	-
Xgeva[2]	Biologic	2017 - 2025	$857	$1,017	2017 - 2022	$364	$405
Neupogen	Biologic	Expired	$839	$765	Expired	$320	$257
Sensipar	Generic	2015 - 2018	$796	$1,040	Expired	$362	$349
Aranesp	Biologic	2024	$794	$901	Expired	$1,136	$1,041
Prolia[2]	Biologic	2017 - 2025	$625	$800	2017 - 2022	$405	$462
Kyprolis	Generic	2025	$306	$468	2025	$25	$50
Vectibix	Generic	2020	$168	$209	2018	$337	$346
Blincyto and others	Biologic	2019 - 2027	$3	$83	2019 - 2026	-	$143

[1] RBC estimates

[2] One of the U.S. patents is eligible for patent term extension with an expiry of Sep 2021

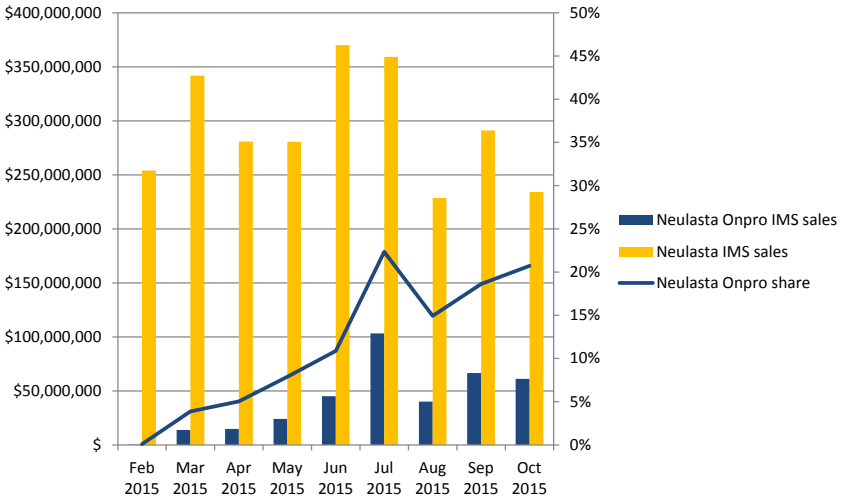
Source: Company reports, RBC Capital Markets estimates

Exhibit 18: Select list of AMGN's partnership and acquisition announcements this past year highlight pursuit of innovation

Company	Ticker	Announced	Type	Program	Indication	Stage	Clinical Trial/Regulatory Timeline
Dezima	Private	Sep-15	Acquisition	TA-8995 (CETP Inhibitor)	Dyslipidemia	Phase IIb	Phase IIb completed; more details to come
Xencor	XNCR	Sep-15	Partnership	CD38 x CD3 5 undisclosed	Cancer/ Inflammatory	Pre-clinical Discovery	**CD38:** IND filings 2016+ (estimated)
Novartis	NVS	Sep-15	Partnership	CNP520 (BACE inhibitor) AMG 334; AMG 301	Alzheimer's Migraine	Phase I/IIa Phase III; Phase I	**CNP520:** Phase I/IIa details imminent **AMG 334:** Data in 2017
Roche	RHHBY	Jun-15	Partnership	Laherparepvec (T-Vec) combo with atezolizumab (MPDL3280A)	Oncolytic Immunotherapy	Phase Ib	**Triple-Neg Breast Cancer:** Initiating **Colectoral Cancer w/ Liver Metastases:** Initiating
Merck	MRK	May-15	Expanded partnership	Laherparepvec (T-Vec) combo with Keytruda (MK-3475)	Oncology	Phase Ib	**SCCHN:** Phase 1 ongoing **Regionally or Mestastic Melanoma:** Phase III primary completion Sep 2018
Kite Pharma	KITE	Jan-15	Partnership	CAR-T	Oncology	Pre-clinical	IND filings 2016+
Astrazeneca	AZN	Apr-12	Partnership	Brodalumab (IL-17) AMG 139 (IL-23) AMG 157 AMG 181 AMG 557	Psoriasis **(ended May'15)** Crohn's Asthma UC/ Crohn's Lupus erythematosus	Phase III Phase II Phase II Phase II Phase Ib	**Brodalumab**: Global submissions YE:15 **(AZN/VRX)** **AMG 139:** Phase II ongoing **AMG 157:** Data YE:16 **AMG 181:** Complete March 2019 **AMG 557:** Safety study data YE:16

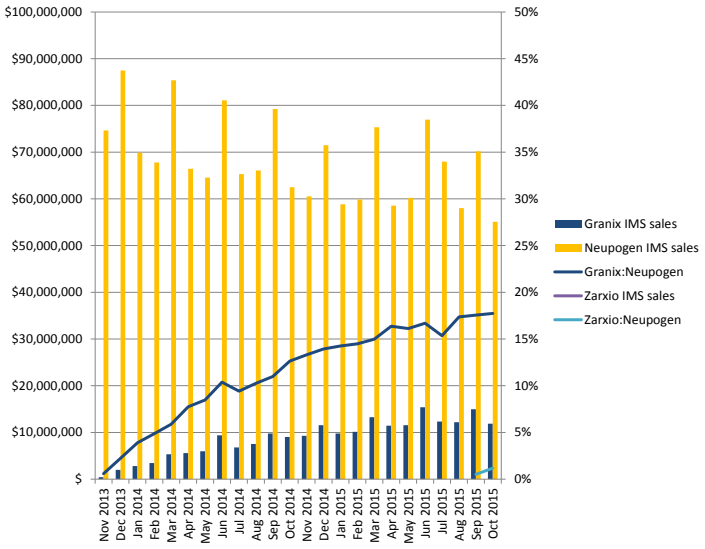
Source: Company reports, RBC Capital Markets estimates

Exhibit 19: Neulasta "on-body" Onpro IMS sales are steadily increasing (21% of total Neulasta sales now)



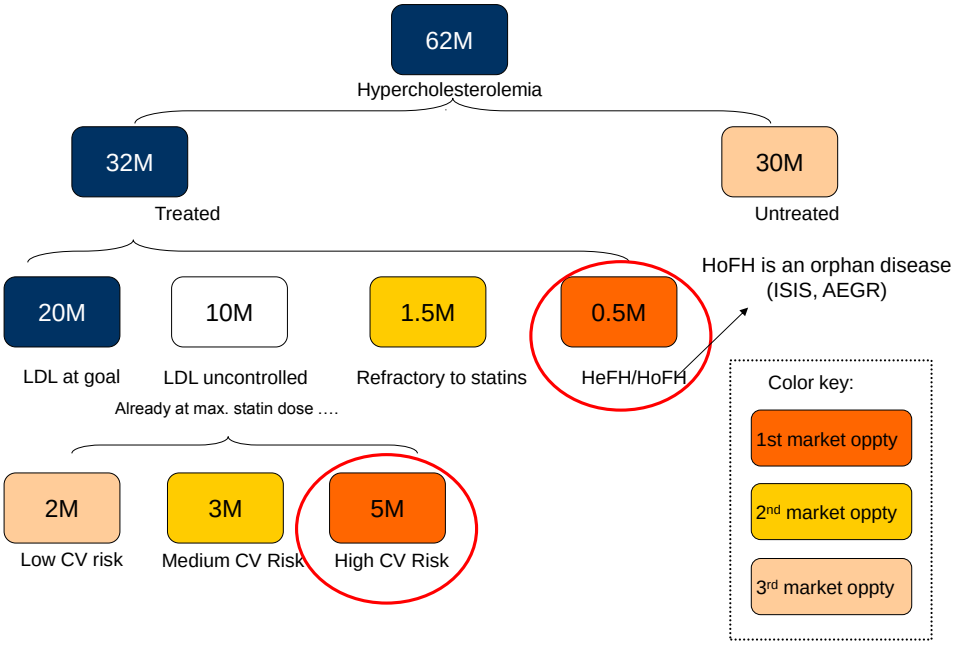
Source: IMS, RBC Capital Markets estimates

Exhibit 20: While Zarxio biosimilar launch is still early, Granix has been duelling shares away from Neupogen (although Granix share is flattening/stabilizing)



Source: IMS, RBC Capital Markets estimates

Exhibit 21: There is considerable unmet need amongst hypercholesterolemia patients



Source: AHA, AMA and RBC Capital Markets estimates

Exhibit 22: Our PCSK9 market model suggests $2B+ in peak sales is reasonable

Probability (AMGN)	100%	85%	85%
Probability (REGN)	100%	85%	85%
Probability (PFE)	90%	85%	77%

Pricing ($)	US	ROW
NET Price of AMG-145 in US ($) per year	$ 12,000	$ 7,000
NET Price of REGN-727 in US ($) per year	$ 12,000	$ 7,000
NET Price of PFE's RN-316 in US ($) per year	$ 12,000	$ 7,000
Price Increase Per Year	3%	0%

Volume (#) for USA Only	US	ROW
How Many People take Statins?	32 M	50 M

	Low	Medium	High
Risk Profile Segmentation (Low - High)	27%	40%	33%
What % Are on Combo Therapy (Statin + x) Already?	10%	28%	48%
What % Still Can't Reach LDL Goals?	18%	23%	27%
What % Has Medical Imperative To Lower LDL?	13%	28%	50%
Theoretical Market Size (# of Patients in '000)	19 K	228 K	684 K
Likely Market Size (# of Patients in '000)	5 K	114 K	445 K

AMGN-145	Peak Sales US ($M)	Peak Sales WW ($M)	$/share (Prob. Adjusted)
Rev. Estimate for Low-Risk Patients ($M)	$ -	$ -	$0
Rev. Estimate for Medium-Risk Patients ($M)	$ 243	$ 372	$1
Rev. Estimate for High-Risk Patients ($M)	$ 2,658	$ 3,417	$10

REGN-727	Peak Sales US ($M)	Peak Sales WW ($M)	$/share (Prob. Adjusted)
Rev. Estimate for Low-Risk Patients ($M)	$ -	$ -	$0
Rev. Estimate for Medium-Risk Patients ($M)	$ 170	$ 300	$2
Rev. Estimate for High-Risk Patients ($M)	$ 2,511	$ 3,421	$27

PFE (RN-316)	Peak Sales US ($M)	Peak Sales WW ($M)	$/share (Prob. Adjusted)
Rev. Estimate for Low-Risk Patients ($M)	$ -	$ -	$0.0
Rev. Estimate for Medium-Risk Patients ($M)	$ 121	$ 186	$0.0
Rev. Estimate for High-Risk Patients ($M)	$ 1,772	$ 2,379	$0.5

	Total	Prob. Adjusted
PCSK9 for AMGN ($/share)	$13	$11
PCSK9 for REGN ($/share)	$35	$30
PCSK9 for SNY ($/share)	$3	$3
PCSK9 for PFE ($/share)	$0.6	$0.5

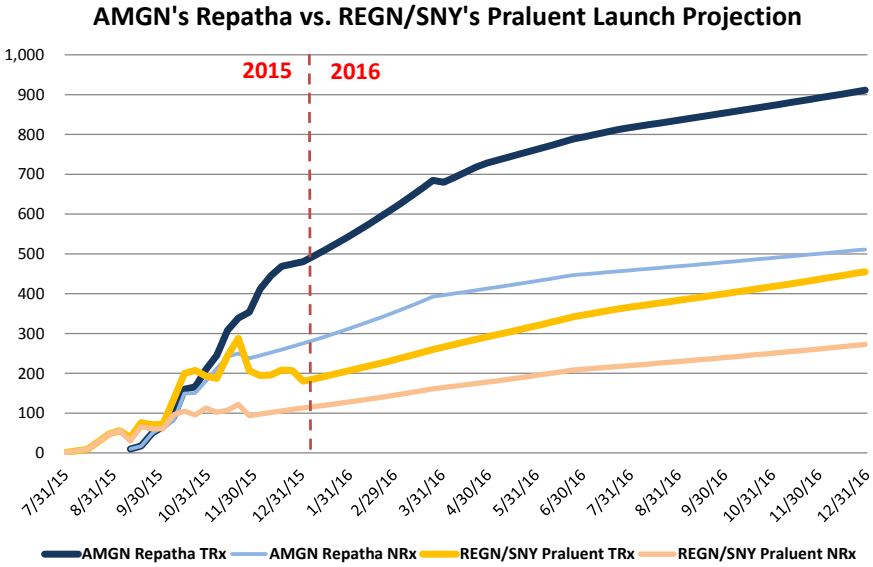
	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
Total REVENUE - Low -Risk Pts ($M)	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -
Total REVENUE - Medium Risk Pts ($M)	$ 30	$ 47	$ 77	$ 102	$ 130	$ 159	$ 190	$ 223	$ 243	$ 263
Total REVENUE - High Risk Pts ($M)	$ 391	$ 550	$ 789	$ 1,047	$ 1,441	$ 1,744	$ 1,898	$ 1,975	$ 2,150	$ 2,339
Total REVENUE - USA ($M)	$ 340	$ 435	$ 621	$ 813	$ 1,100	$ 1,332	$ 1,414	$ 1,500	$ 1,671	$ 1,855
Total REVENUE - ex-US ($M)	$ 82	$ 162	$ 245	$ 336	$ 470	$ 570	$ 673	$ 697	$ 722	$ 748
TOTAL WW REVENUE ($M) for AMG-145	$ 422	$ 597	$ 866	$ 1,149	$ 1,570	$ 1,902	$ 2,087	$ 2,198	$ 2,393	$ 2,603

Source: RBC Capital Markets estimates

Exhibit 23: Our interactive PCSK9 scripts APP initially incorporates modest assumptions at launch and then gradually builds to become a blockbuster product long-term

2016 - Repatha (AMGN)

Repatha Quarterly Estimate	Q1:16E	Q2:15E	Q3:16E	Q4:16E	FY2016
Estimated 1-month Refill Rate	85%	80%	80%	80%	
NRx Weekly Growth	*3.0%*	*1.0%*	*0.5%*	*0.5%*	
Annual cost	$14,100	$14,100	$14,100	$14,100	
Monthly Cost	$1,175	$1,175	$1,175	$1,175	
Gross To Net	20%	20%	20%	20%	
IMS Capture Rate	12%	12%	12%	12%	
TRx Sum	7,500	9,617	11,561	11,496	40,174
NRx Sum	4,300	5,475	6,494	6,450	22,720
Script Predicted Revs ($M)	$59	$75	$91	$90	315
Inventory Build? ($M)	$0	$6	-$3	$8	$11
Repatha Quarterly Sales ($M)	**$59**	**$81**	**$88**	**$98**	**$326**
Consensus ($M)					**$338**
RBC PCSK9 Market Valuation APP					**$340**

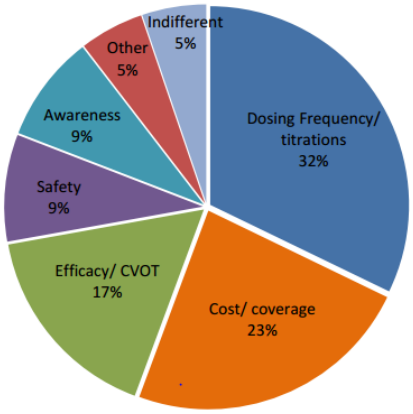


Source: IMS Health, RBC Capital Markets estimates

Exhibit 24: We surveyed 100 US cardiologists after PCSK9s were approved. Survey results indicate that physicians' choice of PCSK9 depends on dosing frequency, payor coverage/cost, efficacy/CVOT data, and ease of use.

Q: Which aspect or factor of the drug will determine your choice of PCSK9 drug?

Dosing Frequency/ titrations	32%
Cost/coverage	23%
Efficacy/ CVOT	17%
Safety	9%
Awareness/ marketing	9%
Other (storage etc)	5%
Indifferent	5%

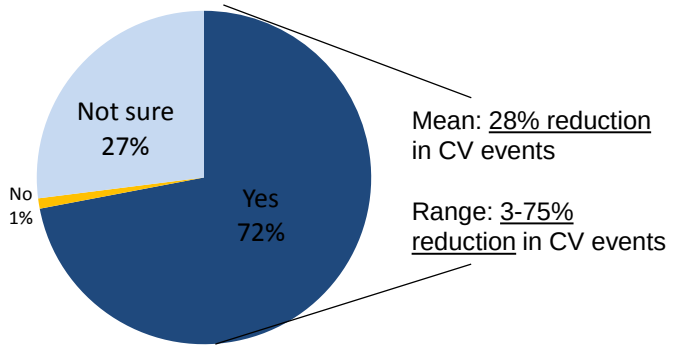


- **Slightly more physicians plan on prescribing Repatha vs Praluent (54% vs 46%):**
  - **Most physicians cited dosing, payor coverage /cost, efficacy/CVOT data, and ease of use as primary reasons for deciding which PCSK9 to prescribe**
  - **Interestingly, a few physicians also cited more interactions with AMGN reps, and one quoted "Sanofi had very difficult application process"**

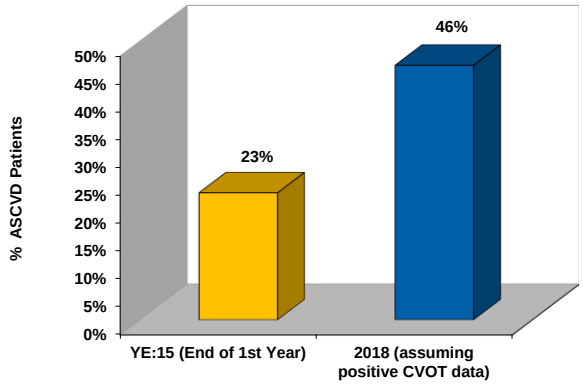
Source: RBC Capital Markets

Exhibit 25: Survey results also indicate that 72% of physicians believe CVOT will be positive, and will increase usage of PCSK9s

Q: Do you think the the PCSK-9 CV outcomes studies will be "positive"?



Q: What % of ASCVD high risk patients are likely to adopt PCSK9s by YE:15 (Year 1) and in 2018 (assuming positive CVOT data read out)?



- 72% of physicians are confident that PCSK9 CVOT data will read out positively by 2017-2018.
- An overwhelming majority of physicians – 80% – predict that PCSK9 usage will increase after outcomes data is available:
  - On average, docs predict PCSK9 usage could increase by ~45% in 2017-2018
  - Predictions for impact on PCSK9 usage range from 10% to 100% higher utilization

Source: RBC Capital Markets

Exhibit 26: Physicians would allocate 20-30% of PCSK9 prescriptions to less frequently dosed drugs

Q: What % of your NEW anti-PCSK9 eligible patients would you start on an every 3 or 4 month anti-PCSK9, such as ALN-PCSsc, if it were available?

Min	Max	Mean	Median	Std Dev
0%	100%	30%	20%	27%

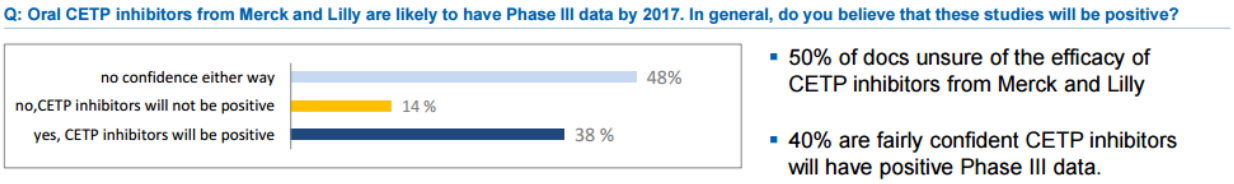
Q: What % of your EXISTING patients on anti-PCSK9 therapy would you transition to an every 3 or 4 month anti-PCSK9 drug when it becomes available?

Min	Max	Mean	Median	Std Dev
0%	100%	32%	25%	26%

- **Many physicians cited dosing among the primary reasons for deciding which PCSK9 to prescribe**
  - **Physicians anticipate prescribing more monthly administrations to patients once/ if available**
  - **Thus it is not surprising that 20-30% of their PCSK9 prescriptions would be for future, potentially less frequently dosed drugs like ALN-PCSsc**

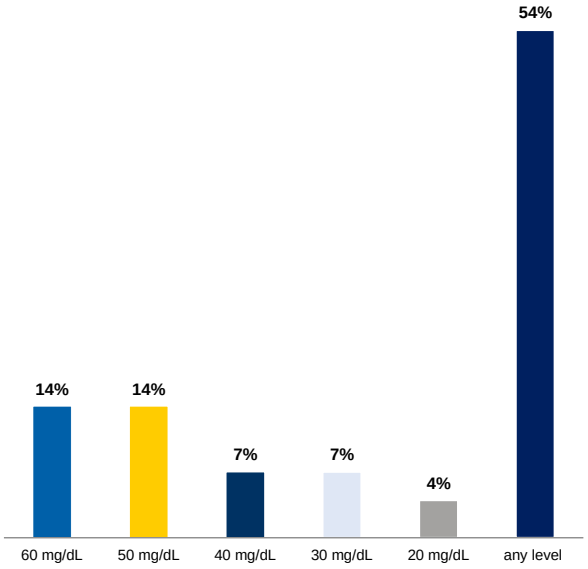
Source: RBC Capital Markets

Exhibit 27: Half of docs do not have confidence in CETP inhibitors yet, but ~40% think oral CETPs will be positive, potentially taking share away from PCSK9s



Source: RBC Capital Markets

Exhibit 28: At the 2015 AHA conference - while some docs (28%) worry on potential side effects of LDL-C levels being too low, 54% said they were confident to use PCSK9s to "any" LDL-C level as long as CVOTs continue to suggest benefits.



Source: AHA 2015, RBC Capital Markets

Exhibit 29: With both an (approved) PCSK9 and CETP inhibitor (Phase IIb), AMGN has multiple shots at the blockbuster cholesterol market

Study	Drug(s)	Dose	Route of Administration	LDL-C reduction	HDL-C increase
AMGN					
GAUSS-2	Repatha (evolocumab)	140, 420 mg	injectable	56% - 61%	-
REGN/SNY					
ODYSSEY ALTERNATIVE	Praluent (alirocumab)	75, 150 mg	injectable	43% - 58%	-
AMGN (Dezima Pharma acquisition)					
TULIP	TA-8995	1, 2.5, 5, 10mg	oral	~45%	up to 179%
TULIP	TA-8995 + 20mg atorvastatin	10 mg	oral	~68%	up to 152%
TULIP	TA-8995 + 10mg rosuvastatin	10 mg	oral	~63%	up to 158%
LLY					
N/A	Evacetrapib	30, 100, 500mg	oral	14% - 36%	up to 129%
MRK					
DEFINE	Anacetrapib	100mg	oral	40%	up to 138.1%
ESPR					
008	ETC1002	120, 180mg	oral	~30%	-
008	ETC1002 + ezetimibe	120, 180mg + 10mg	oral	~48%	-

Source: Companry reports, RBC Capital Markets

Exhibit 30: Table of Kyprolis trials in development. With positive ASPIRE and ENDEAVOR results, the drug will gradually move up towards the second-line setting.

Stage	Trial Name	Phase	N	# Prior Drugs	Regimen	Dosing	Primary Endpoint	Secondary Endpoint	Est. Timing/ Results	Comments
Third Line	**FOCUS**	III	302	≥3	K	20/27 mg/m²	OS	PFS, ORR, CBR, DOR	Missed primary endpoint (Aug '14)	Not sufficiently powered, given crossover risk. Raises question on EU approval.
					vs. corticosteroid (optional Cytoxan)	prednisone 30mg dex 6mg				
	ARROW	III	460	2-3	Kd	20 mg/m² and 70 mg/m² QW or 27 mg/m² BIW	ORR	PFS, OS, safety	~ 2017	Open-label study of once-weekly Kyprolis, initiated May '15
Second Line	**ASPIRE** (SPA)	III	780	1-3	KRd	20/27mg/m² (10min infusion) x 18 cycles R: 25mg, d: 40mg	PFS	OS, ORR, DOR, CBR, TTP, QOL	Hit primary (PFS) at interim (Aug '14). PFS of 26.3 vs. 17.6	To support EU approval and label expansion into 2nd-line in US
					vs. Rd	R: 25mg, d: 40mg				
	ENDEAVOR	III	888	1-3	Kd	20/56 mg/m² (30min infusion) d: 20mg	PFS	OS, ORR, DOR, safety, HR-QOL, neuropathy	Hit primary (PFS) at interim (Mar '15). PFS of 18.7 vs. 9.4	Showed superiority vs. Velcade. Important in EU where Revlimid may be too expensive
					vs. Vd (SQ or IV)	V: 1.3 mg/m² d: 20mg				
	CHAMPION 1	I/II	104	1-3	Kd	20 mg/m² dose escalation to 45, 56, 70, 88 mg/m²	MTD, ORR	CBR, PFS, TTP, DOR	77% ORR, 63% ORR for pts refractory to Velcade (updated at ASH '15)	Determined 70mg/m² as the MTD in a weekly infusion (30mins). Phase II initiated to explore weekly dosing at MTD
Front Line	**CHAMPION 2**	I	27	0	K + Cytoxan + d (followed by K maintenance)	20 mg/m² then MTD x 8 cycles, then 56 mg/m² maintenance	CR rate (sCR+CR)	OS, PFS, ORR, MRD, DOR, safety	~2016	Induction therapy of K + Cytoxan, plus K maintenance
	CLARION	III	882	0	KMP	20/36 mg/m² (30-60min infusion) x 9 cycles	PFS	OS, ORR, CR, HR-QoL, neuropathy, MRD	~2017	For global registration in front-line MM. Going head-to-head vs. Velcade in transplant-ineligible pts
					vs. VMP (SQ or IV)	1.3 mg/m² x 9 cycles				
	ECOG Study (#E1A11)	III	756	0	KRd (followed by R maintenance)	20/36 mg/m² (30min infusion) x 12 cycles	OS	PFS, ORR, MRD, DOR	~2016	Head to head comparison of K vs. V based on ORR and MRD
					vs. VRd (followed by R maintenance)	V: 1.3 mg/m² x 12 cycles				

Source: Company reports, Clinicaltrials.gov, RBC Capital Markets estimates

Exhibit 31: Kyprolis combinations have generally shown deeper responses (>VGPR) compared to Velcade combinations, in line with Kyprolis's superiority over Velcade in ENDEAVOR. Further head-to-head data expected from CLARION in 2017.

Tx Setting	Backbone	Regimen	Stage	N	Prior Tx	ORR	>VGPR	nCR/CR	AE-related discontinuations	
NDMM	Kyprolis	KRd	II	53	-	98%	81%	62%	4%	
		KCd	II	58	-	90%	77%	53%	12%	
		KMP	I/II	66	-	91%	56%	6%	11%	CLARION
	Velcade	VMP	III	344	-	71%	41%	30%	33%	CLARION
	Rev-Vel	RVd	II	35	-	100%	74%	57%		
		IRd	II	56	-	95%	71%	20%	12%	
	Revlimid	MPR			-	80%	45%	33%	24%	
		Rd	III	541	-	73%	43%	14%	13%	
		MPT	III	547	-	62%	28%	9%	14%	
RRMM	Kyprolis	KRd	III	396	2	87%	70%	32%	15%	ASPIRE
		CarPomD	II	30	6	50%	13%	0%		ASPIRE
		Kd	II	257	5	24%	6%	0%	12%	ENDEAVOR
	Revlimid	RD	III	396	2	67%	40%	9%	18%	ENDEAVOR
	Velcade	Vd	III	333	2	38%		6%	25%	ENDEAVOR
	Rev-MAb	Elo-Rd	II	36	2	92%	64%	14%		

Highlighted yellow indicate regimens being explored in pivotal studies

Source: Company reports, ASH 2012, ASH 2013, ASCO 2013, ASH 2014

Key questions and debates for AMGN

1. How much of a risk do biosimilars pose to AMGN?	"Biosimilar risk" is a naturally known long-term headwind, but we believe the base business is more durable than consensus, biosimilars are not as easy as perceived (many delays recently, Hospira received a CRL, and 6mos additional protection from BPCIA), and there are four pipeline programs that are under-appreciated and will likely start to get more credit by the end of 2016. Furthermore, AMGN has their own biosimilar programs but we are not sure how this will play out – first one is Humira and confidence is waning on whether this will actually launch in 2018+ given ABBV commentary on IP and AMGN commentary around potential IP "respect". Another potential threat to AMGN's core business comes from an IPR from the Bass group on a key Enbrel patent (2026+) – possible USPTO decision on institution (review) could come February 2016.
2. How should we view the PCSK9 competition between AMGN's Repatha and REGN's Praluent? What about competition from new orals?	AMGN is ahead of the game, with PCSK9 outcomes data and IVUS imaging data expected to read out H2:16 (Praluent CV outcome study just finished enrollment, data not until 2017). PCSK9 have high expectations and are expected to be positive – CV benefits below 15-20% would arguably be disappointing and may call into question consensus $4B+ in sales and market size of $10B with REGN/SNY. From our survey and KOL work, doctors tend to slightly favor Repatha for ease of administration (longer shelf life, once-a-month Velcro injector coming), as they are not too concerned on titrating down for low LDL (Praluent offers low-dose and high-dose options, but there are at least two case studies of healthy patients with genetic loss of PCSK9 function, negating the need to switch to low doses once LDL drops). Furthermore, AMGN's Repatha currently enjoys a slight advantage with payors – exclusive contracts with CVS and Harvard Pilgrim (vs UNH for Praluent), co-sharing with ESRX, and launch advantages in EU/Canada/Japan.
3. How will AMGN perform in the near-term?	AMGN will likely beat consensus on Q4 earnings in January (typical strong seasonality and buy-up into Q1 price increases, which then makes Q1 a little light). They will also likely benefit from a Q4 R&D tax credit again, which is never in the guidance and thus has boosted Q4 results for last few years. We believe 2016 guidance (given on Q3:15 call) is conservative due to managing expenses much better than expected with new CFO over last year and this is an area of leverage (they may need to raise margin guidance longer-term).

Exhibit 32: Income statement for AMGN

Non-GAAP Income Statement															
Fiscal Year (Ending in December) ($ figures in MM, except per share)	FY12	FY13	FY14	1Q15 Mar-15	2Q15 Jun-15	3Q15 Sep-15	4Q15E Dec-15	FY15E	1Q16E Mar-16	2Q16E Jun-16	3Q16E Sep-16	4Q16E Dec-16	FY16E	FY17E	CAGR 2013 - 2016
Product sales	16,639	18,192	19,327	4,874	5,225	5,516	5,273	20,888	5,028	5,478	5,489	5,618	21,614	22,800	6%
Aranesp	2,040	1,911	1,930	480	479	493	490	1,942	476	470	465	455	1,866	1,836	-2%
Epogen	1,941	1,953	2,031	534	491	489	450	1,964	410	405	400	390	1,605	1,477	-10%
Neulasta	4,092	4,392	4,596	1,134	1,158	1,267	1,160	4,719	1,130	1,150	1,065	1,030	4,375	4,120	-4%
Neupogen	1,260	1,398	1,159	246	256	284	236	1,022	220	224	212	200	856	775	-13%
Enbrel	4,236	4,551	4,688	1,116	1,348	1,459	1,320	5,243	1,139	1,398	1,435	1,477	5,449	5,409	5%
Prolia	472	744	1,030	272	340	320	330	1,262	330	365	371	396	1,463	1,609	16%
Xgeva	748	1,019	1,221	340	331	378	373	1,422	348	363	383	403	1,497	1,670	11%
Sensipar	950	1,089	1,158	334	344	353	358	1,389	356	364	371	379	1,470	1,550	10%
Vectibix	359	389	505	122	160	132	141	555	142	175	172	169	658	711	12%
Kyprolis	-	73	331	108	119	137	154	518	170	195	228	270	863	1,395	62%
Evolocumab	-	-	-	-	-	-	38	38	65	93	108	134	400	840	
US	-	-	-	-	-	-	*33*	*33*	*56*	*78*	*83*	*94*	*311*	*560*	
International	-	-	-	-	-	-	*5*	*5*	*9*	*15*	*25*	*40*	*89*	*280*	
Blincyto and other	-	-	-	15		67	70	226	24	28	34	41	126	190	
T-Vec	-	-	-	-	-	-	5	5	10	17	24	35	86	155	
Ivabradine	-	-	-	-	-	-	5	5	14	16	22	29	80	160	
Nplate	541	673	678	173	125	137	143	578	195	216	199	212	821	904	10%
Other revenues	626	484	736	159	145	207	220	731	200	205	210	215	830	870	
Total Revenues	**17,265**	**18,676**	**20,063**	**5,033**	**5,370**	**5,723**	**5,493**	**21,619**	**5,228**	**5,683**	**5,699**	**5,833**	**22,444**	**23,670**	**5.7%**
Operating expenses															
Cost of sales	2,735	2,870	3,059	735	789	745	765	3,034	704	767	768	787	3,026	3,192	1%
Research and development	3,296	3,929	4,121	856	918	1,086	1,118	3,978	905	986	1,043	1,124	4,058	4,104	0%
Selling, general and administrative	4,717	4,905	4,408	993	1,112	1,206	1,292	4,603	1,041	1,150	1,125	1,348	4,665	4,560	1%
Total expenses	10,748	11,704	11,588	2,584	2,819	3,037	3,174	11,614	2,650	2,903	2,937	3,258	11,748	11,856	0.8%
Operating income	**6,517**	**6,972**	**8,475**	**2,449**	**2,551**	**2,686**	**2,319**	**10,005**	**2,578**	**2,780**	**2,762**	**2,575**	**10,695**	**11,814**	**11.7%**
Interest and other income (expense), net	(428)	(568)	(606)	(146)	(79)	(147)	(152)	(524)	(125)	(125)	(125)	(125)	(500)	(400)	
Income before income taxes	**6,089**	**6,404**	**7,869**	**2,303**	**2,472**	**2,539**	**2,167**	**9,481**	**2,453**	**2,655**	**2,637**	**2,450**	**10,195**	**11,414**	**13.2%**
Provision for income taxes	970	590	1,169	392	495	458	390	1,735	503	558	554	514	2,129	2,397	
Net income	**5,119**	**5,814**	**6,700**	**1,911**	**1,977**	**2,081**	**1,777**	**7,746**	**1,950**	**2,097**	**2,084**	**1,935**	**8,066**	**9,017**	**10.4%**
Non-GAAP EPS - Basic	$6.60	$7.72	$8.82	$2.51	$2.60	$2.75	$2.36	$10.22	$2.60	$2.81	$2.80	$2.61	$10.81	$12.25	
Non-GAAP EPS - Diluted	**$6.51**	**$7.60**	**$8.70**	**$2.48**	**$2.57**	**$2.72**	**$2.33**	**$10.11**	**$2.57**	**$2.78**	**$2.77**	**$2.58**	**$10.70**	**$12.12**	**11.7%**
Shares outstanding - Basic	775.3	752.8	759.5	761.0	760.0	757.0	753.6	757.9	750.5	747.6	744.7	741.7	746.1	736.1	
Shares outstanding - Diluted	786.5	765.0	769.8	770.0	768.0	764.0	763.6	766.4	758.5	755.6	752.7	749.7	754.1	744.1	

Source: Company reports and RBC Capital Markets estimates

Valuation

Our base case of $190/share is based on applying a 17.6x multiple on our 2016 non-GAAP EPS. We believe this multiple is justified, as it is in the mid-range of peer large-cap biopharma companies with modestly slowing growth. We think the mid-range is reasonable given the improving prospects of its pipeline products despite slowing growth on its core products, which remain resilient with rapid declines unlikely in the near future.

Price target impediments

Our price target is dependent on Amgen's ability to stabilize sales on its core franchise, while continuously growing sales from newly launched or pending approval products. Also, the company faces potential competition from generic products inside and outside the US and biosimilars outside the US, which could threaten the company's core product sales, especially if the pathway for "interchangeable" biosimilars gains traction and becomes a readily viable path for generic manufacturers.

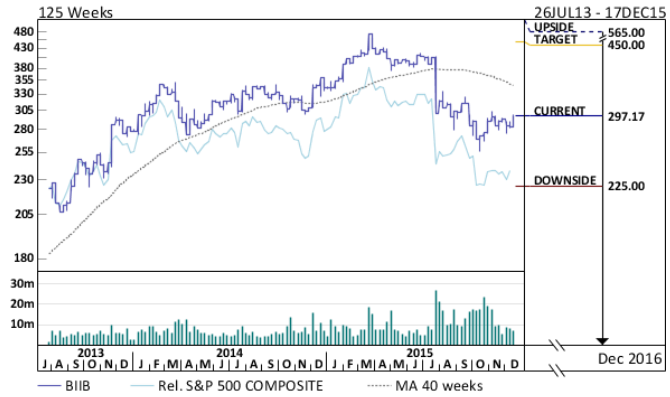
Biogen Idec (BIIB)

Outperform

Price Target USD $450.00

Target/Upside/Downside Scenarios

Exhibit 33: Biogen Idec.



Source: RBC Capital Markets estimates

Target price/base case

Our $450 price target is based on a DCF analysis that values the base business ($266/share) including Tecfidera and hemophilia programs. For various pipeline programs, we add probability adjusted value for anti-LINGO, BIIB037 and Eisai's Alzheimer's programs, MT1303 for IBD/MS, and SMNRx. This is also possible based on a 25x P/E to our 2016E EPS.

Upside scenario

Our upside scenario of $565 is based on similar assumptions as our base case for the core business (Avonex, Rituxan, Tysabri), Tecfidera and the new hemophilia franchise (Eloctate, Alprolix). We assign greater probability adjusted value for the pipeline (5–15% higher for each) as we gain visibility on their prospects in next 12 months. One key driver would be data readouts from anti-LINGO mid-2016, which if positive may drive shares higher toward our upside scenario and increase probability of success

Downside scenario

Our downside scenario of $225 is based on DCF analysis on only the existing core business (Avonex, Rituxan, Tysabri) plus the contribution from Tecfidera and recently launched hemophilia franchise (Eloctate, Alprolix). We do not include any pipeline opportunities as data are limited and many are high-risk. This is also possible based on a 12x P/E on our 2016E EPS, at the lower end of the peer group comparables.

Investment summary

With $10B+ of pipeline data reading out in the next 12 months or more, we would own BIIB for favorable risk/reward. For example, BIIB037 is in Phase III trials for Alzheimer's, and reported robust Phase Ib Alzheimer's, with more titration data coming H2:16. Furthermore, anti-LINGO MS data are due in mid-2016. Long-term, we are keenly tracking the continued uptake of Tecfidera, which may slow down as it enters its third year of launch, and generic Copaxone competing in the MS market. However, we do believe the positive pipeline events will likely outweigh any slowdown in its core MS business.

Potential catalysts for the stock

Series of positive pipeline data: Several of BIIB's key late-stage blockbuster pipeline drugs are expected to read out in the next 12–18 months, beginning with: 1) BIIB037 titration data H2:16, and BAN2401/E2609 (Eisai partnerships) Phase II data coming next spring; and 2) anti-LINGO in MS in mid-'16. Risk/ reward currently favors the upside, in our view, and if any of these data are positive, the stock could move 10% or more.

Risks to our investment thesis

Disappointing Tecfidera sales: Outperformance in the stock in the last two years has largely been driven by the impressive launch and uptake of its oral MS drug, Tecfidera. In Q3:14, it missed consensus estimates for the first time and also reported its first case of a PML-related (progressive multifocal leukoencephalopathy) death. If it continues to miss estimates or new safety signals emerge, this could weigh down the stock.

IP litigation overhang: Tecfidera is protected until 2028 on its dosing patents, but given that other companies (FWP, ALKS) are working on different formulations of the active ingredient DMF, BIIB could get pulled into lengthy patent litigations, which may create an overhang on the stock as Tecfidera is a significant contributor to BIIB's top and bottom lines. BIIB is currently junior party in ongoing interference proceedings with FWP, with oral argument scheduled for January 2017. BIIB will also meet FWP in German court in March 2016. We think a settlement with FWP would be a win-win situation, as a royalty would not meaningfully change our DCF on BIIB.

2016 Thoughts on BIIB

BIIB has experienced the most negative sentiment over the last three to six months and we think that will **turn around as we turn the calendar into 2016 and head into at least four to five potential major clinical catalysts – the most catalysts of ANY of the large cap biotech stocks.**

We predict investors will return to this name and buy it at current depressed levels given the significant upside potential if any of these datasets read out positive.

We think there continues to be investor concern going into 2016 guidance, but we predict that guidance will be fine and encapsulate consensus. Thus, we want to own this stock as guidance will likely be an overhang removed and the **stock should head higher into all these catalysts:**

1. Phase I/II Eisai BAN-2401 Alzheimer's data – safety and efficacy on 600+ patients = spring 2016 (-10% to +10-20%)
2. Phase II LINGO data in MS – mid-2016 (-10% to +20-30%)
3. Phase III ISIS SMN-Rx data in SMA pts – YE:16/early '17 (-5% to +15-20%)
4. LLY's Phase III Alzheimer's data for solanezumab – YE:16 and derivative for BIIB (could be one of the biggest events in all of bio-pharma next year) (BIIB -10-15% to +30-40%)

Bottom line – stock trades within 20-25% of the uber bear case scenario with no pipeline and bearish scenarios on Tecfidera. However, **there is 100% upside potential if one or more of the pipeline programs work – making it have the most upside potential of any large cap biotech.**

Q4 so far looks in line as guidance was for flattish scripts and Tecfidera is indeed mostly flattish. But we don't yet have high conviction in a strong quarter as there was some slight inventory build last quarter and given script trends, don't expect a blow-out quarter. More importantly, 2016 guidance will be issued in January along with earnings and we think guidance will be in-line with consensus for 2016, removing a near-term overhang and shifting focus on clinical catalysts in 2016…..(more important).

Bear case

- All of these catalysts in 2016 are high risk/high reward and few investors have any high confidence in any of them being positive. None are greater than a coin flip likelihood of working, which makes investors feel like they are taking unlikely "bets" in 2016 rather than investing on strong fundamentals and visible growth drivers.
- What if Tecfidera misses another quarter? What if there is another PML case and growth actually declines? What if the base business starts eroding and losing share in 2016? What will Ocrelizumab (Roche) do to the base business starting in 2017?
- Mgmt has been the least aggressive with buybacks versus any of the profitable large cap companies. They have no real organic growth over the next few years and are no longer a "growth" company.
- This company's prospects essentially all lie with Alzheimer's and that's not a program that anyone can get confidence in. If the Eisai data doesn't look good in Spring 2016 – investor sentiment is going to get very negative on BIIB as there is no real BIIB037 data until at least 2018…..so Alzheimer's sentiment will be very bearish.
- LINGO remains an extremely high risk program and it's unlikely to show statistical significance in a mid-size Phase II study – combined with mixed Eisai data – the stock could see $225 as investors will lose faith in the pipeline.
- Why doesn't management get more aggressive? More buybacks? Dutch tender? Acquire some commercial businesses or orphan drug late-stage products that diversify the business away from high risk programs?

Exhibit 34: Expected news flow for BIIB

Timing	Expected News Flow	Program
Q1:16	Commence Phase I clinical study in ALS (SOD-1 ASO)	ALS
early '16	Initiate two Phase III studies for both UC and Crohn's	MT-1303 (Mitsubishi collab)
Spring '16	Potential Phase II data in early AD	BAN2401 (Eisai partnership)
Spring '16	Phase II data in prodromal AD and MCI/Prodromal	E2609 (Eisai partnership)
H1:16	Potential EMA approval for etanercept biosimilar	Samsung Bioepis
H1:16	Potential EMA approval for infliximab biosimilar	Samsung Bioepis
mid-2016	Phase II (SYNERGY) proof-of-concept data for anti-LINGO-1 in remyelaination in MS	BIIB-033 (Anti-LINGO)
mid-2016	Phase I SAD results of BIIB-054 (alpha-synuclein) in healthy volunteer subjects	BIIB-054 (Neurimmune collab)
H2:16	Potential IND filing of XLRP	XLRP (AGTC collaboration)
H2:16	Potential titration dosing data from Phase Ib study (PRIME)	BIIB-037
H2:16	First patient in for Phase III studies in UC and Crohn's (two trials apiece)	MT-1303 (Mitsubishi collab)
YE:16	Estimated completion of Phase I/II study for DMPK in DM1 patients	ISIS-DMPKRx
2016	Estimated primary completion of Phase II double-blind MAD of STX-100 in IPF	STX-100
2016	Initiate dose-ranging Phase IIb trial for Tysabri in stroke	Tysabri
2016	Phase III (ASCEND) data presentation at a scientific meeting	Tysabri
2016	Phase III data in front-line DLBCL (GOYA)	Gazyva (Roche collaboration)
2016	Initiate Phase III trials for trigeminal neuralgia and Phase IIb for lumba radiculopathy	Raxatrigine (CNV1014802)
2016	Potentially initiate Phase II of oral "reparative" (remyelination) treatment for MS	BIIB-061
2016	File IND for treatment in beta-thalassemia	Gene Therapy
2016	Potentially initiate Phase II of dapirolizumab pegol (UCB) in SLE lupus	Anti-CD40 (CDP7657)
late '16/ early '17	Phase III data in Type 1 (infant) pts (ENDEAR)	SMN-Rx
late '16/ early '17	Phase III data in later-onset SMA (CHERISH)	SMN-Rx
2017	Anticipated Phase III readout in front-line iNHL with maintenance (GALLIUM)	Gazyva (Roche collaboration)
2017	File IND for treatment in sickle cell disease	Gene Therapy
H2:17-2018	Potential data from Phase III study in AD (ENGAGE and EMERGE)	BIIB-037
2020	Estimated primary completion of two Phase III studies in AD (ENGAGE and EMERGE)	BIIB-037

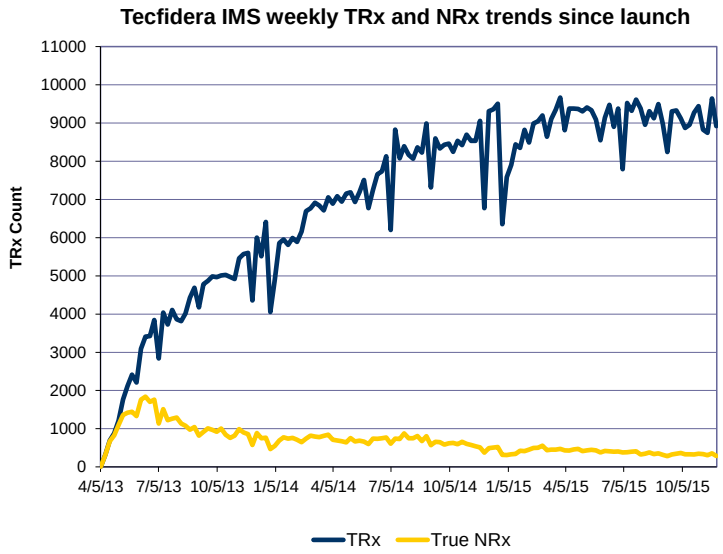
Source: Company reports and RBC Capital Markets estimates

Exhibit 35: Table of key BIIB pipeline events to follow over the next 12-24 months.

Program	Stage	Indication	N	Timing	Key Data Points
BAN2401 (EISAI)	Phase II	Alzheimer's	650+	**Spring '16**	Interim analysis (n=500) was conducted in June 2015. Topline Phase II results for this anti-a-beta protofibrils antibody are expected by spring '16 (Eisai FY ends March 31). Eisai has another Phase II Alzheimer's asset (E2609 BACE in safety stage), results also expected by spring '16.
ANTI-LINGO (BIIB-033)	Phase II	Multiple Scelerosis	419	**mid-16**	Top-line RENEW data showed positive trends on re-myelination and some encouraging results that should help to keep the big drug alive. Importantly consensus did NOT expect statistical significance and did not know what the data could show - so the fact it has some "positive trends" on improving nerve repair is an interesting concept. The company also commented they believe this is encouraging and the first clinical trial to ever show evidence of repair of the CNS and facilitating remyelination...we'll get more Phase II data in the bigger separate MS study in mid-16 (mgmt may have info by YE:15 from internal interim looks of the data).
BIIB037 (aducanumab)	Phase III	Alzheimer's	1350	**H2:17-2018**	On July 22nd, the company updated Phase Ib BIIB-037 AD data for the 6mg dose. In late July, BIIB initiated sites for two Phase III trials (ENGAGE and EMERGE), with plans to reach over 300 sites. The trial design is a randomized, double-blind, placebo-controlled, parallel-group study (n=1350 each). ApoE4 carriers will receive 3mg or 6mg doses, while ApoE4 non-carriers will receive 6mg or 10mg doses. All treatment arms to include titration period. The primary endpoint is CDR-sb and will be measured at ~18 months. Further Phase Ib titration data expected H2:16.
BIIB054	Phase I	Parkinson's Disease	40	**July 2016**	This Phase I, single ascending dose study (5 cohorts) will evaluate the safety and tolerability of BIIB054 administered via IV to healthy volunteers. PK and alpha-synuclein levels in the CSF, and anti-BIIB054 antibodies in serum will also be evaluated.
MT-1303	Phase III	Ulcerative Colitis	TBC	**2016+**	Mitsubishi Tanabe successfully completed a Phase II trial in MS in July 2014. BIIB licensed the drug from Mitsubishi in September 2015, and will evaluate potential further development in MS. BIIB plans to initiate a Phase III trial in UC in early 2016 and may advance Crohn's disease to Phase III in the future.
ISIS-SMNrx	Phase III	Spinal Muscular Atrophy	~110 (infant) ~120 (children)	**late '16/ early '17**	ISIS started two pivotal trials (infant onset, childhood onset) in H2:14. Results from earlier studies suggest encouraging trend in benefit but not quite a life-changing cure as some had hoped.

Source: Company reports, RBC Capital Markets estimates

Exhibit 36: MS weekly Rx trends show flattening Tecfidera, as expected for a product whose early uptake was unprecedentedly rapid and for which BIIB later reported several PML cases. We expect Tecfidera sales to grow ~5-10% next year mostly due to price increases; we'd like to see



2015

Q1:15A		Q2:15A		Q3:15A		Q4:15E	
IMS TRx Sum	113574	IMS TRx Sum	118,685	IMS TRx Sum	118,685	IMS TRx Sum	118,685
Q/Q growth	3%	Q/Q growth	5%	Q/Q growth	0%	Q/Q growth	0%
Price/month	$5,174	Price/month	$5,459	Price/month	$5,568	Price/month	$5,791
G-to-N	20%	G-to-N	20%	G-to-N	21%	G-to-N	21%
Capture	91%	Capture	93%	Capture	92%	Capture	93%
EUTRx/TRx	1.3x	EUTRx/TRx	1.3x	EUTRx/TRx	1.3x	EUTRx/TRx	1.3x
TRx predicted sales	$672	TRx predicted sales	$725	TRx predicted sales	$739	TRx predicted sales	$759
Inventory	-$24	Inventory	-$4	Inventory	$15	Inventory	$0
Sum	**$648**	**Sum**	**$721**	**Sum**	**$754**	**Sum**	**$759**
BIIB reported US sales	**$648**	**BIIB reported US sales**	**$721**	**BIIB reported US sales**	**$754**	**Consensus**	**$744**
Q/Q growth	-13%	*Q/Q growth*	11%	*Q/Q growth*	5%	*Q/Q growth*	1%

Total (2015)	**$2,881**
Consensus	**$2,865**

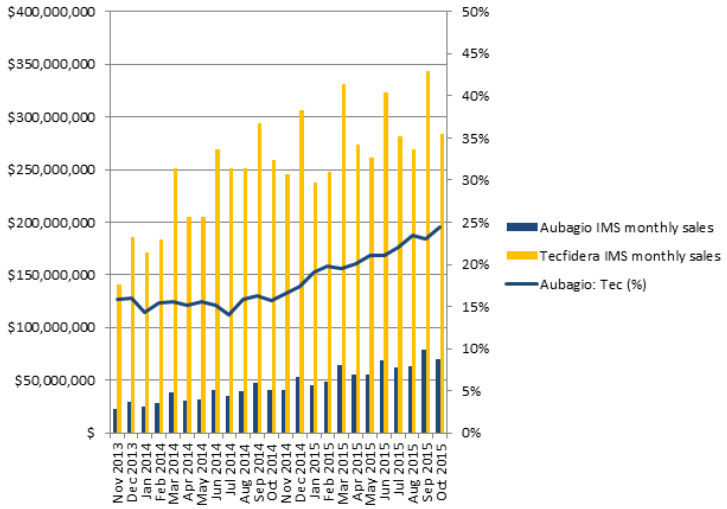
2016

Q1:16E		Q2:16E		Q3:16E		Q4:16E	
IMS TRx Sum	118,685	IMS TRx Sum	118,685	IMS TRx Sum	118,685	IMS TRx Sum	117,498
Q/Q growth	0%	Q/Q growth	0%	Q/Q growth	0%	Q/Q growth	-1%
Price/month	$5,791	Price/month	$6,138	Price/month	$6,138	Price/month	$6,507
G-to-N	21%	G-to-N	23%	G-to-N	23%	G-to-N	25%
Capture	93%	Capture	93%	Capture	93%	Capture	93%
EUTRx/TRx	1.3x	EUTRx/TRx	1.3x	EUTRx/TRx	1.3x	EUTRx/TRx	1.3x
TRx predicted sales	$759	TRx predicted sales	$754	TRx predicted sales	$754	TRx predicted sales	$771
Inventory	-$9	Inventory	$6	Inventory	$16	Inventory	$4
Sum	**$750**	**Sum**	**$760**	**Sum**	**$770**	**Sum**	**$775**
Consensus	**N/A**	**Consensus**	**N/A**	**Consensus**	**N/A**	**Consensus**	**N/A**
Q/Q growth	-1%	*Q/Q growth*	1%	*Q/Q growth*	1%	*Q/Q growth*	1%

Total (2016)	**$3,055**	6% YoY
Consensus	**$3,072**	

Source: IMS Health, RBC Capital Markets estimates

Exhibit 37: Tecfidera continues to face growing competition - Aubagio has been continuously gaining shares (24% of Tecfidera in Oct '15 vs just 20% six months ago).



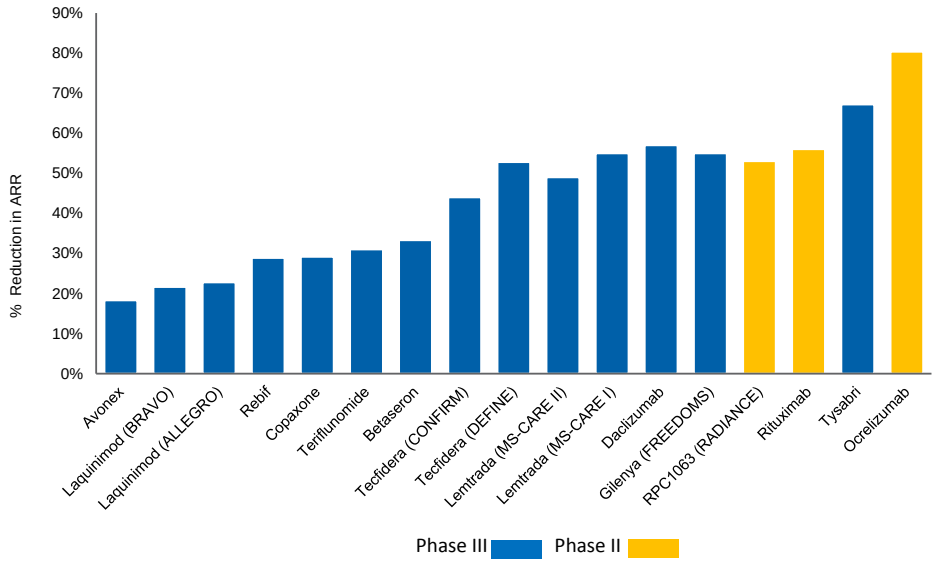
Source: IMS Health, RBC Capital Markets estimates

Exhibit 38: Absolute and Comparative % ARR for MS Drugs

	% ARR	% ARR (Comparator)	ARR (Drug)	ARR (Placebo)	ARR (Comparator)
Avonex	18%		0.67	0.82	
Laquinimod (BRAVO)	22%	27%	0.29	0.37	0.27
Laquinimod (ALLEGRO)	23%		0.31	0.40	
Rebif	29%		1.73	2.56	
Copaxone	29%		1.19	1.68	
Teriflunomide	31%		0.37	0.54	
Betaseron	33%		0.42	0.63	
Tecfidera (CONFIRM)	44%	29%	0.22	0.40	0.29
Tecfidera (DEFINE)	53%		0.17	0.36	
Ocrelizumab (OPERA I)		46%			
Ocrelizumab (OPERA II)		47%			
Lemtrada (MS-CARE II)	49%				
Lemtrada (MS-CARE I)	55%				
Daclizumab	57%		0.2	0.5	
Gilenya (FREEDOMS)	55%		0.18	0.40	
RPC1063 (RADIANCE)	53%		0.24	0.50	
Rituximab	56%		0.37	0.84	
Tysabri	67%		0.22	0.67	
Ocrelizumab	80%		0.13	0.64	

Source: Company reports, RBC Capital Markets estimates

Exhibit 39: Percent reduction of ARR in MS therapies



Source: Company Reports and RBC Capital Markets estimates

Exhibit 40: Comparison of efficacy data between aducanumab (Biogen), solanezumab (Eli Lilly) and crenezumab (Roche) highlights potential for aducanumab to work in early Alzheimer's disease

	BIIB037 (Aducanumab)		Solanezumab			Crenezumab	
Company	Biogen		Eli Lilly			Roche	
Status	Phase I	Phase Ib	Phase III			Phase II	Phase II
Indication	mild/ moderate AD	prodromal or mild AD	mild/ moderate AD	mild/ moderate AD	mild AD	mild/ moderate AD	amyloid positive AD
Trial	single-ascending dose	PRIME (multi-dose)	EXPEDITION 1	EXPEDITION 2	EXPEDITION 3	ABBY	BLAZE
Prim Endpt Time	6 months (0.5 yr)	126 weeks (2.4 yrs)	80 weeks	80 weeks	80 weeks	73 weeks	69 weeks
Treatment duration		52 weeks	80 weeks	80 weeks	76 weeks	72 weeks	68 weeks
Dosage	0.03, 1, 3, 10, 20, 30, 60 mg/kg IV	1, 3, 6, 10 mg/kg IV QM	400 mg IV QM	400 mg IV QM	400 mg IV QM	300 mg SC Q2W, 15mg/kg IV Q4W	300 mg SC Q2W, 15mg/kg IV Q4W
Enrollment	53	194	1012	1040	2100	431	91
Primary endpoint	safety/ tolerability	safety/ tolerability	ADAS-Cog11, ADCS-ADL	ADAS-Cog14	ADAS-Cog14, ADCS-iADL	ADAS-Cog12, CDR-SOB	changes in brain amyloid load by florbetapir-PET
Secondary endpoint	PK, immunogenicity	18F-AV-45F-AV-45 PET, PK, immunogenicity	CDR, NPI, vMRI, MMSE, RUD-Lite, EQ-5D Proxy, QoL-AD, amyloid	CDR, NPI, vMRI, MMSE, RUD-Lite, EQ-5D, QoL-AD, amyloid, ADAS-Cog12, ADAS-Cog11, ADCS-ADL	CDR, NPI, vMRI, MMSE, RUD-Lite, EQ-5D Proxy, QoL-AD, plasma amyloid, ADAS-Cog11, ADCS-ADL, FAQ, florbetapir PET, CSF amyloid	ADCS-ADL, volumetric MRI, CSF biomarkers	ADAS-Cog12, CDR-SOB, CSF, vMRI, ADCS-ADL
Efficacy trends?		-stat sig dose- and time-dependent amyloid reduction -stat sig cognition at 54 weeks (MMSE, CDR)	-slowing by 34% in cognitive decline (ADAS-Cog14 and MMSE) at 80wks in mild, pooled analysis			BLAZE, ABBY did not meet co-primary endpoints in mild/moderate, but positive trend in coginition in mild AD	
MMSE (in mild): pbo-adj mean change from baseline		-2.25 pbo-adj in 10mg high dose (drug=-0.56; week 52, p<0.05); -0.85 pbo-adj in 6mg dose (drug = -1.96; week 52); -2.11 pbo-adj in 3mg dose (drug=-0.70; week 52; p<0.05); -0.64 pbo-adj in 1mg dose (drug =-2.18; week 52) -2.81 pbo (week 52)	-0.12 (pbo= -0.30 vs drug= -0.18; week 28, p=0.468) -0.42 (pbo= -1.43 vs drug= -1.01; week 52, p=0.051) -0.93 (pbo= -2.76 vs drug = -1.83; week 80, p=0.001)			-0.70 (pbo=-2.22 vs drug =-1.52; wk 73; p=0.351)	
CDR-SOB (in mild)		-1.24 pbo-adj in 10mg high dose (drug=0.63; week 54, p<0.05); -0.76 pbo-adj in 6mg dose (drug=1.11; week 54); -0.50 pbo-adj in 3mg dose (drug=1.37; week 54); -0.15 pbo-adj in 1mg dose (drug =1.72; week 54) pbo=1.87 (week 54)	+0.1 (pbo=1.8 vs drug=2.0; wk 80, p=0.51, **mild/mod** AD)	-0.3 (pbo=1.6 vs drug=1.3; wk 80, p=0.22, **mild** AD)		-0.02 (-1.0%; wk 73; p=0.964)	-41.5%; wk 73; p=0.44 (high-dose IV drug)
Safety	no amyloid-related imaging abnormalities (ARIA) in doses up to 30 mg/kg	ARIA mild-moderate, self-resolving; dose- and APoE4-dependent (5-55% in APoE4 carriers vs 9-17% in ApoE4 non-carriers); 65% of ARIA-E asymptomatic	1% ARIA-E (vasogenic edema) in treated, 0.5% placebo (not stat sig)			single case of ARIA-E in IV-treated patient across both studies	
Timeline	completed	initiate Phase 3 (EMERGE, ENGAGE) in early AD in 2015	did not meet primary endpts	did not meet primary endpts	complete ~Dec 2016	completed	completed

*MMSE scoring:	27-30	normal
	20-26	**mild**
	10-19	moderate
	0-9	severe

*CDR-SOB scoring	0	normal
	0.5-2.5	questionable impairment
	3.0-4.0	very mild dementia
	4.5-9.0	**mild dementia**
	9.5-15.5	moderate dementia
	16.0-18.0	severe dementia

Source: Company reports, RBC Capital Markets estimates

Key questions and debates for BIIB

1. Tecfidera scripts haven't picked up yet, and additional PML-related deaths are not helping. Is 2016 guidance at risk? Could ocrelizumab pose further risk?

BIIB has experienced the most negative sentiment over the last three to six months and we think that will turn around as we turn the calendar into 2016 and head into at least four major clinical catalysts – the most catalysts of ANY of the large cap biotech stocks. We think there continues to be investor concern going into 2016 guidance but we predict that guidance will be fine and encapsulate consensus. Thus we want to own this stock as guidance will be an overhang removed and the stock should head higher into 2016 catalysts. We predict investors will return to this name and buy it at current depressed levels given the significant upside potential if any of these datasets read out positive.

On ocrelizumab, Roche reported high efficacy Phase III data in RRMS and PPMS. However, we don't view ocrelizumab as a major threat to our LT thesis on BIIB: Ocrelizumab won't be on the market until early 2017. Roche will need to hire its own salesforce and it will be used primarily by academic centers and where there are IV capabilities (i.e. not oral pill); further safety details (not until late '16 or early '17) are needed; BIIB gets a ~20% royalty on US sales of ocrelizumab so this offsets half the economic impact, and positive ocrelizumab data could have a positive halo effect for BIIB.

2. What should investors focus on for 2016?

Stock trades within 20-25% of the uber bear case scenario with no pipeline and bearish scenarios on Tecfidera. However, there is 100% upside potential if one or more of the pipeline programs work – making it have the most upside potential of any large cap biotech. We believe the stock should head higher into all these catalysts:

1. Phase I/II Eisai BAN-2401 Alzheimer's data – safety and efficacy on 600+ patients = spring 2016 (-10% to +10-20%)
2. Phase II LINGO data in MS – mid-2016 (-10% to +20-30%)
3. Phase III ISIS SMN-Rx data in SMA pts – YE:16/early '17 (-5% to +15-20%)
4. LLY's Phase III alzheimer's data for solanezumab – YE:16 and derivative for BIIB (could be one of the biggest events in all of bio-pharma next year) (BIIB -10-15% to +30-40%)

3. All of the catalysts in 2016 are high risk/ high reward, with none greater than a 50/50 likelihood of working. What happens if none of the pipeline programs work out?

This company's prospects essentially all lie with Alzheimer's and that's not a program that anyone can get confidence in. If the Eisai data doesn't look good in Spring 2016 – investor sentiment is going to get very negative on BIIB as there is no real BIIB-037 data until at least 2018…..so Alzheimer's sentiment will be very bearish. Also, LINGO remains an extremely high risk program and it's unlikely to show statistical significance in a mid-size Phase II study – combined with mixed Eisai data – the stock could see $225 as investors will lose faith in the pipeline.

4. How should we think about BIIB stock near-term?

Q4 so far looks in-line as guidance was for flattish scripts and Tecfidera is indeed mostly flattish. We don't yet have high conviction in a strong quarter as there was some slight inventory build last quarter and given script trends, don't expect a blow-out quarter. More importantly, 2016 guidance will be issued in January along with earnings; we think guidance will be in line with consensus for 2016, removing a near-term overhang and shifting focus on clinical catalysts in 2016…..(more important).

Exhibit 41: Income statement for BIIB

Fiscal Year (Ending in December) ($ figures in MM, except per share)	FY13	1Q14 Mar-14	2Q14 Jun-14	3Q14 Sep-14	4Q14 Dec-14	FY14	1Q15 Mar-15	2Q15 Jun-15	3Q15 Sep-15	4Q15E Dec-15	FY15E	1Q16E Mar-16	2Q16E Jun-16	3Q16E Sep-16	4Q16E Dec-16	FY16E	FY17E
Avonex + Plegridy	3,004.9	761.5	773.8	745.2	777.1	3,057.6	754.5	689.7	784.8	742.4	2,971.4	736.7	735.8	735.1	755.1	2,962.7	2,775.0
Tecfidera	876.0	505.7	700.4	787.1	916.0	2,909.2	824.9	883.3	937.4	949.0	3,594.9	945.0	960.0	980.0	990.0	3,875.0	4,079.2
US	*674.4*	*460.0*	*585.0*	*638.0*	*743.0*	*2,426.0*	*648.0*	*721.0*	*754.0*	*759.0*	*2,882.0*	*750.0*	*760.0*	*770.0*	*775.0*	*3,055.0*	*3,177.2*
International	*9.6*	*45.7*	*115.4*	*149.1*	*173.0*	*483.2*	*176.9*	*163.0*	*183.0*	*190.0*	*712.9*	*195.0*	*200.0*	*210.0*	*215.0*	*820.0*	*902.0*
Rituxan + Gazyva	1,126.6	296.9	303.3	290.7	304.5	1,195.4	330.6	337.5	337.2	325.6	1,330.9	339.0	342.3	345.7	349.0	1,376.0	1,393.1
Tysabri	1,526.6	441.0	533.4	501.2	483.9	1,959.6	462.6	463.1	479.7	483.0	1,888.7	486.8	490.7	494.1	497.0	1,968.6	2,007.2
US	*700.6*	*234.0*	*250.0*	*275.0*	*266.0*	*1,025.0*	*273.0*	*268.5*	*284.0*	*285.0*	*1,110.5*	*287.9*	*290.7*	*293.6*	*296.6*	*1,168.8*	*1,192.2*
International	*713.0*	*207.0*	*283.4*	*226.2*	*217.9*	*934.6*	*189.6*	*194.6*	*196.0*	*198.0*	*778.2*	*198.9*	*199.9*	*200.4*	*200.4*	*799.8*	*815.0*
Fampyra (Ex-US)	74.0	19.0	22.3	20.4	18.5	80.2	20.0	21.1	21.0	21.0	83.1	20.0	20.0	20.0	20.0	80.0	80.0
Eloctate	-	-	-	21.6	36.8	58.4	53.6	74.3	90.6	92.0	310.5	95.0	100.0	105.0	112.5	412.5	490.0
Alprolix			10.4	25.3	40.3	76.0	43.1	54.4	65.7	68.0	231.2	69.0	70.0	72.0	75.0	286.0	320.0
Oral fumarate (Psoriasis)	60.2	15.6	16.0	16.5	14.4	62.5	13.6	12.7	12.5	12.0	50.8	10.0	10.0	10.0	10.0	40.0	35.0
Contracts and other sales	78.2	52.2	21.5	36.3	17.8	127.8	32.2	47.0	40.0	35.0	154.2	20.0	20.0	20.0	20.0	80.0	80.0
Royalties	185.8	37.9	40.3	67.1	31.4	176.7	19.8	8.6	9.0	9.0	46.4	10.0	10.0	10.0	10.0	40.0	80.0
Total Revenues	**6,932.3**	**2,129.8**	**2,421.5**	**2,511.4**	**2,640.7**	**9,703.3**	**2,554.9**	**2,591.7**	**2,777.8**	**2,737.0**	**10,662.1**	**2,731.5**	**2,758.8**	**2,791.8**	**2,838.6**	**11,120.8**	**11,339.5**
Cost of goods sold	857.7	279.2	291.9	302.6	297.3	1,171.0	312.4	286.1	310.0	319.5	1,228.1	319.9	322.6	325.4	330.0	1,297.9	1,310.8
Research and development	1,439.7	526.6	446.1	415.9	499.1	1,887.7	460.5	490.7	519.9	625.0	2,096.1	532.6	538.0	544.4	553.5	2,168.6	2,182.8
Sales, general & administrative	1,706.8	509.1	540.1	569.0	572.5	2,190.7	560.4	491.9	477.8	600.0	2,130.1	505.3	510.4	516.5	525.1	2,057.3	2,097.8
Collaboration profit (loss) sharing	85.4	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Total Expenses	3,246.3	1,039.1	990.0	988.7	1,077.4	4,095.3	1,024.3	987.8	1,001.8	1,228.0	4,241.9	1,041.0	1,051.3	1,063.9	1,081.7	4,237.9	4,292.6
Operating Income	**2,844.8**	**808.4**	**1,143.4**	**1,224.5**	**1,270.6**	**4,447.0**	**1,218.2**	**1,317.7**	**1,466.1**	**1,189.5**	**5,192.1**	**1,370.6**	**1,384.9**	**1,402.5**	**1,426.9**	**5,585.0**	**5,759.0**
Other Income (net)	(7.7)	(5.8)	4.9	(16.3)	(8.8)	(26.0)	(17.4)	(10.9)	(15.4)	(73.8)	(117.4)	(73.8)	(73.8)	(73.8)	(73.8)	(295.0)	(305.0)
Pretax Income	2,837.1	802.6	1,148.3	1,208.2	1,261.9	4,421.0	1,200.8	1,306.8	1,450.6	1,115.8	5,074.7	1,296.9	1,311.1	1,328.8	1,353.2	5,290.0	5,454.0
Provision for taxes	694.0	215.4	308.6	304.0	296.9	1,124.9	304.5	309.6	347.8	278.9	1,240.8	324.2	327.8	332.2	338.3	1,322.5	1,363.5
Net Income	**2,135.8**	**587.2**	**837.8**	**898.8**	**964.7**	**3,288.5**	**897.2**	**992.4**	**1,096.0**	**836.8**	**3,823.0**	**972.7**	**983.4**	**996.6**	**1,014.9**	**3,967.5**	**4,090.5**
Net income adjusted for diluted EPS calculati	2,135.8	587.2	829.1	899.6	965.6	3,281.1	899.6	994.8	1,042.1	836.8	3,823.0	972.7	983.4	996.6	1,014.9	3,967.5	4,090.5
EPS - Basic (Non-GAAP)	$9.01	$2.48	$3.50	$3.81	$4.10	$13.91	$3.82	$4.23	$4.49	$3.87	$16.64	$4.53	$4.62	$4.72	$4.85	$18.72	$19.91
EPS - Diluted (Non-GAAP)	**$8.96**	**$2.47**	**$3.49**	**$3.80**	**$4.09**	**$13.83**	**$3.82**	**$4.22**	**$4.48**	**$3.86**	**$16.61**	**$4.52**	**$4.61**	**$4.71**	**$4.83**	**$18.67**	**$19.85**
Shares outstanding - Basic	236.9	236.8	236.7	236.2	235.5	236.4	235.0	235.3	232.2	216.3	229.7	214.5	212.8	211.1	209.4	211.9	205.5
Shares outstanding - Diluted	238.3	237.8	237.4	237.0	236.3	237.2	235.6	235.7	232.6	216.9	230.2	215.1	213.4	211.7	210.0	212.5	206.1

Source: Company reports and RBC Capital Markets estimates

Valuation

Our $450 price target is based on a DCF analysis that values the base business ($266/share) including Tecfidera and hemophilia programs. For various pipeline programs, we add probability adjusted value for anti-LINGO, BIIB037 and Eisai's Alzheimer's programs, MT1303 for IBD/MS, and SMNRx. This is also possible based on a 25x P/E to our 2016E EPS.

Price target impediments

Risks to our thesis are disappointing Tecfidera growth and sales, worse than expected erosion of Avonex/Plegridy franchise, and less than projected growth in Tysabri. However, we think that competition, market share loss, and new oral MS drugs are well known already by the Street and reflected in estimates. Failure of BIIB's pipeline programs (anti-LINGO for re-myelination, BIIB037 and Eisai programs for Alzheimer's, SMN-Rx for spinal muscular atrophy) to have successful data readouts in the next one to t hree years would also contribute to downside, given that BIIB's premium valuation to peers reflects some expectation of success in continued generations of blockbuster therapies.

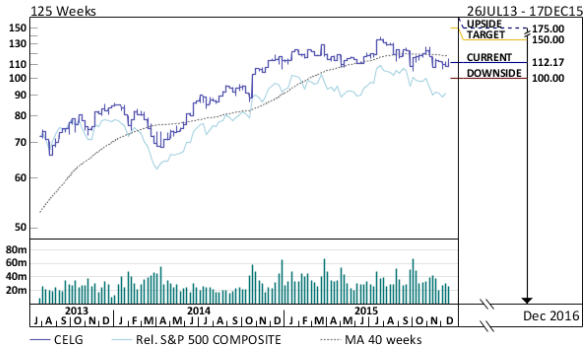
Celgene (CELG)

Outperform

Price Target USD $150.00

Target/Upside/Downside Scenarios

Exhibit 42: Celgene.



Source: RBC Capital Markets estimates

Target price/base case

Our base case of $150/share is derived through our DCF on a robust pipeline. We expect double digit growth in the base business for the next five to eight years (Revlimid, Pomalyst, Abraxane, Apremilast) as well as 95% probability that Revlimid polymorph holds until 2026. We also believe CELG's partnered assets (AG-221/AG-120 for leukemia, GED-0301 for Crohn's, etc.) are under-appreciated assets that are likely to help maintain CELG's healthy growth into 2020+. Our base case is also supported by applying a 25x multiple to our 2016E EPS. With CELG's above peer group EPS CAGR of 20%+ we believe this premium multiple is warranted.

Upside scenario

Our upside scenario of $175/share incorporates a higher multiple of 2016E EPS. This may be warranted if we make the same assumptions as our base case, except that we assume 100% (instead of 95%) probability that the 2026 polymorph patent holds, and we assume higher probability of success of 50%+ on pipeline programs.

Downside scenario

Our downside scenario of $100/share incorporates a lower 17x multiple of 2016E EPS. This may be justified in the scenario using same assumptions as our base case, but with lower probability (60% vs 95%) that the 2026 polymorph patent will hold. Additionally, we do not include any value for early-stage pipeline, which would make growth in outer years more challenging and likely result in a lower multiple.

Investment summary

Our positive investment thesis on Celgene is based on five key drivers: 1) successful transition to a diversified story beyond Revlimid with new product launches (Pomalyst, Otezla) and supported by deep pipeline of 25+ partnered assets, 2) potential Revlimid IP settlement with Actavis/AGN, removing a key overhang, 3) Revlimid's increasing duration of therapy appears under-estimated in long-term models, 4) evolving capital allocation/earnings growth with continued buybacks and potential for dividends in 2016+, and 5) new 2020 guidance over $13/share, which at historical 19-20x multiple could get the stock towards $200 over time.

Potential catalysts for the stock

Financial guidance revision: More evolving data such as ASPIRE and PD-1 combo data from ASH '15 (American Society of Hematology) show increasing durations with Revlimid and Pomalyst continues robust uptake. Upwards revision to Revlimid and other guidance would boost investor confidence on the impressive growth trajectory.

Select pipeline read-outs that would be upside: GED-0301 Phase III data could finally be positive in 2017 – this is a $1-2B franchise that Street had turned more lukewarm on since CELG hasn't disclosed any endoscopy data. AGIO's third IDH drug now starting Phase I could work in solid tumors, OMED's pancreatic antibody on top of Abraxane in Phase I/II, VentiRX immunotherapy Phase II ovarian cancer data YE:16.

Risks to our investment thesis

Disappointing expansion of Revlimid into NDMM: Key variable in meeting 2017 guidance remains Revlimid's robust expansion into NDMM in the US and EU. Largest room for growth lies in EU and given the price-conscious dynamic there and challenge in changing practice patterns, the growth in Revlimid sales may not meet expectations.

Lackluster uptake in Otezla: Otezla launch remains early, yet it accounts for a meaningful portion ($1.5-2B) of CELG's 2017 top-line guidance. Consensus remains below company expectations and based on how launch continues, it could determine whether the drug could become a meaningful contributor to the company or not.

Lack of settlement with Actavis (AGN) on Revlimid: Given Revlimid accounts for approximately two-thirds of its revenues, patent litigation with generic manufacturer Actavis (AGN) remains an overhang on the stock.

2016 thoughts on CELG

CELG remains **one of the best "growth" stories in large cap biotech** and with the stock down around 20% off the highs, we think this is an attractive opportunity for the one- to two-year horizon to own one of the premier growth names, with a potential to remove one of the longest running overhangs (IP settlement) and a **very big early-mid stage pipeline**.

While there isn't one specific catalyst to point to on the horizon, we do think there are **a number of positive drivers in 2016-17** that could continue to strengthen the long-term fundamental growth story:

1. A Revlimid IP settlement with AGN in 2016 with a base case generic launch farther out than 2025 (or with economics on anything earlier).
2. Abraxane should actually get stronger over the long-term due to "chemo-combo" I/O regimens that have moved to Phase III (Roche atezolizumab + abraxane) in front line lung cancer – updated Phase II data at ASCO could further build the bull case that this is one of the best front-line regimens in lung cancer.
3. CELG's own PD-1 combos (using AZN PD-L1) with Revlimid/Pom all show great data from ASH and this is a $1B franchise that isn't in the long-term CELG models. This is one of the $1B franchises growing beyond 2020.
4. GED-0301 Phase III data could finally be positive in 2017 – this is a $1-2B franchise that Street had turned more lukewarm on since CELG hasn't disclosed any endoscopy data.
5. Select early/mid stage pipeline programs that would be upside and could see read-outs: AGIO's third IDH drug now starting Phase I could work in solid tumors, OMED's pancreatic antibody on top of Abraxane in Phase I/II, VentiRX immunotherapy Phase II ovarian cancer data YE:16.

We maintain a **positive "5x5" thesis** that supports our longer-term positive outlook:

- Successful transition to a more diversified story beyond Revlimid with new product launches (Pomalyst, Otezla) and a deep pipeline of ~28 partnered assets, including RCPT, JUNO CAR-T, AZN PD-1 and more.
- Revlimid's increasing duration of therapy could be under-estimated in long-term models, especially post AMGN ASPIRE data, ABBV Elo myeloma data and new RVd triple data at ASH.
- Evolving capital allocation/earnings growth with continued buybacks ($2.8B repurchased YTD).
- 2020 guidance over $13/share, which implies $200 over time with a historical 15-20x multiple.
- Potential Revlimid IP settlement with Actavis, removing a key overhang.

Thinking about guidance

With CELG management historically guiding conservatively, we expect conservative guidance next year, although they may raise 2020 guidance. For FY16, we are estimating non-GAAP EPS of $5.65 vs cons $5.68 (range $5.04-6.08), taking into account the higher interest expense from an $8B debt offering related to the RCPT deal – CELG management guided to $480-500M interest expense next year.

Bear case

- No catalysts on the stock other than patent settlement, which remains murky at best – why would AGN settle now and it will soon be moving out from under them as part of the generics business sale.
- 2016 guidance uncertainty and risk to Abraxane estimates in 2016 (along with decreasing confidence on longer-term Abraxane guidance given recent lackluster sales.
- No settlement is likely anytime soon given expert discovery doesn't finish until mid-January, the AGN generics sale closes in Q1 and timing is too close/tight, and AGN is in the process of merging with PFE now. So a settlement is unlikely to be a priority at this time with AGN.
- Raising guidance for 2020 is unlikely to be a major catalyst as duration of therapy for Revlimid only adds to the increased weight and importance of Revlimid to the long-term and thus importance for a settlement, which isn't anytime soon.
- Company continues to pull out up-front payments from the pro-forma, EPS which makes non-GAAP EPS 20-25%+ higher than including them (or at least 1-2 P/E turns more expensive than peers). They also have higher stock option expense than peers that further makes "true" EPS lower than peers on a GAAP basis.
- Higher P/E stock could continue to see relative outflows vs peers if the biopharma sector continues to remain under pressure or if "pricing" rhetoric continues into 2016.

Exhibit 43: Expected news flow for CELG

Timing	Expected News Flow	Program
I & I Franchise		
H1:16	Positive registration study in Japan and NDA filing	Otezla
mid-16	Complete Phase II trial in moderate-to-severe atopic dermatitis (CC-10004-AD-001)	Otezla
H2:16	Phase III data for patients with untreated moderate-to-severe late stage psoriatic arthritis (PSA-006)	Otezla
H1:17	Complete Phase II trial in Ulcerative Colitis	Otezla
H2:17	Complete Phase III trial in Behcet's disease (BCT-002/RELIEF)	Otezla
YE:15/early '16	Initiate Phase II program in Crohn's disease	Ozanimod
H1:17	Phase II/ III data in relapsing multiple sclerosis (RADIANCE)	Ozanimod
H1:17	Phase III data in relapsing multiple sclerosis (SUNBEAM)	Ozanimod
2018	Phase III top-line data in moderate-to-severe Ulcerative Colitis (TRUE NORTH)	Ozanimod
Q4:15	Initiate Phase III patient randomization in Crohn's disease (CD-002)	GED-0301
Q4:15	Initiate Phase II proof of concept study in UC (UC-001)	GED-0301
YE:15	Complete Phase III enrollment in registration-enabling endoscopy trial	GED-0301
H1:16	Initiate Phase III trials in Crohn's disease (CD-003)	GED-0301
2017	Potential Phase III data for treatment of Active Crohn's disease	GED-0301
Hematology & Oncology Franchise		
Q4:15	Receive Russia Federal RRMM tender	Revlimid
Dec '15	Present Phase I results of MK-3475 (Pembro) + Revlimid + Low-Dose Dex in MM at ASH (KEYNOTE-023)	Revlimid/MK-3475
Dec '15	Present Phase II data of Pemrbo + Revlimid + Dex in R/R MM patients at ASH	Revlimid/MK-3475
YE:15	Phase III enrollment completion of CLL patients; maintenance in 2nd line CLL (CONTINUUM)	Revlimid
YE:15	Japan decision for NDMM approval	Revlimid
Apr '16	PDUFA date for non-deletion 5q low risk/ INT-1 transfusion-dependent MDS patients	Revlimid
H1:16	Obtain reimbursement from rest of G5 NDMM	Revlimid
Q3:16	Phase III maintenance readout of elderly patients with DLBCL and treated with R-CHOP (REMARC)	Revlimid
YE:16/2017	Phase III top-line data in R/R follicular lymphoma patients (AUGMENT/NHL-007)	Revlimid/Rituximab
H1:17	Potential data from Phase III trial in newly diagnosed patients with follicular lymphoma (RELEVANCE)	Revlimid/Rituximab
mid '17	Potential data from Phase III maintenance trial following VMP induction therapy in NDMM (ARUMM)	Revlimid
H2:17	Phase III maintenance data in ASCT eligible patients (MYELOMA XI)	Revlimid
mid '18	Phase III top-line data in patients with untreated activated B-cell DLBCL (ROBUST/DLC-002)	Revlimid/R-CHOP
2021	Phase III top-line data in patients with R/R indolent lymphoma (MAGNIFY/NHL-008)	Revlimid/Rituximab
H1:18	Phase III data in relapsed or refractory MM patients	Pomalyst/Imnovid
YE:15	Expected CHMP recommendation in elderly newly diagnosed AML (AZA-AML-001)	Vidaza
Dec '15	Phase I results in TNBC expected at San Antonio Breast Cancer Symposium (SABCS)	Abraxane
mid '16	Phase III top-line data for patients with first-line stage IIIB / IV squamous NSCLC (NSCL-003/Abound.sqm)	Abraxane/carboplatin
YE:16	Phase II/III data in patients with first-line triple negative metastatic breast cancer (ABI-007-MBC-001)	Abraxane/gemcitabine
2016	Enrollment completion of combination Phase III trials of Abraxane with PD-L1 in NSCLC and TNBC	Abraxane/PD-1
mid '18	Phase III data on post induction AML maintenance patients in complete remission	CC-486
mid '19	Phase III data for patients with Low risk/INT-1 transfusion-dependent MDS (AZA-MDS-003)	CC-486
Partnered Programs		
Nov 2015	Present Phase II interim data of sotatercept in patients with renal anemia at ASN	Sotatercept
YE:15	Initiate pivotal Phase III study in beta-thalassemia	Luspatercept
YE:15	Initiate pivotal Phase III program in IDH2 mutated AML	AG-221
YE:15/early '16	Complete enrollment for Phase IIa trial of CC-220 in systemic lupus erythematosus (SLE)	CC-220
H1:19	Phase III data of AG-221 in older subjects with late stage AML harboring an ID2H mutation	AG-221
Revlimid IP Litigation Timelines		
Jan '16	Close of expert discovery begins	Natco
mid 2016	Trial begins few months after expert discovery ends	Natco

Source: Company reports and RBC Capital Markets estimates

Exhibit 44: Table of CELG partnerships. (*Please contact us for a more detailed table*)

Company	Ticker	Announced	Program	Indication	Stage	Clinical Trial Timeline
Nurix	-	Sep-15	Small Molecule Drug Discovery	Oncology, Inflammation, Immunology	Pre-clinical	IND filings 2016+
Epizyme	EPZM	Jul-15; Apr-12	3 Predefined Targets; DOTL1	To be Determined; MLL	Phase Is; Phase I/II	**MLL:** Dose escalation enrollment in pediatric patients 2H:15
Juno Therapeutics	JUNO	Jun-15	CD19 and CD22 CAR-T	Cancer, Autoimmune Diseases	Phase I	**CD19:** B-ALL data Q1:16; B-NHL data Q2:16; r/r Leukemia data Q1:17; two additional studies in pre-clinical **CD22:** r/r B-cell malignancies data Q1:17
Lycera	-	Jun-15	LYC-30937	Immuno-oncology	Phase I	**IBD:** Complete YE:15
AstraZeneca (MedImmune)	AZN	Apr-15	MEDI4736	Cancer Hematology	Phase I/ II*	**Myelodysplastic Ph I**: Topline Q4:15
Zymeworks		Jan-15		Immuno-oncology	Pre-clinical	IND filings 2016-2018
Sutro Biopharma	-	Oct-14; Dec-12	Antibody Discovery	Undisclosed Immuno-oncology	Pre-clinical	IND filings 2016+
Nogra Pharma	-	Apr-14	GED-0301	Crohn's disease	Phase III	Inititate Phase III trials 2H:15
Abide Therapeutics	-	Feb-14	AB101131; Drug Discovery	Inflammation; Immunology	Pre-clinical	IND filings 2016+
NantBioScience	-	Jan-14	NTB-011, NTB-010; nab-based molecules	Cancer	IND-ready; Pre-clinical	Initiate Phase I trials 2015
OncoMed	OMED	Dec-13	Demicizumab; 6 anti-CSC Products	Solid tumors, NSCLC, Pancreatic	Phase I/II	**Tumors:** Phase I/II antibody data 2016
PharmAkea	-	Oct-13	Small-molecule Discovery	Cancer, Fibrotic disease	Pre-clinical	Equity (private)
Adimab	-	Aug-13	Antibody Discovery	Undisclosed	Pre-clinical	IND filings 2016+
Acetylon	-	Jul-13	Ricolinostat; ACY-738	Cancer; Hematology	Phase I/II	**Ricolinostat:** data 2H:15 **ACY738:** IND 2016+
Array Biopharma	ARRY	Jul-13	-	Inflammation	Pre-clinical	IND filings 2016+
Tengion	TNGN	Jul-13	Neo-Kidney Augment Program	CKD	Phase I	Phase I terminated 4Q:14
Concert Pharma	CNCE	May-13	CTP-730	Inflammation	Phase I	Completed May-June 2015
FORMA therapeutics	-	Apr-13	-	Protein Homeostasis	Pre-clinical	IND filings 2016+
BlueBird Bio	BLUE	Jun-15 Mar-13	CAR-T Cell BCMA	Hematology	Pre-clinical	**bb2121:** Initiate Phase I early 2016
Presage Biosciences	-	Mar-13	Drug-Discovery Platform	Solid tumors	Pre-clinical	IND filings 2016+
VentiRx	-	Oct-12	VTX-2337	Solid tumors	Phase I/II	Phase II data H2:16
InhibRx	-	Jun-12	Antibody Discovery	Undisclosed	Pre-clinical	Phase I data Q4:17
AnaptysBio	-	Apr-12	Antibody Discovery	Cancer, Inflammation	Pre-clinical	IND filings with clinical read-outs 2016-2017
Quanticel Pharmaceuticals	-	Nov-11	-	Cancer	Pre-clinical	IND filing early 2016
Agios	AGIO	Dec '13; Oct -11; Apr-10	AG-221, AG-120	IDH2/1 Mutant Cancers	Phase I	Solid tumor data at AACR-NCI-EORTC in Nov 5-9
GlobeImmune	GBIM	May-09	GI-6301, GI-6207, GI-4000	Oncology	Phase I/II/IIb	Initiate MTC Phase II trial in 2H:16
Acceleron	XLRN	Feb-08	Sotatercept, Luspatercept	Beta-Thalassemia, MDS, CKD	Phase II	Initiate Phase III trials in β-thalassemia and MDS in 2H:15

*(Phase I for Myeloma)

Source: Company reports

Exhibit 45: Table of Revlimid's US patent portfolio. The polymorph patent '800 is the most important in CELG's litigation vs. generic manufacturer NatCo (Actavis/Allergan) as it provides the longest protection out to 2027.

Type	Patent #	Patent Expiration	In Suit?	Description	Patent Title	Orange Book	Drug Sub	Drug Prod
Composition of Matter	6,281,230	7/24/2016	Y	R/S configuration	Isoindolines, method of use, and pharmaceutical compositions	Y		
	6,555,554	7/24/2016	Y	R/S configuration	Isoindolines, method of use, and pharmaceutical compositions	Y		Y
	7,119,106	7/24/2016	Y		Pharmaceutical compositions of 1-oxo-2-(2,6-dioxopiperidin-3-yl)-4-aminoisoindoline	Y		Y
	8,288,415	7/24/2016	Y	Unit dosage form	Pharmaceutical compositions of 3-(4-amino-1-oxoisoindolin-2yl)-piperidine-2,6-dione	Y	Y	Y
	5,635,517	10/4/2019	Y	Farthest COM patent	Method of reducing TNF.alpha. levels with amino substituted 2-(2,6-dioxopiperidin-3-yl)-1-oxo- and 1,3-dioxoisoindolines	Y	Y	Y
Method (Distribution)	6,045,501	8/28/2018	Y		Methods for delivering a drug to a patient while preventing the exposure of a foetus or other contraindicated individual to the drug	Y		
	6,561,976	8/28/2018	Y		Methods for delivering a drug to a patient while preventing the exposure of a foetus or other contraindicated individual to the drug	Y		
	6,908,432	8/28/2018			Methods for delivering a drug to a patient while preventing the exposure of a foetus or other contraindicated individual to the drug	Y		
	8,204,763	8/28/2018			Methods for delivering a drug to a patient while preventing the exposure of a foetus or other contraindicated individual to the drug	Y		
	8,589,188	8/28/2018			Methods for delivering a drug to a patient while preventing the exposure of a foetus or other contraindicated individual to the drug	Y		
	6,315,720	10/23/2020	Y		Methods for delivering a drug to a patient while avoiding the occurrence of an adverse side effect known or suspected of being caused by the drug	Y		
	6,561,977	10/23/2020	Y		Methods for delivering a drug to a patient while restricting access to the drug by patients for whom the drug may be contraindicated	Y		
	6,755,784	10/23/2020	Y		Methods for delivering a drug to a patient while restricting access to the drug by patients for whom the drug may be contraindicated	Y		
	8,315,886	10/23/2020	Y		Methods for delivering a drug to a patient while restricting access to the drug by patients for whom the drug may be contraindicated	Y		
	8,626,531	10/23/2020			Methods for delivering a drug to a patient while restricting access to the drug by patients for whom the drug may be contraindicated	Y		
Method (Treatment)	7,189,740	4/11/2023	Y		synergistic mixture of amino-1,3-dihydroisoindol-2-yl)piperidin-2,6-dione compound as immunomoderator and another active drug	Y		
	8,404,717	4/11/2023	Y		Methods of treating myelodysplastic syndromes using lenalidomide	Y		
	8,530,498	5/15/2023			Methods for treating multiple myeloma with 3-(4-amino-1-oxo-1,3-dihydroisoindol-2-yl)piperidine-2,6-dione	Y		
	8,648,095	5/15/2023			Methods for treating multiple myeloma using 3-(4-amino-1-oxo-1,3-dihydroisoindol-2-yl)-piperidine-2,6-dione in combination with proteasome inhibitor	Y		
	7,468,363	10/7/2023			Methods for treating multiple myeloma using 3-(4-amino-1-oxo-1,3-dihydroisoindol-2-yl)-piperidine-2,6-dione in combination with proteasome inhibitor	Y		
	7,968,569	10/7/2023	Y		Anticancer agents; angiogenesis inhibitor; side effect reduction	Y		
Polymorph	8,431,598	9/3/2024	Y	"Form A" anhydrous	Polymorphic forms of 3-(4-amino-1-oxo-1,3 dihydro-isoindol-2-yl)-piperidine-2,6-dione	N		
	8,193,219	9/3/2024	Y	"Form A" anhydrous	Polymorphic forms of 3-(4-amino-1-oxo-1,3 dihydro-isoindol-2-yl)-piperidine-2,6-dione	N		
	7,855,217	11/24/2024	Y		Polymorphic forms of 3-(4-amino-1-oxo-1,3 dihydro-isoindol-2-yl)-piperidine-2,6-dione	Y	Y	Y
	7,977,357	1/8/2025	Y	"Form A" anhydrous	Polymorphic forms of 3-(4-amino-1-oxo-1, 3 dihydro-isoindo1-2-yl)-piperidine-2,6-dione	N		
	7,465,800	April 27, 2027	Y	"Form B" hemihydrate	Polymorphic forms of 3-(4-amino-1-oxo-1,3 dihydro-isoindol-2-yl)-piperidine-2,6-dione	Y	Y	Y

Source: Celgene 2013 10-K, FDA Orange Book

Exhibit 46: Overview of select IBD drugs under development

Company	Partner?	Name	Disease	Trial	Timeline	MOA
CELG		Ged0301	Crohn's	Phase 3	initiating in H2:15	oral antisense DNA oligo targeting Smad7 mRNA
			UC	Phase 2	initiating in H2:15	
		Ozanimod (RPC1063)	UC	Phase 3	initiated in July '15; prim completion listed ~Sept '18	oral S1P 1 and 5 receptor modulator
			Crohn's	Phase 2	initiate in Sept '15	
		Otezla	UC	Phase 2	prim completion listed ~Feb '17	small molecule inhibitor of PDE4
PFE		tofacitinib	UC	Phase 3	multiple OCTAVE studies completing 2015-2016	oral JAK1 and JAK3 inhibitor
GLPG	GILD	filgotinib (GLPG0634)	Crohn's	Phase 2	topline 20-wk data in Q1:16	oral JAK1 inhibitor
		GLPG1205	UC	Phase 2a	topline data in Q1:16, enrollment completed	oral GPR84 inhibitor
GILD		GS-5745	UC	Phase 2/3	prim completion listed ~Feb '18	MMP9 mAb inhibitor
			Crohn's	Phase 2	prim completion listed ~Dec '16	
ARNA		APD334	UC	Phase 2	initiated July '15; prim completion ~ Nov '16	oral S1P1 modulator
BIIB	MTPC	MT-1303	Crohn's	Phase 2	initiated March '15; prim completion ~ Aug '16	oral S1P modulator
			UC	Phase 1	completed in July '14 for IBD; BIIB to initiate next study	
Qu Biologics		QBECO	UC	Phase 2	Initiated Phase 2 in July 2015; timeline TBD	Site specific immunomodulators
			Crohn's	Phase 2	Data in H1:16	
AZN		AMG 139	Crohn's	Phase 2	study ongoing; AMGN suspended co-dev w AZN in April	monoclonal antibody against IL-23
	AMGN	AMG 181	Crohn's	Phase 2	study ongoing; final primary data collected	monoclonal antibody against alpha4/beta7
			UC	Phase 2	study ongoing; primary completion ~Oct 2017	
BMY		BMS-936557 (MDX-1100)	Crohn's	Phase 2	completed in June '14	anti-IP-10 antibody
			UC	Phase 1	completed in Dec '12	
Lycera	CELG	LYC-30937	UC	Phase 1	initiated in May '15; potential data YE:15	oral ATPase modulator

Source: Company reports, RBC Capital Markets estimates

Exhibit 47: Our Crohn's APP yields base case $1B+ for GED-0301

GED0301 in Crohn's Disease INTERACTIVE MODEL—> You can change the assumptions in blue in the Box here.

Price of therapy in US ($/month)	$3,500
Price Growth	3%
Gross to net	12%
Price of therapy in EU ($/month)	$2,100
Price Growth	1%
Gross to net	15%
Prob. of Pivotal Trial Start	75%
Prob of Regulatory Approval	70%
Prob. of Getting to Market	53%

		Prob. Adjusted	$/share
Peak Revenue Estimate (US; $M)	$1,207	$634	**$1.7**
Peak Revenue Estimate (EU; $M)	$349	$183	**$0.5**
Total Peak Revenue Estimate ($M)	$1,557	$817	**$2.2**

	2014	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E
Total REVENUE - USA ($M)	$ -	$ -	$ -	$ -	$ 101	$ 288	$ 476	$ 734	$ 954	$ 1,072	$ 1,116	$ 1,160	$ 1,207
Total REVENUE - ROW ($M)	$ -	$ -	$ -	$ -	$ -	$ 23	$ 98	$ 158	$ 239	$ 305	$ 336	$ 342	$ 349
TOTAL WW REVENUE ($M)	**$ -**	**$ -**	**$ -**	**$ -**	**$ 101**	**$ 311**	**$ 574**	**$ 892**	**$ 1,193**	**$ 1,377**	**$ 1,451**	**$ 1,503**	**$ 1,557**
Prob. Adjusted Revenue Estimates													
Total REVENUE - USA ($M)	$ -	$ -	$ -	$ -	$ 53	$ 151	$ 250	$ 385	$ 501	$ 563	$ 586	$ 609	$ 634
Total REVENUE - ROW ($M)	$ -	$ -	$ -	$ -	$ -	$ 12	$ 51	$ 83	$ 125	$ 160	$ 176	$ 180	$ 183
TOTAL WW REVENUE ($M)	**$ -**	**$ -**	**$ -**	**$ -**	**$ 53**	**$ 163**	**$ 301**	**$ 468**	**$ 627**	**$ 723**	**$ 762**	**$ 789**	**$ 817**

US Market		2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026
Moderate-to-Severe (Pre-Biologic)														
Crohn's Disease Prevalence	565,000													
% Moderate-to-severe	50%													
% Treated	60%													
Growth Rate	1.0%													
# Eligible Patients		169,500	171,195	172,907	174,636	176,382	178,146	179,928	181,727	183,544	185,380	187,233	189,106	190,997
GED0301 Market Share (%)		0%	0%	0%	0%	1%	3%	5%	8%	10%	10%	10%	10%	10%
Duration of therapy (in months)		0	0	0	0	4	9	9	9	9	9	9	9	9
# Pts treated on GED-0301		0	0	0	0	5,650	5,344	8,996	14,538	18,354	18,538	18,723	18,911	19,100
Post-Biologic														
% Mod-to-Severe on anti-TNF	30%													
# Treated with anti-TNF	50,850													
# Eligible Patients		50,850	51,359	51,872	52,391	52,915	53,444	53,978	54,518	55,063	55,614	56,170	56,732	57,299
GED0301 Market Share (%)		0%	0%	0%	0%	5%	10%	15%	20%	25%	30%	30%	30%	30%
Duration of therapy (in months)		0	0	0	0	4	8	8	8	8	8	8	8	8
# Pts treated on GED-0301		0	0	0	0	2,543	5,344	8,097	10,904	13,766	16,684	16,851	17,020	17,190

Source: RBC Capital Markets estimates

Exhibit 48: The competitive landscape for Crohn's disease

Company	Drug	Type	Trial	Study design	Time	Arm	N	Remission*	vs. Pbo	Response**	vs. Pbo
Abbvie (ABBV)	Humira	subQ, TNF-alpha blocker	CD-I	treatment-naïve	Week 4	Humira	76	36%	24%	58%	24%
						placebo	74	12%		34%	
			CD-II	Remicade refractory	Week 4	Humira	129	21%	14%	52%	18%
						placebo	166	7%		34%	
			CD-III	open label long term study	Week 4	Humira	854			58%	
				"maintenance of response" after 4 wks	Week 26	Humira	172	40%	23%	54%	26%
						placebo	170	17%		28%	
				"maintenance of response" after 4 wks	Week 56	Humira	172	36%	24%	43%	25%
						placebo	170	12%		18%	
Janssen (JNJ)	Remicade	IV, TNF-alpha blocker		single-dose; prior failures	Week 4	Remicade	108	48%	44%	81%	65%
						placebo	108	4%		16%	
			ACCENT I	multidose; prior failures	Week 2	Remicade	545			57%	
				"maintenance of response" after 2 wks (5 mg/kg)	Week 30	Remicade	104	39%	14%		
				"maintenance of response" after 2 wks (10 mg/kg)		Remicade	105	46%	21%		
						placebo	102	25%			
Biogen (BIIB)	Tysabri	IV, itegrin receptor antagonist	CD 1	moderate to severe Crohn's	Week 10	Tysabri	717			56%	7%
						placebo	179			49%	
			CD 2	elevated serum CRP	wks 8+12	Tysabri	259	26%	10%	48%	16%
						placebo	250	16%		32%	
			CD 3	"maintenance of response" from CD1 after 12 wks	Month 9	Tysabri	>128	45%	19%	61%	32%
						placebo	>118	26%		29%	
				"maintenance of response" from CD1 after 12 wks	Month 15	Tysabri	>128	40%	25%	54%	34%
						placebo	>118	15%		20%	
UCB	Cimzia	subQ, TNF-alpha blocker	CD1	randomized, placebo-controlled	Week 6	Cimzia	331	22%	5%	35%	8%
						placebo	328	17%		27%	
				randomized, placebo-controlled	Week 26	Cimzia	331	29%	11%	37%	10%
						placebo	328	18%		27%	
			CD2	"maintenance of response" after 6 wks	Week 26	Cimzia	215	48%	19%	63%	27%
						placebo	210	29%		36%	
Millennium (TKPYY)	Entyvio	IV, integrin receptor antagonist	CD 1	moderate to severe Crohn's	Week 6	Entyvio	220	15%	8%		
						placebo	148	7%			
			CD 2	76% had prior failures, intolerance to TNF blockers	Week 6	Entyvio	158	15%	3%		
						placebo	157	12%			
			CD 3	"maintenance of response" from CD1 or open-label after 6 wks	Week 52	Entyvio	154	39%	17%	44%	14%
						placebo	153	22%		30%	
				"maintenance of response" (6 wks) subgroup that discontinued	Week 52	Entyvio	82	32%	16%		
						placebo	82	16%			
Celgene (CELG)	GED-0301	oral oligo, antisense to Smad7	Phase I	open-label, prior failures	Week 1	GED-0301	15	80%		100%	
					Week 4			86%		100%	
					Week 12			60%			
			Phase II	randomized, placebo-controlled	Week 4	GED-0301 10mg	166	12%	3%	37%	20%
						GED-0301 40mg		55%	46%	58%	41%
						GED-0301 160mg		65%	56%	72%	55%
						placebo		10%		17%	
					Week 12	GED-0301 10mg		29%	8%		
						GED-0301 40mg		63%	41%		
						GED-0301 160mg		67%	46%		
						placebo		21%			
Galapagos (GLPG)	filgotinib (GLPG0634)	oral JAK1 inhibitor	Phase II (FITZROY)	double-blind, randomized, placebo-controlled	Week 10	'0634 200mg	180	48%	25%	60%	19%
						'0634 100mg + placebo					
						placebo		23%		41%	
					Week 20	'0634 200mg					
						'0634 100mg + placebo					
						placebo					

**Clinical remission defined by CDAI < 150*

***Clinical response defined by decrease in baseline CDAI ≥70 pts (except for Cimzia, Entyvio 'week 52', GED-0301 and filgotinib, which were decrease ≥ 100 pts)*

Source: Company reports, RBC Capital Markets estimates

Exhibit 49: Current drugs for Crohn's disease come with many safety warnings, underscoring the need for more treatment options

Drug	Boxed warning	Warnings and Precautions		
HUMIRA	Infections and malignancy	serious infections (TB) lymphoma, blood problems nervous system problems (MS)	HBV reactivation heart failure liver problems	allergic reactions immune reactions (lupus-like) psoriasis
REMICADE	Tuberculosis, bacterial sepsis, histoplasmosis; lymphoma, fatal HSTCL and other malignancies	hematologic events hypersensitivity CNS demyelinating disorders (MS)	HBV reactivation lupus-like syndrome infections	acute liver failure/jaundice/ cholestasis
TYSABRI	Progressive multifocal leukoencephalopathy	significant liver injury allergic reactions gastroenteritis	pneumonia vaginal infection tooth and other infections	encephalitis and meningitis serious urinary tract infection
CIMZIA	Serious infections (TB) and malignancy (lymphoma)	invasive fungal infections HBV reactivation demyelinating disease	heart failure anaphylaxis lupus-like syndrome	cyotpenias, pancytopenia upper repiratory, urinary tract infections
Entyvio		infusion-related reactions progresssive multifocal leukoencephalopathy (PML)	hypersensitivity	infections liver injury

Source: Company reports, RBC Capital Markets

Exhibit 50: The competitive landscape for Ulcerative Colitis

Company	Drug	Trial	Study design	Study Type	Time	Arm	N	Remission*	vs. Pbo	Response**	vs. Pbo
Abbvie (ABBV)	Humira	UC-I	Randomized, double-blind, placebo-controlled	Induction	Week 8	Humira (160/80mg)	130	19%	9%	42%	8%
						placebo	130	9%		35%	
				Sustained	Weeks 8, 52	Humira (160/80mg)	130	N/A	N/A	N/A	N/A
						placebo	130	N/A		N/A	
		UC-II	Randomized, double-blind, placebo-controlled	Induction	Week 8	Humira (160/80mg)	248	17%	7%	50%	15%
						placebo	246	9%		35%	
				Sustained	Weeks 8, 52	Humira (160/80mg)	248	9%	4%	24%	12%
						placebo	246	4%		12%	
Janssen (JNJ)	Remicade	UC-I	Randomized, double-blind, placebo-controlled	Induction	Week 8	Remicade (5mg/kg)	121	39%	24%	69%	32%
						Remicade (10mg/kg)	122	32%	17%	62%	25%
						placebo	121	15%		37%	
					Week 30	Remicade (5mg/kg)	121	34%	18%	52%	22%
						Remicade (10mg/kg)	122	37%	21%	51%	21%
						placebo	121	16%		30%	
					Week 54	Remicade (5mg/kg)	121	35%	18%	45%	25%
						Remicade (10mg/kg)	122	34%	17%	44%	24%
						placebo	121	17%		20%	
				Sustained	Weeks 8, 30	Remicade (5mg/kg)	121	23%	15%	49%	26%
						Remicade (10mg/kg)	122	26%	18%	46%	23%
						placebo	121	8%		23%	
					Weeks 8, 30, 54	Remicade (5mg/kg)	121	20%	13%	39%	25%
						Remicade (10mg/kg)	122	20%	13%	37%	23%
						placebo	121	7%		14%	
		UC-II	Randomized, double-blind, placebo-controlled	Induction	Week 8	Remicade (5mg/kg)	121	34%	28%	65%	36%
						Remicade (10mg/kg)	120	28%	22%	69%	40%
						placebo	123	6%		29%	
					Week 30	Remicade (5mg/kg)	121	26%	15%	47%	21%
						Remicade (10mg/kg)	120	36%	25%	60%	34%
						placebo	123	11%		26%	
					Week 54	Remicade (5mg/kg)	121	N/A	N/A	N/A	N/A
						Remicade (10mg/kg)	120	N/A	N/A	N/A	N/A
						placebo	123	N/A		N/A	
				Sustained	Weeks 8, 30	Remicade (5mg/kg)	121	15%	13%	41%	26%
						Remicade (10mg/kg)	120	23%	21%	53%	38%
						placebo	123	2%		15%	
					Weeks 8, 30, 54	Remicade (5mg/kg)	121	N/A	N/A	N/A	N/A
						Remicade (10mg/kg)	120	N/A	N/A	N/A	N/A
						placebo	123	N/A		N/A	
Janssen (JNJ)	Simponi	UC-1	Randomized, double-blind, placebo-controlled	Induction	Week 6	Simponi (200/100mg)	253	18%	11%	51%	21%
						placebo	251	6%		30%	
		UC-2	Randomized, double-blind, placebo-controlled	Sustained	Week 54	Simponi (100mg)	154	28%	12%	50%	19%
						placebo	151	16%		31%	
Takeda (TKPYY)	Entyvio	UC Trial 1	Randomized, double-blind	Induction	Week 6	Entyvio	225	17%	12%	47%	21%
						placebo	149	5%		26%	
		UC Trial 2	Randomized, double-blind; patients in clinical response at Week 6	Sustained	Week 52	Entyvio	122	42%	26%	N/A	N/A
						placebo	126	16%		N/A	
					Weeks 6, 52	Entyvio	122	21%	12%	57%	33%
						placebo	126	9%		24%	
Celgene (CELG)	Ozanimod (RPC1063)	Phase II	randomized, double-blind, placebo-controlled	Induction	Week 8	RPC1063 1mg	67	16%	10%	57%	20%
						RPC1063 0.5mg	65	14%	8%	54%	17%
						placebo	65	6%		37%	
				Sustained	Week 32	RPC1063 1mg	67	21%	15%	51%	31%
						RPC1063 0.5mg	65	26%	20%	35%	15%
						placebo	65	6%		20%	
		Phase III	Randomized, double-blind, placebo-controlled	Induction	Week 10	RPC1063 1mg	900				
						placebo					
				Sustained	Week 52	'RPC1063 1mg					
						placebo					
Galapagos (GLPG)	GLPG1205	Phase II	Randomized, double-blind, placebo-controlled	Induction	Week 8	GLPG1205 100mg	64				
						placebo					

** Defined as Mayo score ≤ 2 with no individual subscores > 1.*

*** Defined as a decrease from baseline in the Mayo score of ≥30% and ≥3 points, accompanied by a decrease in the rectal bleeding subscore of ≥1 or a rectal bleeding subscore of 0 or 1.*

Source: Company reports, RBC Capital Markets estimates

Exhibit 51: Timelines for ongoing Revlimid IP litigation has been pushed out, but settlement could still come next year

Timelines			
	Post 10/13/15 conf call	Post 8/15/15 conf call	Post 6/29/15 meeting
Responsive Expert Reports	-	22-Sep-15	14-Aug-15
Reply Expert Reports	06-Nov-15	09-Oct-15	16-Sep-15
Close of Expert Discovery	15-Jan-16	20-Nov-15	20-Nov-15

Source: USPTO and RBC Capital Markets

Key questions and debates for CELG

1. What is our "5x5" thesis for CELG that supports our longer-term positive outlook?

Our "5x5" longer-term, positive investment thesis on Celgene is based on 5 key drivers we see over the next 5 years: 1) successful transition to a more diversified story beyond Revlimid with new product launches (Pomalyst, Otezla) and a deep pipeline of ~28 partnered assets, including RCPT, JUNO CAR-T, AZN PD-1 and more; 2) Revlimid's increasing duration of therapy could be under-estimated in long-term models, esp post AMGN ASPIRE data, ABBV Elo myeloma data and new RVd triple data at ASH; 3) evolving capital allocation/earnings growth with continued buybacks ($2.8B repurchased YTD), 4) 2020 guidance over $13/share, which implies $200 over time with a historical 15-20x multiple, 5) potential Revlimid IP settlement with Actavis, removing a key overhang.

2. What are some positive drivers for CELG in 2016-2017?

While there isn't one specific catalyst to point to on the horizon, we do think there are a number of positive drivers in 2016-17 that could continue to strengthen the long-term fundamental growth story:

- GED-0301 Phase III data could finally be positive in 2017 – this is a $1-2B franchise that Street had turned more lukewarm on since CELG hasn't disclosed any endoscopy data.
- Select early/mid stage pipeline programs that would be upside and could see read-outs: Pivotal Phase III **Revlimid DLBCL** study w/ maintenance Revlimid (REMARC). (data in H2:16 and could be filed to FDA and EMA), which represents a $1B+ potential with four more various NHL etc studies also coming; **AGIO**'s third IDH drug now starting Phase I could work in solid tumors (first solid tumor data possible by YE:16); **BLUE** partnered BCMA CAR-T for myeloma - IND filed and Phase I starting now (we could see data in 2016); **OMED**'s pancreatic antibody on top of Abraxane in Phase I/II; **VentiRX** immunotherapy Phase II ovarian cancer data YE:16 (CELG has option to acquire); PD-L1 durvalumab from **AZN** $1B+ opportunity now starting Phase I/II studies as mono/combo with Revlimid.
- Abraxane should actually get stronger over the long-term due to "chemo-combo" I/O regimens that have moved to Phase III (Roche atezolizumab + abraxane) in front line lung cancer – updated Phase II data at ASCO could further build the bull case that this is one of the best front-line regimens in lung cancer.
- CELG's own PD-1 combos (using AZN PD-L1) with Revlimid/Pom all show great data from ASH and this is a $1B franchise that isn't in the long-term CELG models. This is one of the $1B franchises growing beyond 2020
- A Revlimid IP settlement with AGN in 2016 with a base case generic launch farther out than 2025 (or with economics on anything earlier)

3. Could a settlement be reached in the Revlimid patent litigation versus Actavis/AGN (Natco)?

Bears argue that no settlement is likely anytime soon given expert discovery has been pushed out and doesn't finish until mid-January, the AGN generics sale closes in Q1 and timing is too close/tight, and AGN is in the process of merging with PFE now. So a settlement is unlikely to be a priority at this time with AGN. However, CELG is "far enough along" in the expert discovery process that it's theoretically possible a settlement could occur and recent delays are apparently more "administrative" in nature; if court proceedings begins in the summer, then a settlement could occur before then.

Exhibit 52: Income statement for CELG

Fiscal Year Ends December	1QA Mar-14	2QA Jun-14	3QA Sep-14	4QA Dec-14	FYE 2014	1QA Mar-15	2QA Jun-15	3QA Sep-15	4QE Dec-15	FYE 2015	1QA Mar-16	2QA Jun-16	3QE Sep-16	4QE Dec-16	FYE 2016	FYE 2017
REVENUES:																
Revlimid	1144	1214	1300	1323	4980	1343	1444	1454	1610	5850	1650	1680	1700	1717	6747	7680
U.S.	642	716	760	798	2916	811	873	895	930	3509	960	980	990	1005	3935	4407
ROW	502	498	540	525	2064	532	571	558	680	2342	690	700	710	712	2812	3273
Thalomid	58	54	52	57	221	47	48	45	46	186	38	38	37	37	150	128
Vidaza	148	152	158	154	612	144	152	148	154	597	143	148	152	157	600	614
Abraxane	185	215	212	236	848	223	244	230	265	963	260	320	340	355	1275	1518
Istodax	16	17	16	17	66	17	18	17	19	70	19	19	19	20	76	82
Pomalyst	136	161	181	202	680	199	235	257	285	975	275	305	333	360	1273	1570
Otezla	0	5	18	48	70	60	90	139	165	454	185	205	230	255	875	1488
Others	21	27	21	19	87	23	24	24	20	91	20	20	20	20	80	60
Total product sales	1708	1845	1957	2055	7564	2055	2254	2313	2564	9185	2590	2735	2831	2921	11076	13139
Collaborative agreements and other revenue	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Royalty Revenue	23	28	25	31	107	26	24	22	22	93	24	24	25	25	98	100
Total Revenue	**1730**	**1873**	**1982**	**2086**	**7670**	**2081**	**2278**	**2334**	**2586**	**9278**	**2614**	**2759**	**2856**	**2946**	**11174**	**13239**
EXPENSES:																
Cost of Sales	80	93	91	96	360	97	93	101	123	415	133	157	164	175	628	810
Research and Development	358	397	419	478	1651	431	477	488	545	1940	525	575	595	624	2319	2431
Sales, General & Administrative	418	440	441	479	1778	463	541	474	540	2018	555	580	585	599	2319	2562
Total Expenses	856	930	951	1052	3789	991	1110	1063	1208	4373	1213	1311	1343	1398	5265	5803
Income from operations (EBIT)	**875**	**943**	**1031**	**1033**	**3881**	**1089**	**1167**	**1271**	**1377**	**4905**	**1400**	**1448**	**1513**	**1548**	**5909**	**7436**
Total Other Income	-30	-52	-69	-41	-192	-32	55	-100	-110	-186	-105	-90	-135	-135	-465	-510
Pre-tax income	845	890	962	993	3690	1058	1222	1172	1267	4719	1295	1358	1378	1413	5444	6926
Taxes	140	143	156	152	591	167	204	160	209	740	214	224	227	233	898	1143
Net Income	**705**	**748**	**806**	**840**	**3099**	**891**	**1019**	**1011**	**1058**	**3979**	**1082**	**1134**	**1151**	**1180**	**4546**	**5783**
EPS Basic - Non-GAAP	$ 0.87	$ 0.94	$ 1.01	$ 1.05	$ 3.86	$ 1.12	$ 1.28	$ 1.28	$ 1.34	$ 5.02	$ 1.38	$ 1.46	$ 1.49	$ 1.54	$ 5.87	$ 7.50
EPS Diluted - Non-GAAP	**$ 0.83**	**$ 0.90**	**$ 0.97**	**$ 1.01**	**$ 3.71**	**$ 1.07**	**$ 1.23**	**$ 1.23**	**$ 1.29**	**$ 4.82**	**$ 1.33**	**$ 1.40**	**$ 1.43**	**$ 1.48**	**$ 5.65**	**$ 7.22**
Shares Outstanding - Basic	811	800	800	800	803	799	793	791	788	793	781	777	772	768	775	771
Shares Outstanding - Diluted	845	831	833	835	836	834	825	824	820	826	811	807	802	798	805	801

Source: Company reports and RBC Capital Markets estimates

Valuation

Our base case of $150/share is derived through our DCF on a robust pipeline. We expect double-digit growth in the base business for the next five to eight years (Revlimid, Pomalyst, Abraxane, Apremilast) as well as 95% probability that Revlimid polymorph holds until 2026. We also believe CELG's partnered assets (AG-221/AG-120 for leukemia, GED-0301 for Crohn's etc) are under-appreciated assets that are likely to help maintain CELG's healthy growth into 2020+. Our base case is also supported by applying a 25x multiple to our 2016E EPS. With CELG's above peer group EPS CAGR of 20%+ we believe this premium multiple is warranted.

Price target impediments

Our price target is significantly dependent on the clinical, regulatory, and commercial success of Revlimid, Pomalyst, Abraxane, and Otezla in both the US and Europe. Impediments to our current price target include: 1) regulatory delays or setbacks; 2) slower-than-expected commercial growth; and 3) competition from Velcade, Kyprolis and other competitor pipeline candidates. These issues would increase the discount rate for our future projections and potentially make our estimates unachievable.

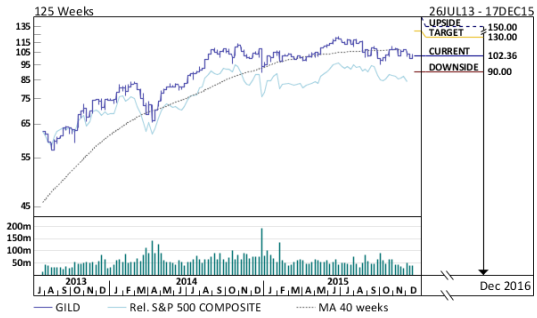
Gilead (GILD)

Outperform

Price Target USD $130.00

Target/Upside/Downside Scenarios

Exhibit 53: Gilead Sciences, Inc.



Source: RBC Capital Markets estimates

Target price/base case

Our base case of $130/share is derived from applying a 12x multiple to forward 2016E EPS. We believe this multiple is reasonable as it is in-line with comparable low-growth large-cap pharma and also reflects the lack of visibility on the long-term trajectory of its HCV franchise as well as pipeline opportunities such as simtuzumab antibody for fibrosis-related diseases (idiopathic pulmonary fibrosis (IPF), nonalcoholic steatohepatitis (NASH)).

Upside scenario

Our upside scenario of $150 is based on applying a 14x multiple on our forward 2016E EPS. We believe this scenario is possible if its HCV franchise continues to beat expectations in the next 12 months, mitigating any concerns on its long-term sustainability due to reimbursement, competition and market size. Pipeline success such as simtuzumab data next year would also contribute to this scenario. Then investors will be more likely to apply a 14x PE multiple, bringing it more on par with its peer group, which have better perceived long-term growth prospects.

Downside scenario

Our downside scenario of $90 is based on applying a lower 8x multiple on our forward 2016E EPS. This is usually the very low end of peer multiples for companies where long-term growth prospects are uncertain. We think this may result if GILD's HCV franchise fails to impress and its competitiveness decreases due to evolving competition and reimbursement pressure.

Investment summary

We believe the stock will continue to trend higher over the next 6-12 months, albeit more modestly (+15-20%) than in the past years post the VRUS acquisition in 2011. The stock is fairly inexpensive at around P/E of 9-11x 2015E EPS and we believe there is still a general upside bias to estimates due to margins and ex-US sales. Continued aggressive stock buyback will likely provide support for the stock, while the stock dividend could attract new investors. However, for the stock to see meaningful upside from P/E expansion, we would likely need another major acquisition or pipeline development. At the same time, we don't see a large acquisition anytime soon but instead expect tuck-in and earlier stage deals focused in oncology.

Potential catalysts for the stock

HCV upside levers ex-US: We think ex-US HCV sales could ramp up higher than consensus for GILD.

Positive pipeline development: GILD has several assets under development for lung fibrosis, NASH, and portal hypertension. Positive data readouts from these other candidates would provide investor confidence on diversification and sustainability in long-term revenues.

Risks to our investment thesis

- **Volatility and pressure on the HCV franchise:** Key debate will likely remain focused on GILD's HCV franchise (Harvoni and Sovaldi) given it accounts for ~ 50% of the company's top line and even more on the bottom line. With uncertainty on payor dynamics and competition (MRK, ABBV), the stock may remain volatile until more clarity is available or sales continue to beat estimates.
- **Lack of positive pipeline development and diversification to product mix:** Commercial products for GILD are concentrated in HIV and HCV, whose long-term sustainability remains debatable from patent expirations and the evolving competitive landscape. GILD has yet to show where its next leg of growth lies, although it has said that it is committed to oncology. Simtuzumab has high investor interest for its potential in NASH, but it remains early and high risk.

2016 Thoughts for GILD

We believe the stock may be a bit range-bound through the first part of 2016 but could rally by mid-year or into H2:16 as the Street gets more comfort with durability of Hep C in USA, stronger Hep C sales OUS, and a pipeline catalyst in simtuzumab later in YE:16 that could be 5-10%+ upside if data looks good.

Overall, we think the stock is in fact a bit defensive and attractive, particularly to value-based investors or those who don't want high expectation stocks or high-risk/high reward pipeline issues to deal with. We think GILD is cheap, has very low expectations, and the P/E already prices in and assumes a lot of negative sentiment towards the core business and pipeline.

There are three key positive "pillars" to our thesis:

1. **Hep C business more durable and OUS is a major source of longer-term revenue opportunity**
   a. Consensus is modeling only +6% Y/Y for OUS sales in 2016 yet Harvoni hasn't even come on in most countries and Japan is a $1-2B long term opportunity and hasn't even ramped yet. We think OUS could be $1-2B higher than expectations in 2016-17.
   b. In USA, 50% of scripts written are for healthier F0-2 patients and only 20-25% on average get reimbursed. Thus, there is significantly more demand (nearly 25-40% more) than what reported revenues are showing in USA. These pts will come back in due time and thus create a longer tail.
2. **2016 Pipeline optionality on simtuzumab and MMP-9 antibodies and NASH drug**
   a. Phase II/III cirrhotic study in portal hypertension pts – key data readout YE:16 - $1-2B+ opportunity and read-through to other indications.
   b. Phase IIB IPF lung fibrosis study – data YE:16.
   c. Other NASH indications ongoing in combination with ASK-1 oral pill.
   d. MMP-9 antibody also in multiple Phase II studies across cancer and immunology – data throughout 2016.
   e. Phenex acquisition led to Phase I oral FXR agonist now in Phase I for NASH with some data possible in YE:16 – identical drug as ICPT but possibly without pruritus and cholesterol increases.
3. **M&A or deal making optionality given strongest balance sheet in biotech**
   a. While they have significant capacity to do deals, we think they are likely to be more patient and do smaller early/mid stage deals rather than a large transformational deal.
   b. We think GILD is most likely to take a longer-term approach and continue to look at Phase I/II companies where GILD can add value over the longer term (e.g., VRTX is already commercial and launched around the world and doesn't really add any pipeline).
   c. These deals would give GILD call options over the longer term.
   d. We don't believe GILD will make a large transformational deal in 2016 (eg >$15-20B price) and that the few companies that could fit this bill are unlikely (VRTX, INCY, BMRN, REGN, etc).
   e. We think the recent GLPG Jak deal was an incremental positive but not a major development as this is a competitive area and it also suggests to us some uncertainty about what GILD really wants to do and what they want to be as they haven't really done anything in cancer and their BTK inhibitor is still in Phase I despite others like Acerta moving well into Phase III.

To be clear, we do think that, near-term, there is ongoing investor nervousness about upcoming Merck Hep C approval around Jan 28th and the subsequent pricing (rebates), managed care contracting, and market share this drug will get in the following months and quarters. There is also some short-term worry about 2016 guidance and how confident the company can be given script trends and a new competitor coming in 2016.

Bear case

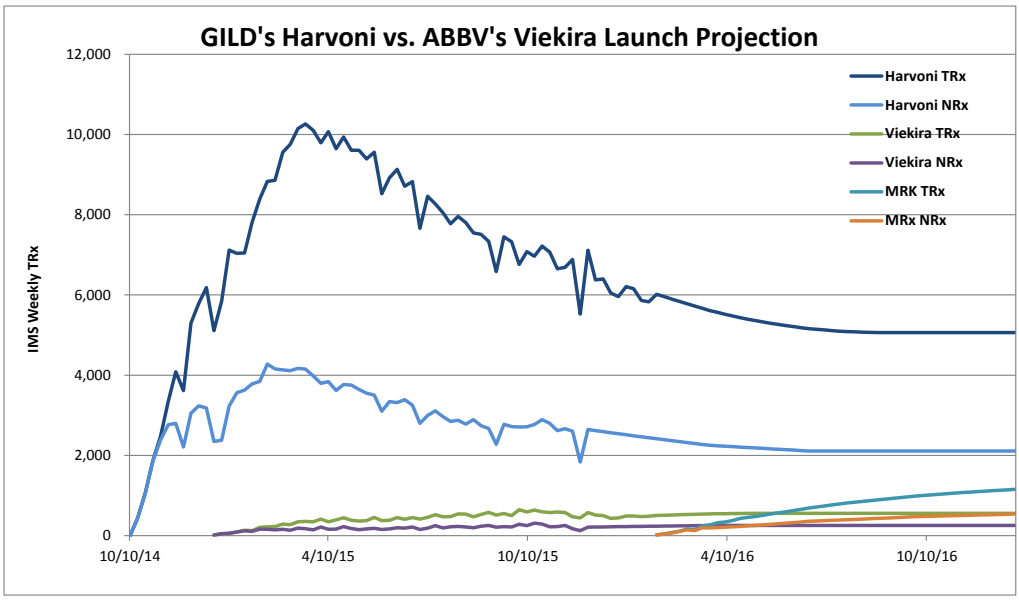
- 2016 USA Hep C consensus sales too high by up to $1B or more. Q4 looks to be $200-400M shy of consensus on US sales ($2.4B vs cons $2.8B) which, if true, would make the 2016 USA run-rate around $10.0B – yet 2016 USA consensus is $10.3B. Flat could be too high, particularly if the market is static and Merck is coming in and taking 5-10% share and price falls by 5-10%. This would imply USA sales could fall 10-20% in theory or $1-2B Y/Y – and make EPS $1 too high.
- Merck is going to be aggressive with price and marketing and has a history of this in Hep C with Peg-Intron (vs Roche's Pegasys) and Victrelis (vs VRTX Incivek). In both cases, MRK was able to get 20%+ share with an arguably inferior product. And don't forget JNJ and ABBV are all still coming with new and improved regimens as well.
- GILD won't do any major acquisitions and investors are expecting a "deal" and when they don't do any big deal they will be disappointed and may sell the stock.
- Pipeline is very bare compared to its other large cap peers – there is limited visibility on simtuzumab and the pancreatic cancer data was quite negative and other indications are also very challenging.
- At $25-30B in revenues now with declining USA HCV scripts there is a significant challenge to grow the top line at this point. It will be very difficult for GILD to ever become a "growth" stock again.

Exhibit 54: Expected news flow for GILD

Timing	Expected News Flow	Program
HCV		
Feb 2016	US sNDA approval for decompenstated cirrhotics and post-transplant patients (PDUFA Feb '16)	Harvoni
Feb 2016	Label update for decompensated cirrhotics and post-transplant patients (PDUFA Feb '16)	Sofosbuvir / Harvoni
HIV		
Mar 1, 2016	Approval of R/F/TAF in the U.S. (used priority voucher for US NDA on July 1, 2015) (PDUFA Mar 1, 2016)	R/F/TAF
April 7, 2016	Approval of F/TAF in the U.S. (PDUFA Apr 7, 2016)	F/TAF
Q2:16	Approval of F/TAF in the EU	F/TAF
H1:16	Topline data from Phase I study in HIV cure	GS-9620
Q3:16	Approval of R/F/TAF in the EU	R/F/TAF
HBV		
Q4:15	Phase III readout of TAF vs Viread in Antigen-Negative and Antigen-Positive HBV	GS-7340 (TAF)
Q4:15	Initiate Phase II study in treatment naïve patients	GS-9620
Q1:16	Potential top-line data from Phase II study for HBV in virally supressed patients	GS-9620
Q1:16	Submit US NDA and EU MAA for TAF	GS-7340 (TAF)
Q3:16	Phase II topline data for treatment-naïve patients	GS-4774
NASH		
Q4:15	48-week interim analysis for futility by DSMB	Simtuzumab
Q4:16	Reach 96-week endpoint of Phase II study	Simtuzumab
Hematology / Oncology		
Q4:15	Complete enrollment in Phase III study vs best available treatment for myelofibrosis	Momelotinib
H2:16	Interim data from Phase III study for CLL frontline with bendamustine + rituximab	Idelalisib
Inflammation/ Respiratory		
H1:16	Topline data from IPF Phase 2 study	Simtuzumab
Q2:16	Complete enrollment in Phase II study for Crohn's disease	GS-5745
Q2:16	Initiate Phase II study in RA	GS-5745
H2:16	Complete enrollment in Phase II/III study for ulcerative colitis	GS-5745
Q4:16	Topline data from RSV Phase II studies in adults with infection in upper or lower respiratory tracts	Presatovir (GS-5806)
Cardiovascular		
H1:16	Complete enrollment of Phase III study in LQT-3 Syndrome	Eleclazine (GS-6615)
H1:16	Potentially complete enrollment of Phase II study in HCM	Eleclazine (GS-6615)
H1:16	Complete enrollment of Phase II study in VT/VF	Eleclazine (GS-6615)
H2:16	Complete Phase II study in adults with PAH	GS-4997

Source: Company reports and RBC Capital Markets estimates

Exhibit 55: With MRK competition coming January '16, we conservatively model flattening/declining GILD scripts next year



2016 - Harvoni + Sovaldi (GILD)

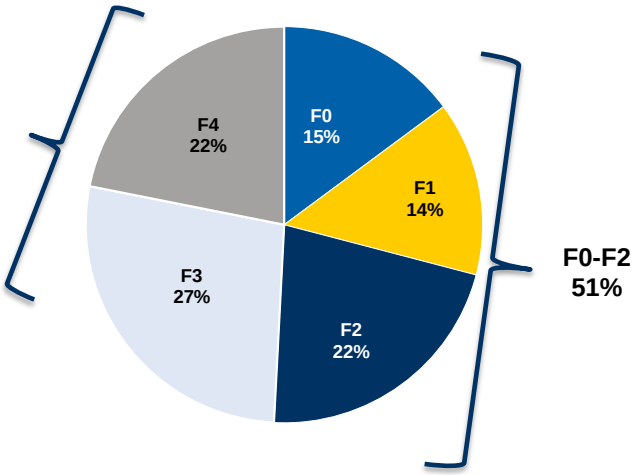
Harvoni Quarterly Estimate	Q1:16E	Q2:16E	Q3:16E	Q4:16E
Estimated 1-month Refill Rate	80%	80%	80%	80%
Ramp of Harvoni NRx vs. Sovaldi at launch				
NRx Weekly Growth	*-1%*	*-1%*	*0.0%*	*0.0%*
12-week Treatment Cost	$94,500	$94,500	$94,500	$94,500
Monthly Cost	$31,500	$31,500	$31,500	$31,500
Gross To Net	46%	46%	46%	46%
IMS Capture Rate	78%	78%	78%	78%
	22,451	22,212	22,074	19,866
TRx Sum	76,500	69,410	71,171	65,833
NRx Sum	31,119	28,273	29,540	27,430
Script Predicted Revs ($M)	$1,668	$1,514	$1,552	$1,436
VA sales	$100	$100	$100	$100
Inventory Build? ($M)	$50	$50	$0	$100
Harvoni Quarterly Sales ($M)	**$1,818**	**$1,664**	**$1,652**	**$1,636**
Sovaldi Quarterly Sales ($M)	$531	$525	$512	$500
GILD Total US HCV Sales ($M)	**$2,349**	**$2,189**	**$2,164**	**$2,135**

Total US GILD HCV Revs for 2016 ($B)	**$8.8**	**vs**	**Cons**	**$10.3**

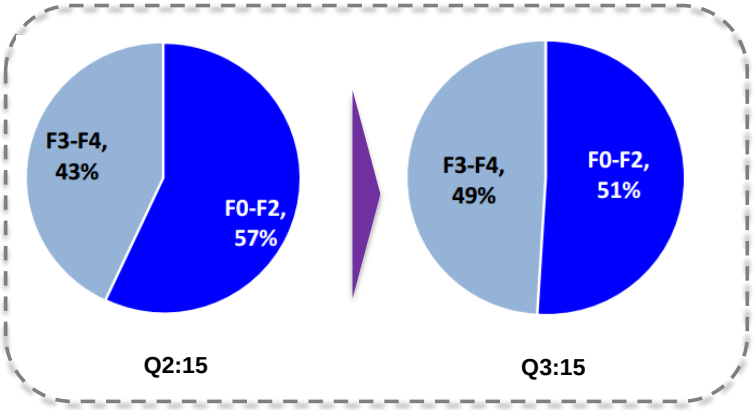
Source: IMS Health, RBC Capital Markets estimates

Exhibit 56: We surveyed 50 liver experts right before AASLD '15 – docs wrote as many scripts for F0-F2 as for F3-F4 patients

Q: In 2015, among your patients you wrote a script for, what was the breakdown of the patients by fibrosis stage?



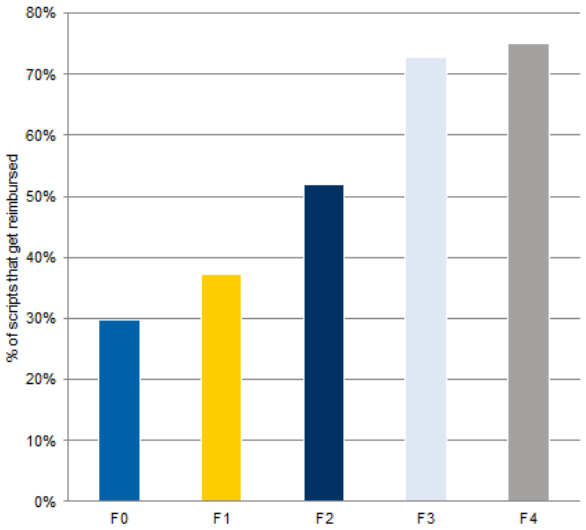
Data according to GILD



Source: RBC Capital Markets proprietary survey, company reports

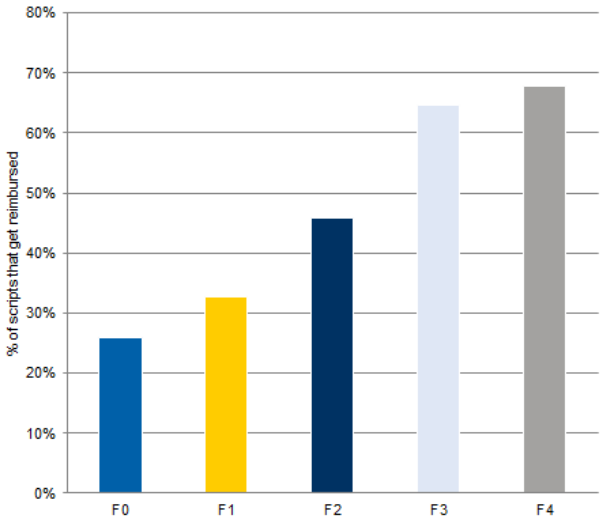
Exhibit 57: 70-75%+ of sick patients get reimbursed but only 10-30% of healthier patients are getting reimbursed - still a significant gating factor

Q: What percentage of Gilead Harvoni scripts written actually get reimbursed for the following type of patient?



Stage	Mean	Median
F0	30%	13%
F1	37%	25%
F2	52%	50%
F3	73%	80%
F4	75%	90%

Q: What percentage of ABBV Viekira Pak scripts written actually get reimbursed for the following types of patient?

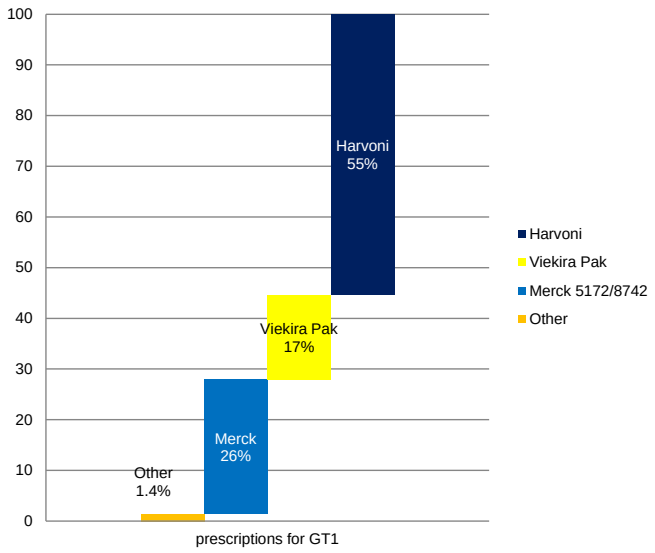


Stage	Mean	Median
F0	26%	8%
F1	33%	25%
F2	46%	50%
F3	65%	75%
F4	68%	80%

Source: RBC Capital Markets proprietary survey

Exhibit 58: Docs project ABBV's Viekira Pak will be used in up to 17% of GT1 HCV patients, and MRK's new drug could be used in 26% of GT1 HCV patients in 2016

Q: Assuming a scenario where Merck could get fairly similar coverage to Gilead Harvoni, what percentage of your GT1 patients in 2016 will get a script for the following drugs?

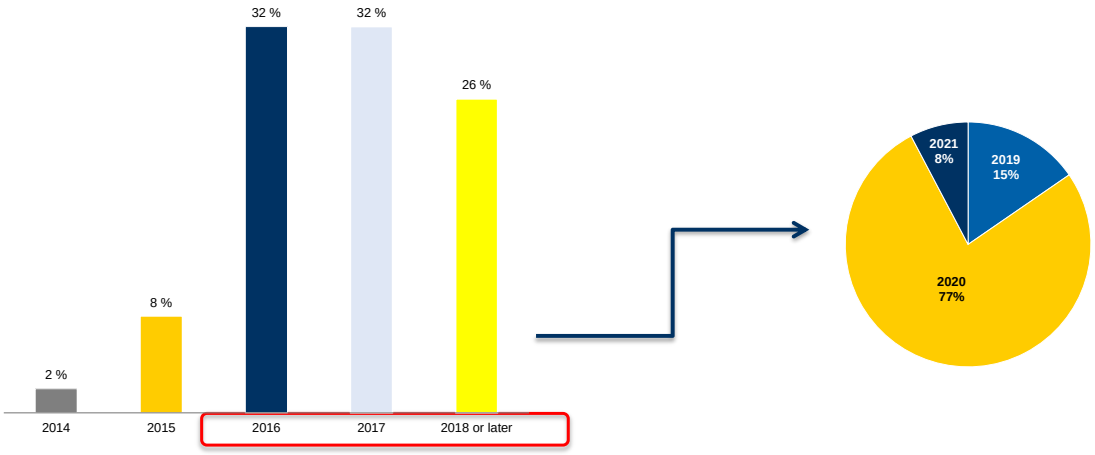


- Based on the survey, docs project approx. 50-60% of GT1 HCV pts will be prescribed a GILD regimen (Sovaldi/ Harvoni) vs. 20% on ABBV's Viekira Pak, and 26% would get the MRK regimen
- "Other" category: BMY's Daklinza and INF were listed under "other treatments"

Source: RBC Capital Markets proprietary survey

Exhibit 59: Surprisingly, docs seem to think the peak and tail in HCV volume is more sustainable than what the Street may believe

Q: When do you think the volume of HCV patients treated at your center will peak?



- Interestingly, 90% of docs think the volume in HCV treated patients in the US will peak in 2016 or later.
- In fact, an overwhelming majority of docs who selected "later" believe HCV volume won't peak until 2020
- We believe this is quite different from Wall Street consensus estimates, where investors worry about flattening IMS scripts and payor restrictions that may prevent the bathtub from "refilling"

Source: RBC Capital Markets proprietary survey

Key questions and debates for GILD

1. With flattening/declining Hep C scripts, how should we think about the stock?

We believe stock may be a bit range-bound through first part of 2016 due to Street concerns on MRK approval and market share over the first part of 2016. But it could rally a bit by mid-year or into H2:16 as (a)Street gets more comfort with durability of Hep C in USA, (b)stronger Hep C sales OUS, and (c)a pipeline catalyst in simtuzumab later YE:16 that could be 5-10%+ upside if data looks good; furthermore, MMP-9 antibody is also in multiple Phase II studies across cancer and immunology, with data throughout 2016. Overall, we think the stock is in fact a bit defensive and attractive particularly to value-based investors or those who don't want high expectation stocks or high-risk/high reward pipeline issues to deal with. We think GILD is cheap, has very low expectations, and the P/E already prices in and assumes a lot of negative sentiment towards the core business and pipeline.

2. Will GILD do a transformational deal next year?

While GILD has significant capacity to do deals, we think they are likely to be more patient and do smaller early/mid stage deals rather than a large transformational deal – rather, we think GILD would continue to look at Phase I/II companies where GILD can add value over the longer term in order to give GILD call options over the longer term. Thus, the few companies that would fit a large transformational deal next year (VRTX, INCY, BMRN, REGN, etc) seem unlikely to us.

We think the recent GLPG Jak deal was an incremental positive but not a major development as this is a competitive area and it also suggests to us some uncertainty about what GILD really wants to do and what they want to be as they haven't really done anything in cancer and their BTK inhibitor is still in Phase I despite others like Acerta moving well into Phase III. In addition, we do NOT see a large acquisition anytime soon due to a limited number of options and while some make sense on paper (we believe VRTX could be a very accretive candidate and build Boston presence, etc, and would be a big win for both VRTX and GILD investors) they are very unlikely to do a deal like that. We see tuck-in deals and Phase I/II deals focused in immunology and oncology (StemCentrx or others)

Exhibit 60: Income statement for GILD

($ in millions, except per share)	FYA	1QA	2QA	3QA	4QE	FYE	1QE	2QE	3QE	4QE	FYE	FYE
Fiscal Year Ends December	2014	Mar-15	Jun-15	Sep-15	Dec-15	2015	Mar-16	Jun-16	Sep-16	Dec-16	2016	2017
Sovaldi	10,283	972	1,291	1,466	1,305	5,034	1,230	1,195	1,160	1,125	4,710	4,100
Harvoni + Next gen HCV	2,127	3,579	3,608	3,332	2,850	13,369	2,900	3,000	3,075	3,150	12,125	11,350
Truvada (Emtriva/Viread)	3,339	771	849	903	880	3,403	690	750	710	680	2,830	2,745
Atripla (Emtriva/Viread/Sustiva)	3,470	734	782	818	815	3,149	700	740	700	700	2,840	2,755
Complera (TMC-278/Emtriva/Viread)	1,228	320	367	360	400	1,447	400	435	470	495	1,800	1,913
Stribild (QUAD)	1,198	356	447	511	580	1,894	560	600	630	660	2,450	2,930
Viread	1,058	234	271	297	316	1,118	240	275	270	273	1,058	915
Hepsera/ Other antiviral	81	22	16	15	12	65	10	9	9	8	35	28
Elvitegravir	-	-	-	-	-	-	-	-	-	-	-	-
Cobicistat	-	-	-	-	-	-	-	-	-	-	-	-
Total Antiviral Franchise	22,791	6,988	7,631	7,702	7,178	29,499	6,780	7,084	7,139	7,261	28,263	27,585
Zydelig (iNHL/CLL)	23	26	30	36	40	132	55	80	108	135	402	670
AmBisome (ex-US)	389	85	103	88	90	366	80	95	90	85	350	250
Letairis	595	151	176	181	160	668	150	145	140	135	570	500
Ranexa	510	117	141	161	140	559	130	125	125	120	500	450
Other	131	38	45	43	50	176	35	40	40	45	170	158
Total Product Sales	24,474	7,405	8,126	8,211	7,658	31,400	7,230	7,569	7,642	7,781	30,255	29,613
Royalties & contracts	395	189	118	84	100	491	100	100	100	100	400	300
Total Revenues	**24,890**	**7,594**	**8,244**	**8,295**	**7,758**	**31,891**	**7,330**	**7,669**	**7,742**	**7,881**	**30,655**	**29,913**
Total COGS	3,788	882	998	1,064	1,078	4,022	985	1,028	1,031	1,047	4,091	3,658
Research and development	2,854	696	818	743	853	3,110	733	844	890	946	3,413	3,350
Selling, general & administrative	2,983	645	812	903	931	3,291	733	882	890	946	3,451	3,290
Total Operating Expenses	**9,625**	**2,223**	**2,628**	2,710	2,862	10,423	2,451	2,753	2,812	2,938	10,954	10,299
Operating Income (Loss)	**15,265**	**5,371**	**5,616**	5,585	4,896	21,468	4,879	4,916	4,930	4,942	19,701	19,614
Total Other Income (Expense)	(408)	(132)	(105)	(113)	(129)	(479)	(213)	(213)	(213)	(213)	(853)	(803)
Pretax Income	**14,856**	**5,239**	**5,511**	5,472	4,767	20,989	4,666	4,703	4,717	4,730	18,847	18,811
Provision for taxes	2,797	907	1,014	880	858	3,659	859	865	868	870	3,468	3,574
Net Income	**12,101**	**4,333**	**4,492**	4,600	3,912	17,337	3,812	3,842	3,853	3,863	15,395	15,255
EPS - Basic (GAAP)	$7.95	$2.91	$3.05	$3.14	$2.68	$11.79	$2.60	$2.63	$2.65	$2.67	$10.57	$10.73
EPS - Diluted (GAAP)	$7.35	$2.76	$2.92	$3.06	$2.61	$11.35	$2.50	$2.53	$2.55	$2.56	$10.17	$9.93
EPS - Diluted (Non-GAAP)	**$8.09**	**$2.94**	**$3.15**	**$3.22**	**$2.80**	**$12.10**	**$2.69**	**$2.71**	**$2.73**	**$2.75**	**$10.89**	**$10.44**
Shares Outstanding - Basic (MM)	1,522.3	1,488.0	1,472.0	1,463.0	1,457.3	1,470.1	1,464.4	1,458.7	1,453.4	1,448.2	1,456.2	1,421.8
Shares Outstanding - Diluted (MM)	1,647.0	1,568.0	1,540.0	1,503.0	1,497.5	1,527.1	1,521.7	1,516.3	1,511.4	1,506.4	1,513.9	1,536.6

Detailed HCV Sales Summary	FYE	1QA	2QA	3QA	4QE	FYE	1QE	2QE	3QE	4QE	FYE	FYE
	2014	Mar-15	Jun-15	Sep-15	Dec-15	2015	Mar-16	Jun-16	Sep-16	Dec-16	2016	2017
Sovaldi												
US	8,507	421	615	692	568	2,296	530	520	510	500	2,060	1,800
RoW	1,776	551	676	774	737	2,738	700	675	650	625	2,650	2,300
Worldwide Sales	10,283	972	1,291	1,466	1,305	5,034	1,230	1,195	1,160	1,125	4,710	4,100
Harvoni												
US	2,001	3,016	2,826	2,541	1,850	10,233	1,700	1,700	1,675	1,650	6,725	6,600
RoW	126	563	782	791	1,000	3,136	1,200	1,300	1,400	1,500	5,400	4,750
Worldwide Sales	2,127	3,579	3,608	3,332	2,850	13,369	2,900	3,000	3,075	3,150	12,125	11,350
Total												
US	10,508	3,437	3,441	3,233	2,418	12,529	2,230	2,220	2,185	2,150	8,785	8,400
RoW	1,902	1,114	1,458	1,565	1,737	5,874	1,900	1,975	2,050	2,125	8,050	7,050
Worldwide Sales	12,410	4,551	4,899	4,798	4,155	18,403	4,130	4,195	4,235	4,275	16,835	15,450

Source: Company reports and RBC Capital Markets estimates

Valuation

Our base case of $130/share is derived from applying a 12x multiple to forward 2016E EPS. We believe this multiple is reasonable as it is in line with comparable low-growth large-cap pharma and also reflects the lack of visibility on long-term trajectory of its HCV franchise as well as pipeline opportunities such as simtuzumab antibody for fibrosis-related diseases (IPF, NASH).

Price target impediments

Risks to our price target and possible impediments include: 1) market factors such as competition and payor restrictions that lead to disappointing HCV sales; 2) greater than expected HIV revenue erosion post generic entrance in 2018; 3) material legal disputes that delay or increase cost of goods; and 4) inability of the oncology franchise to emerge as $2B+ material.

Additional Company profiles – (Yee)

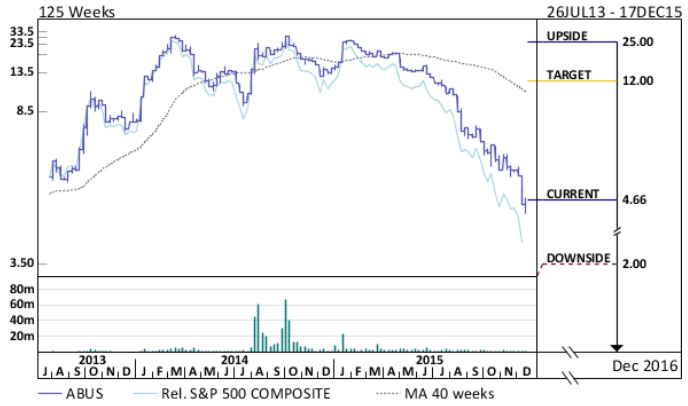
Arbutus Biopharma Corp. (ABUS)

Outperform, Speculative Risk

Price Target USD $12.00

Target/Upside/Downside Scenarios

Exhibit 61: : Arbutus Biopharma Corp.



Source: RBC Capital Markets estimates

Target price/base case

We are lowering our price target to $12 (from $20) based on lower probabilities of success and lower revenue opportunity for "conservatism". Our $12 PT is a SOTP analysis of probability-adjusted value of its pipeline candidates and royalty on partnered programs. 1) We assign 6% probability for its combined HBV pipeline to become a ~$4B+ global opportunity. 2) NPV from partnered programs and ALN-TTR02 yields about $1/share, using a 3–7x multiple of probability-adjusted peak royalties.

Upside scenario

Our upside scenario of $25/share (lowered from $47/share) is due to using lower probabilities of success and lower revenue opportunity for "conservatism". We assume $28/share for HBV pipeline based on a 13% probability of success, which could be justified on the presentation of pre-clinical data or early safety data from healthy patients. We account for valuations on royalties ($1/share) and other pipeline candidates ($1/share).

Downside scenario

Our downside scenario of $2/share (lowered from $5/share) is due to using lower probabilities of success for "conservatism". We assume less than $60M in value from RNAi platform and zero value from other programs in the pipeline.

Investment summary

We rate Arbutus Biopharma (formerly Tekmira Pharmaceuticals) as Outperform, Speculative Risk because of its long-term potential in Hepatitis B and numerous drug programs that could be combined to produce a functional cure over time. ABUS has several HBV program catalysts over the next 1–2 horizon, and we think potential positive data readouts could help to establish HBV as a field ripe for M&A, similar to how Hep C played out. We see at least another one to two years before multiple Hep B programs reach IND, Phase I and Phase II, and before ABUS begins combination therapies (expected 2017). We believe longer-term investors can get several HBV assets for cheap right now, as ABUS is particularly inexpensive with ~70% of the stock in cash.

Potential catalysts for the stock

TKM-HBV Phase II efficacy data in H2:16: Results will include data on HBsAg reduction in chronically infected HBV patients.

Several INDs expected in 2016: Over the next 12 months, ABUS will move multiple HBV programs including the clinic, including a cccDNA formation inhibitor, capsid assembly inhibitor, and a TLR9 agonist (CYT003).

Various combo studies: Various "combination" studies with TKM-HBV are expected to start in 2017.

The following are risks to our investment thesis

Failure of TKM-HBV to generate proof-of-concept data for successful RNAi knockdown of HBsAg: This would be a large setback because this is the mechanistic basis of its lead program as well as a demonstration of viability and applicability of its RNAi delivery-platform technology.

Failure to demonstrate causality link between reduction in HBsAg and immune de-repression: This is a central issue that determines whether TKM-HBV is a novel 'adjuvant' therapy to be used to lower HBsAg or a truly differentiated HBV therapy that could effect functional cures. While there is not yet consensus on this issue, empirical data support the hypothesis that reduction of HBsAg should help in the process of immune viral clearance. Evidence and proportion of TKM-HBV treated patients who achieve seroconversion directly affect our assigned probability of success of the program, which would affect our price target.

Emergence of serious safety signal that precludes continued development of TKM-HBV: Liver, renal, or other off-target toxicities, such as severe immunological reactions, could result in termination of this key program. Tissue delivery, stability of therapeutic, and control of off-target toxicities are common challenges for RNAi-based therapy.

Other oral competitors advancing: ASMB's trials in 2016-17, Novira's Phase II, and Spring Bank's immune modulator SB9200 Phase II starting)

2016 thoughts on ABUS

ABUS is attractive but will require at least a one- to two-year long-term view to see multiple Hep B programs through IND and Phase I and Phase II and at least in some forms of combination therapy, which may take into 2017. However, this is largely priced in and investors with a long-term timeframe can get numerous Hep B assets for cheap right now, as ABUS is particularly inexpensive with 70% of the stock in cash now. ABUS is differentiated from other Hep B players in that it has many different candidates in-house and these could be combined in different variations to target different parts of the virus and more completely come up with a functional cure.

Although still early (Phase I or earlier), ABUS has sufficient cash to run several concurrent trials in mono and combos over the next one to two years. We continue to believe if data looks good, this is a field ripe for M&A similar to how Hep C played out and we are watching JNJ start to get aggressive here and GILD and others are watching this area closely.

In an interesting HBV industry development, JNJ acquired privately-held Novira, a capsid inhibitor company that had completed early Phase I/II studies. While terms weren't announced, we estimate based on channel checks that it was $100M+ with one primary early-stage program. However, this acquisition was positive for ABUS as it helps validate the overall value proposition and makes ABUS inexpensive at a $100M EV itself with 6-7 programs. As a reminder, Novira's lead candidate, NVR 3-778, is a direct acting antiviral that inhibits HBV core protein (capsid) function, and the drug is planned for combo studies with nukes and IFN.

At JNJ's analyst event, they mentioned HBV was an area they remain interested in and was aligned with their acquisition of Alios for Hep C (JNJ said they had screening programs in Hep B ongoing). GILD has also identified HBV as an important field, having established an active screening program to find oral small molecules against cccDNA. If HBV combinations start to show promise, we could see a period of some more consolidation by 2017

We lowered our price target from $20 to $12 based on more conservative assumptions on TKM-HBV's probability of success and revenue opportunity. We are reducing TKM-HBV's probability of success to 6% on a $4B WW drug, down from $5B+ previously. In addition, this is more consistent with JNJ's acquisition of Novira (estimated to be $100-$200M) and its Phase II asset. At a $12 price target, that would imply $500M market cap for ABUS, which has TKM-HBV soon to be in Phase II and five other earlier-stage HBV candidates.

Bear case

- Hep B and ABUS are very early-stage and there aren't a lot of data catalysts right now; Lead is Phase I/II and other products are IND-prep.
- Lack of proof of concept in mono or in combos; No current efficacy data yet for lead product TKM-HBV.
- Hep B more difficult than Hep C and most investors don't understand or fully appreciate that; even with S-antigen knockdown it's not clear what level will lead to cures and what levels of other antigens and markers will lead to what level of cure.
- Other oral competitors advancing (e.g. ASMB's trials in 2016-17, Novira's (JNJ) Phase II, and Spring Bank's immune modulator SB9200 Phase II starting). ARWR recently reported a number of incrementally positive findings from their ongoing Phase II ARC-520.

Key questions and debates for ABUS

1. How is TKM-HBV differentiated from ARWR's ARC-520?

The two products are similar in that both are RNAi therapies aiming to knock down HBsAg potentially to lead to "functional cures" for chronic HBV. However, key differences exist between its delivery technology (ABUS's LNP versus ARWR's DPC) and payload (different siRNA combinations). ABUS also uses 3rd and 4th generation LNP technology and has potentially higher potency. ABUS is using less than 1mg/kg while ARWR was using up to 3-4mg/kg, implying that ABUS's drug uses 10x less drug to see equal results.

Until we see the data, we will not know whether these differences lead to a superior drug. Until then, what we know is that for ABUS, the payload will be a cocktail of two to three siRNAs for potent efficacy across genotypes and decreased risk of viral resistance. In terms of dosing, we expect the 3rd generation LNP formulation to enable infrequent (monthly) IV dosing without the need for immunosuppressive agents.

2. Hep B and ABUS are very early-stage and there aren't a lot of data catalysts right now

Although ABUS is still early, we believe investors will come back to this name in 2016-2017 as the company embarks on building out a rich portfolio of drugs over the next year. In addition, we believe if data looks good, this is a field ripe for M&A similar to how Hep C played out. JNJ acquired privately-held Novira, a capsid inhibitor company that had early Phase I studies. We view this acquisition as a positive for ABUS as it helps validate the overall value proposition and makes ABUS inexpensive with 6-7 programs.

3. How much are the royalties worth on its partnered programs?

ABUS' LNP technology has been tested and proven efficacious in multiple sites outside the liver. ABUS licensed its LNP technology for use in SPPI's Marqibo and three of ALNY's pipeline products. Marqibo was approved for treatment of Ph-ALL, and ABUS is entitled to an estimated 3% royalty on net sales. ALNY's ALN-TTR02 is in Phase III studies for TTR-FAP (data expected Q1:17), and we estimate 2-3% royalties here as well. Both products combined have peak sales estimates of $800M, which with 2-3% royalty yields an additional $2/share for TKMR.

Exhibit 62: ABUS's news flow

Time	Expected News Flow	Program
YE:15	Potential data for Phase IIa in GI-NET and ACC	TKM-PLK1
YE:15	Results from Phase IIa dose-escalation HCC expansion corhort	TKM-PLK1
YE:15	Begin multi-dosing Phase II in chronic infected HBV patients stable on nuc therapy	TKM-HBV (ARB-1467)
YE:15	Update from Phase II clincal efficacy trial of TKM-Ebola-Guinea (suspended)	TKM-Ebola
H1:16	Potential interim results of Phase II multi-dosing trial in HBV patients stable on nuc	TKM-HBV (ARB-1467)
H2:16	File IND (or equivalent) for cccDNA formation inhibitor	cccDNA formation inhibitor
H2:16	File IND (or equivalent) for capsid assembly inhibitor	capsid assembly inhibitor
H2:16	HBsAg reduction results from Phase II trial in chronic infected HBV patients stable on nuc	TKM-HBV (ARB-1467)
2016	Start clinical development of CYT003 (TLR9 agonist)	CYT003 (TLR9 agonist)
2016	File IND for a surface antigen secretion inhibitor	Antigen secretion inhibitor
2017	Include TLR9 agonist CYT003 in combination studies	CYT003 (TLR9 agonist)
2017	Include cccDNA formation inhibitor in combination studies	cccDNA formation inhibitor
2017	Start multiple combination studies in HBV	Various

Source: Company reports and RBC Capital Markets estimates

Exhibit 63: ABUS's pipeline

Drug (Target)	Indication	Stage	Est. Year to Market
Non-HBV Assets			
TKM-PLK1	GI-NET, ACC, HCC	Phase II	2017/2018+
TKM-Marburg	Marburg virus	Pre-clinical	2019+
TKM-ALDH2	Alcohol-use disorder	Pre-clinical	N/A
TKM-HTG	Rare forms of hypertriglyceridemia	Pre-clinical	N/A
TKM-GSD	Glycogen storage disorder type IV	Pre-clinical	N/A
HBV Assets			
TKM-HBV	Hepatitis B	Phase I	2019+
TKM-PLK1	Hepatitis B	Phase I	2019+
CYT003*	Hepatitis B	Pre-clinical	2019/2020+
cccDNA formation inhibitor	Hepatitis B	Pre-clinical	N/A
capsid assembly inhibitor	Hepatitis B	Pre-clinical	N/A
surface antigen secretion inhibitor	Hepatitis B	Pre-clinical	N/A
cccDNA epigenetic modifier	Hepatitis B	Pre-clinical	N/A
STING agonist	Hepatitis B	Pre-clinical	N/A
Partnered programs			
Marqibo (SPPI)	Adult relapsed Ph- ALL	Approved	N/A
ALN-TTR02 (ALNY)	TTR amyloidosis	Phase III	2017/2018
ALN-VSP (ALNY)	Liver cancer	Phase I	N/A
DCR-PH1 (Dicerna)	Primary Hyperoxaluria Type 1	Phase I	N/A
ALN-PCS (ALNY)	High cholesterol	Phase I	N/A

**has been tested in 400+ human subjects to date for non-HBV indication*

Source: Company reports and RBC Capital Markets estimates

Exhibit 64: ABUS's income statement

($ in millions, except per share) Fiscal Year Ends December	FYA 2011A	FYA 2012A	FYA 2013A	FYA 2014A	1QA Mar-15	2QA Jun-15	3QA Sep-15	4QE Dec-15	FYE 2015E	1QE Mar-16	2QE Jun-16	3QE Sep-16	4QE Dec-16	FYE 2016E	FYE 2017E
Revenues:															
Tekmira product sales	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Collaborations, contracts, milestones	16.3	12.1	10.4	12.1	4.7	3.4	4.1	4.7	16.9	5.7	5.2	5.4	5.7	22.0	28.6
Total Revenues, net	**16.8**	**14.1**	**15.5**	**15.0**	**4.7**	**3.4**	**4.1**	**4.7**	**16.9**	**5.7**	**5.2**	**5.4**	**5.7**	**22.0**	**28.6**
Costs and expenses:	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Cost of product sales	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Research and development	20.1	18.0	21.5	38.7	10.6	9.7	16.4	18.4	55.1	17.0	19.0	22.0	25.0	83.0	99.6
Selling, general and administrative	6.4	8.1	5.5	8.7	2.7	7.7	7.7	8.0	26.1	7.0	8.0	9.5	10.7	35.2	38.7
Depreciation	1.0	0.9	0.6	0.5	0.1	0.1	0.2	0.2	0.6	0.2	0.2	0.2	0.2	0.8	0.9
Total operating costs and expenses	27.5	27.0	27.6	48.0	22.7	17.8	62.3	26.6	129.4	24.2	27.2	31.7	35.9	119.0	139.2
Income (loss) from operations	**(10.7)**	**(12.9)**	**(12.2)**	**(33.0)**	**(18.0)**	**(14.4)**	**(58.2)**	**(21.9)**	**(112.5)**	**(18.5)**	**(22.0)**	**(26.3)**	**(30.2)**	**(97.0)**	**(110.6)**
Other income:	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Interest and other income	0.1	65.2	0.5	13.3	6.0	-	14.0	3.0	23.0	5.0	7.0	9.0	12.0	33.0	39.6
Interest and other expense	0.5	(22.6)	(2.5)	19.1	-	0.5	-	-	0.5	-	-	-	-	0.5	0.5
Total other expense	0.6	42.6	(1.9)	(5.8)	6.0	(0.5)	14.0	3.0	22.5	5.0	7.0	9.0	12.0	32.5	39.1
Provision for Income Tax	-	-	-	-	-	-	(15.2)	-	-	-	-	-	-	-	-
Net income attributable to ABUS	**(10.1)**	**29.6**	**(14.1)**	**(38.8)**	**(12.0)**	**(14.9)**	**(29.0)**	**(18.9)**	**(90.0)**	**(13.5)**	**(15.0)**	**(17.3)**	**(18.2)**	**(64.5)**	**(71.5)**
EPS (basic)	(0.89)	2.16	(0.92)	(1.80)	(0.44)	(0.27)	(0.57)	(0.38)	(1.98)	(0.28)	(0.31)	(0.37)	(0.40)	(1.36)	(1.57)
EPS (diluted)	(0.89)	2.07	(0.92)	(1.80)	(0.44)	(0.27)	(0.57)	(0.38)	(1.98)	(0.28)	(0.31)	(0.37)	(0.40)	(1.36)	(1.57)
Shares outstanding:	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Basic	11.3	13.7	15.3	21.6	27.0	54.3	50.9	49.9	45.5	48.9	47.9	46.9	46.0	47.4	45.5
Diluted	11.3	14.3	15.8	22.7	27.0	54.3	50.9	49.9	45.5	48.9	47.9	46.9	46.0	47.4	45.5

Source: Company reports and RBC Capital Markets estimates

Valuation

Our $12 price target is a SOTP analysis of the probability-adjusted value of its pipeline candidates and royalties on partnered programs. 1) We assign 6% probability for its combined HBV pipeline to become a ~$4B opportunity. 2) NPV on 3x-7x multiple of probability-adjusted peak royalties from partnered programs, Marqibo and ALN-TTR02 ($1/share). We removed pipeline programs such as Ebola due to discontinuation or our view of lack of likelihood of advancing to late stage.

Price target impediments

Failure of TKM-HBV to generate proof-of-concept data for successful RNAi knockdown of HBsAg: This would be a large setback because this is the mechanistic basis of its lead program as well as demonstration of viability and applicability of its RNAi delivery-platform technology.

Failure to demonstrate causality link between reduction in HBsAg and immune derepression: This is a central issue that determines whether TKM-HBV is a novel "adjuvant" therapy to be used to lower HBsAg or a truly differentiated HBV therapy that could effect functional cures. While there is not yet consensus on this issue, empirical data support the hypothesis that reduction of HBsAg should help in the process of immune viral clearance. Evidence and proportion of TKM-HBV treated patients who achieve seroconversion directly affects our assigned probability of success of the program, which would affect our price target.

Emergence of serious safety signal that precludes continued development of TKM-HBV: The development of liver, renal, or other off-target toxicities, such as severe immunological reactions, could result in termination of this key program. Tissue delivery, stability of therapeutic, and control of off-target toxicities are common challenges for RNAi-based therapy

Other oral competitors advancing: ASMB's trials in 2016-17, Novira's Phase II, and Spring Bank's immune modulator SB9200 Phase II starting.

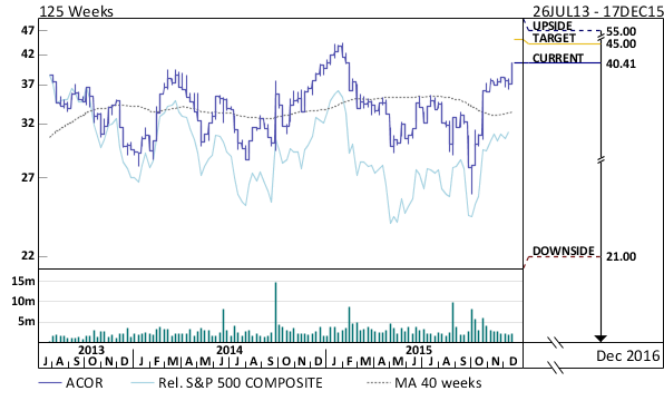
Acorda Therapeutics (ACOR)

Outperform, Speculative Risk

Price Target USD $45.00

Target/Upside/Downside Scenarios

Exhibit 65: Acorda Therapeutics Inc.



Source: RBC Capital Markets estimates

Target price/base case

Our target price of $45/share is supported by a DCF valuation for Ampyra alone in the US with IP extended to February 2026 (but using full expense structure), royalties on Ampyra sales ex-US, and optionality value in Ampyra in the post-stroke indications (20% probability on doubling of Ampyra franchise sales). We also account for the recently acquired CVT-301 for Parkinson's OFF episodes based on 35% probability of $500M peak sales discounted back.

Upside scenario

Our upside scenario of $55 assumes Amypra gets protection out to 2026-27 like the recent settlements and then wiping out SG&A and R&D from the Ampyra P&L, which gets to $40-45 on this MS indication alone. Including Civitas of around $10-15/ share and with net cash of around zero, this yields $55. All other pipeline could also present upside, including Ampyra stroke QD program and rHgM22 for re-myelination.

Downside scenario

Our downside scenario of $21 assumes stagnant US Ampyra sales growth, peaking at ~$400M in 2015 and patent exclusivity expiring at the end of 2018. We then include $10-15 for the Civitas programs and net zero cash.

Investment summary

We rate Acorda shares Outperform, Speculative Risk. We believe sentiment is turning as 2016 catalysts start to come into play. We see ACOR stock generally appreciating over time due to: 1) likely positive Phase III trials for new Civitas CVT-301 inhaled L-Dopa for Parkinson's disease, and 2) potential positive Phase IIb data for Ampyra in new post-stroke walking deficit disorder indication. Each of these could add $500M+ in potential sales – as much as $1B theoretical peak – and double the company's sales vs current ~$400M in sales for just Ampyra in multiple sclerosis alone today. In addition, there is also interesting potential for their Phase I re-myelinating antibody rHIgM22 data next year, which may get attention depending on how BIIB's own LINGO antibody looks in mid-16. We do not anticipate any issues arising from the remaining paragraph IV litigations. ACOR could be a potential takeout candidate for firms interested in neurology.

Potential catalysts for the stock

Potential upside from IP and takeout value: We think patents will go out to 2027 vs. consensus estimates of a generic entry in 2018-2020+. Upside from IP and takeout value could be as high as 50%.

Ampyra stroke data in 2016: ACOR has three prototypes for QD formulation, and will move all into Phase I (PK studies) by YE:15, with data in early '16. The Phase IIb interim data in post-stroke walking deficit is expected in 2016. ACOR will also initiate Phase III based on potential positive QD dosing data.

CVT-301 Phase III data YE:16: ACOR has reiterated several times that CVT-301 is their "highest priority" program. This program will take time to play out although it should be a positive de-risking catalyst.

Risks to our investment thesis

Ampyra generic challenge overhang: Although ACOR agreed to settle on 3 of up to 8 first-to-file paragraph IVs for a 2027 launch, there are at least 7 other generic filers left (8 filed in 2014 and 2 in 2015). Patent litigation may create an overhang on the stock given Ampyra is currently the sole commercial drug for ACOR and comprises more than 50% of its valuation.

CVT-301 Phase III data: The clinical, regulatory and commercial risks still need to play out. We estimate a 10-20% swing if Phase III data of CVT-301 (acquired by ACOR for $600M) does not read out positively.

Continued regulatory delay in diazepam nasal spray (Plumiaz): ACOR originally submitted a New Drug Application (NDA) for diazepam nasal spray in Nov 2013 on a 505(b)2 pathway but received a CRL from the FDA in May 2014. ACOR believes Plumiaz could reach $100M+ peak sales. However, if it continues to face regulatory delays, then it could be a dent to management's credibility and its confidence on the regulatory path for Ampyra for post-stroke and CVT-301.

2016 thoughts on ACOR

We think ACOR could continue to move higher in 2016 due to better visibility on the patent situation, new opportunities to expand the market into stroke deficits, and Phase III data for their second drug from Civitas for Parkinson's disease. Overall, in the longer term, ACOR could be at least 50%+ higher if: (1) patents hold until 2027; (2) Phase II post-stroke program starts panning out more positive from current low expectations today (there will be some Phase II interim data and QD-new formulation data by mid-year and this could double the sales opportunity over time); and (3) acquired Civitas Parkinsons' drug pans out; this program will take some time to play out although the data are expected by YE:16 and should be a positive de-risking catalyst.

Potential upside from IP and takeout value could be 50% higher. From the patent situation alone, they've settled on three of the up to eight first-to-file paragraph IV filings for a 2027 launch and this should further de-risk the patent situation creating significant value if the IP really goes out to 2027 (vs worst case scenario 2017-18). Adding nine years of patent extension literally doubles the value of the DCF versus the seven years they had of just "orphan protection". If we go to 2026 protection from 2017 and then wipe out expenses in a takeout scenario (presuming that's what would happen), then the DCF on Ampyra alone goes from $23 to around $40-45 on this MS indication alone. Bottom line is we do believe patents will go out towards 2027, whereas consensus and the stock is suggesting generic entry 2018-2020+.

In addition to potential IP upside and takeout opportunity, we look forward to several key catalysts in 2016: (1) Phase I QD dosing data (early '16, minimal downside but +5-7% if positive scenario), (2) CVT-301 Phase III Parkinson's data (YE:16, +/- 10-20% scenario), although this program will take some time to play out but should be a positive de-risking catalyst, and (3) interim on Ampyra Phase IIb post-stroke (2016, +/- 10% scenario given they still want to re-do this with once-daily, not twice-daily currently in use).

Bear case

- Although two IPR petitions from the Hayman group (Bass) have been dismissed, more IPR institution decisions are pending throughout Spring 2016.
- There were 10 total generic filers and 7 of them have not yet settled and continue to litigate. The filers included Actavis, Accord Healthcare, Alkem Laboratories Ltd., Apotex, Inc., Aurobindo Pharma Ltd., Mylan Pharmaceuticals, Inc., Roxane Laboratories, Inc., Teva Pharma, and Sun Pharma.
- Why did ACOR get Civitas if it was so competitive and such a great asset? The clinical, regulatory, and commercial risks still need to play out.
- There is unknown chronic toxicity safety with long-term dosing of L-dopa on the lungs via inhalation technology.
- Heart failure drug had serious toxicity at high doses and its therapeutic window is unknown.
- ACOR's pipeline and business development have disappointed historically.

Key questions / debates for ACOR

1. It seems likely that if the Phase III data are positive, CVT-301 should get approved easily. What are the risks that CVT-301 may not get approved?

Inhaled drugs delivered directly to the lungs, especially if it's an old drug, would need chronic toxicity studies, animal toxicity data and likely carcinogenicity studies. We do not know yet what happens if L-dopa is chronically inhaled. Also, the hurdle for getting an existing drug approved via a new route of administration can be tricky given there may be less urgency to approve the new drug when it is already available orally (i.e. risk/benefit) and the primary benefit is better route of administration. For example, MNKD's inhaled insulin had prior FDA delays and ALXA's vaporized loxapine (Adasuve) was delayed due to prior safety and pulmonary tox risks and FDA panel concerns. Both of these were older, already FDA-approved drugs. In addition, giving or administering an inhaled drug to a Parkinson's patient undergoing an "OFF" episode could be tricky.

2. Will management seek ex-US BD opportunities?

With debt capacity, ACOR could be looking at OUS deals, especially those with commercial infrastructure or spec pharma companies, now that global industry valuations have come down. However, we think this will come after CVT-301 data are available as we don't recommend any major deal until there is visibility on the Civitas data and post-stroke indication.

3. What is the recent status of the Paragraph IV filings, timing, and settlement situation?

ACOR has settled on three of the (possibly up to eight first-to-file sponsors) paragraph IV filings now, including Actavis, Sun and Aurobindo. We think more could come in 2016, helping to resolve the litigation and generic risk of up to 10 years. A Markman hearing is scheduled for March 7th, 2016 but ultimately we think more settlements will happen given that the ones to date have faced an uphill litigation battle and incurred substantial costs to pursue this litigation. The timing for additional settlements could go through 2016, as court would not begin until 2017.

Exhibit 66: Expected news flow for ACOR

Timing	Expected News Flow	Program
YE:15	Topline data from Phase Ib study in chronic heart failure	Cimaglermin alfa (GGF2)
March 2016	Markman hearing (US District Court in Delaware) for ANDA challenges to Ampyra	Legal
H1:16	Phase I PK data from healthy volunteers for migraine	CVT-427
H1:16	Phase I PK dose (three QD versions) data in humans	Ampyra (stroke)
Sept 2016	Trial date for ANDA challenges to Ampyra (US District Court in Delaware)	Legal
YE:16	Potential results from Phase III in Parkinson's Disease	CVT-301
YE:16	Initiate Phase III based on potential positive QD dose data	Ampyra (stroke)
2016	Potential Phase IIB interim look at post-stroke walking deficit	Ampyra (stroke)
2016	Potential results from Phase I trial in acute relapse MS	rHIgM22
Q1:17	Refiling of NDA of Plumiaz following three clinical trials	Plumiaz
H1:17	File NDA for Parkinson's Disease	CVT-301
July 2017	Expiration of 30-month stay on generic Ampyra (MS)	Legal

Source: Company reports and RBC Capital Markets estimates

Exhibit 67: ACOR's income statement

Fiscal Year (Ending in December) ($ figures in MM, except per share)	FY13	1Q14 Mar-14	2Q14 Jun-14	3Q14 Sep-14	4Q14 Dec-14	FY14	1Q15 Mar-15	2Q15 Jun-15	3Q15 Sep-15	4Q15E Dec-15	FY15E	1Q16E Mar-16	2Q16E Jun-16	3Q16E Sep-16	4Q16E Dec-16	FY16E	FY17E
REVENUES:																	
Ampyra (US Sales)	302.5	72.5	87.4	96.4	109.9	366.2	92.4	105.5	117.0	120.0	434.9	103.0	115.0	125.0	130.0	473.0	510.8
Fampyra (ex-US Royalties & Milestones)	9.3	2.4	2.8	2.5	2.3	10.0	2.3	2.5	2.5	2.5	9.8	2.5	2.5	2.5	2.5	10.0	10.0
Zanaflex (authorized generic Royalties)	11.2	1.4	2.3	2.7	2.7	9.1	1.8	1.4	2.1	2.0	7.3	2.1	2.2	2.3	2.4	9.0	9.0
Zanaflex	4.2	1.7	2.1	1.8	0.5	6.1	0.8	1.8	23.9	1.7	28.2	1.8	1.8	1.9	1.9	7.3	7.6
Qutenza (capsaicin 8% patch)	0.3	0.3	0.3	0.3	0.2	1.0	0.3	0.2	0.4	0.4	1.4	0.4	0.5	0.5	0.6	1.9	2.2
Plumiaz (diazepam nasal spray for epilepsy	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
License Revenue	9.1	2.3	2.3	2.3	2.3	9.1	2.3	2.3	2.3	2.3	9.1	2.3	2.3	2.3	2.3	9.2	9.2
Total Revenue	**$336.5**	**$80.5**	**$97.1**	**$106.0**	**$117.9**	**$401.5**	**$99.9**	**$113.7**	**$148.2**	**$128.9**	**$490.7**	**$112.1**	**$124.3**	**$134.5**	**$139.7**	**$510.4**	**$548.8**
EXPENSES:																	
Cost of Sales	66.0	15.5	18.9	20.6	25.0	80.0	18.4	22.7	24.7	25.2	91.1	21.6	24.2	26.3	27.3	99.3	107.3
Research and Development	53.9	14.5	16.4	16.6	25.9	73.5	30.6	31.2	43.4	48.0	153.2	50.0	52.0	54.0	56.0	212.0	243.8
SG&A	185.5	46.9	50.6	47.8	56.5	201.8	48.8	52.8	51.1	57.0	209.6	52.0	53.0	54.0	55.0	214.0	220.4
Change in fair value of acquired continge	-	-	-	-	2.2	-	3.1	1.1	3.2	3.2	10.6	3.2	3.2	3.2	3.2	12.8	12.0
Total Expenses	306.1	77.1	86.2	85.1	116.7	365.1	101.1	108.0	122.5	133.6	465.2	127.0	132.5	137.6	141.7	538.8	584.1
Income from operations (EBIT)	**30.4**	**3.4**	**11.0**	**20.8**	**1.2**	**36.4**	**(1.3)**	**5.7**	**25.7**	**(4.7)**	**25.5**	**(14.9)**	**(8.3)**	**(3.2)**	**(2.0)**	**(28.4)**	**(35.3)**
Total Other Income	(1.5)	0.1	(0.3)	(4.3)	(3.9)	(8.4)	(3.9)	(3.6)	(4.0)	(4.0)	(15.4)	(4.0)	(4.0)	(4.0)	(4.0)	(15.9)	(15.9)
Pre-tax income	28.9	3.5	10.7	16.5	(2.7)	28.0	(5.1)	2.1	21.7	(8.6)	10.1	(18.9)	(12.2)	(7.1)	(6.0)	(44.3)	(51.2)
Taxes	12.4	2.8	6.0	4.5	(3.0)	10.3	(2.0)	1.1	17.8	-	16.9	-	-	-	-	-	-
Net Income	**16.5**	**0.7**	**4.7**	**12.0**	**0.3**	**17.7**	**(3.1)**	**1.0**	**3.9**	**(8.6)**	**(6.8)**	**(18.9)**	**(12.2)**	**(7.1)**	**(6.0)**	**(44.3)**	**(51.2)**
EPS Basic	$0.41	**$0.02**	**$0.11**	**$0.29**	**$0.01**	$0.43	**($0.07)**	**$0.02**	**$0.09**	**($0.20)**	($0.16)	**($0.44)**	**($0.29)**	**($0.17)**	**($0.14)**	($1.04)	($1.19)
EPS Diluted*	**$0.40**	**$0.02**	**$0.11**	**$0.28**	**$0.01**	**$0.42**	**($0.07)**	**$0.02**	**$0.09**	**($0.20)**	**($0.16)**	**($0.44)**	**($0.29)**	**($0.16)**	**($0.14)**	**($1.01)**	**($1.16)**
Shares Outstanding - Basic	40.2	40.9	41.0	41.1	41.5	41.2	42.0	42.1	42.2	42.3	42.2	42.5	42.7	42.9	43.0	42.8	43.0
Shares Outstanding - Diluted	41.4	42.2	42.4	42.4	43.1	42.5	43.6	43.3	43.4	43.5	43.5	43.7	43.9	44.1	44.2	44.0	44.2

Ampyra Y/Y % Growth	FY13	1Q14	2Q14	3Q14	4Q14	FY14	1Q15	2Q15	3Q15	4Q15E	FY15E	1Q16E	2Q16E	3Q16E	4Q16E	FY16E	FY17E
US	14%	16%	12%	24%	30%	21%	27%	21%	21%	9%	19%	11%	9%	7%	8%	9%	8%

*Basic shares used to calculate diluted EPS when earnings are negative
Source: Company reports and RBC Capital Markets estimates

Valuation

Our target price of $45/share is supported by a DCF valuation for Ampyra alone in the US with IP extended to February 2026, royalties on Ampyra sales ex-US, and optionality value in Ampyra in the post-stroke indications (20% probability on doubling of Ampyra franchise sales). We also account for the recently acquired CVT-301 for Parkinson's OFF episodes based on 35% probability of $500M peak sales discounted back.

Price target impediments

Our price target is partially dependent on the commercialization success of Fampridine SR. Impediments to our current price target include: 1) commercial setbacks or regulatory delays in Europe; 2) unexpected new safety signals; and 3) slower-than-expected uptake in the market. These issues would increase the discount rate for our future projections and potentially make our estimates not achievable.

Ampyra generic challenge overhang: Although ACOR agreed to settle on three of up to eight first-to-file paragraph IVs for a 2027 launch, there are at least seven other generic filers left (eight filed in 2014 and two in 2015). Patent litigation may create an overhang on the stock given Ampyra is currently the sole commercial drug for ACOR and comprises more than 50% of its valuation.

CVT-301 Phase III data: The clinical, regulatory and commercial risks still need to play out. We estimate a 10-20% swing if Phase III data of CVT-301 (acquired by ACOR for $600M) does not read out positively.

Continued regulatory delay in diazepam nasal spray (Plumiaz): ACOR believes Plumiaz could reach $100M+ peak sales. However, if Plumiaz continues to face regulatory delays, then it could be a dent to management's credibility and its confidence on the regulatory path for Ampyra for post-stroke and CVT-301.

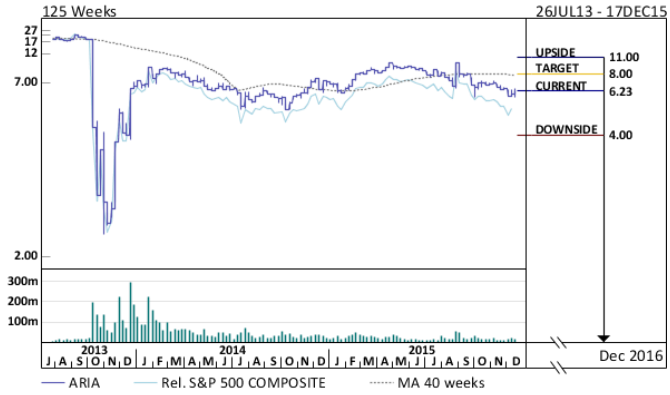
Ariad Pharmaceuticals (ARIA)

Sector Perform, Speculative Risk

Price Target USD $8.00

Target/Upside/Downside Scenarios

Exhibit 68: Ariad Pharmaceuticals.



Source: RBC Capital Markets estimates

Target price/base case

Our base case of $8/share values Iclusig assuming $350M sales in second/third-line and T315I patients, for whom Iclusig remains the only effective treatment for some chronic myelogenous leukemia (CML) patients. Separately, we value '113 (brigatinib) as a $150M anaplastic lymphoma kinase (ALK) lung cancer drug based on competitive Phase I/II data seen to date, although ALK is a more competitive therapeutic space. We do not assign valuation to ponatinib optionality in GIST or FGFR lung cancer.

Upside scenario

Our upside scenario of $11 values Iclusig as a $500M drug, assuming optimal commercial execution and the optionality of a takeout. We also include ponatinib's optionality in second line GIST (Phase II proof-of-concept data in H1:14), given the unmet need after patients fail Nexavar.

Downside scenario

Our downside scenario of $4 assumes Iclusig remains a niche $100M drug reserved for T315i patients.

Investment summary

We rate ARIA shares Sector Perform, Speculative Risk. A possible takeout scenario valuing ARIA as high as $12-$13 could make the stock a reasonable contrarian long due to 50-75% upside potential. Fundamentally, however, we think the stock is fairly valued for now because: (1) $1B+ enterprise value is already Iclusig's 3x peak sales out in 2018-19; (2) Iclusig theoretically needs to get to a $300M sales run-rate to "break-even" and needs to show clear trajectory in getting there, given ARIA's need to raise capital in ~2017; (3) new "dose ranging" study using lower doses will help inform safety/efficacy but going back to big dream of $1-2B "front line" opportunity is still far off; (4) quarterly net-new patient additions are not meaningfully surpassing expectations; (5) proof-of-concept in other indications (e.g. AP32788) is still fairly far off; and (6) we question the value of continuing to plow more capital into '113 as the third or fourth ALK drug in a modest-sized niche market, particularly given high cost of capital and high expense structure.

Potential catalysts for the stock

Potential M&A target: The company had already received at least one offer from BXLT for around $10/share (stock currently around $6). However, we think ARIA believes this offer undervalues the company. Comparable analyses (e.g. M&A in past two years) show ARIA could be acquired for $12-13/share.

Brigatinib Phase II data in June 2016: If the results from pivotal trial (ALTA) is positive at ASCO, ARIA could file an accelerated marketing approval in the following year.

CEO Berger's departure on December 31st: We think discussions on ARIA's strategic options could be further accelerated following the departure of the CEO. Founding CEO Berger has deep ties to the company and may be tied historically to the perception of fair value.

Strong uptick in Iclusig sales: Iclusig's re-launch in 2014 was rather tepid as it required regaining confidence from physicians and EU regulators who remained cautious. There were encouraging signs indicating broad use of Iclusig in earlier lines of treatment. EU PRAC recommendation was fairly liberal on the revised indication. If Iclusig sales show a reacceleration beyond the temporary effect from high cost of 30mg dose, it could prove to be a positive catalyst.

Risks to our investment thesis

Modest Iclusig sales growth: Sales have only met or missed most quarters since launch and visibility on $300-$400M in sales is not yet assured to justify prices over $13/share.

2016 thoughts on ARIA

Consistent with prior written notes, we think it is very reasonable that ARIA could be acquired in H1:16 for its FDA approved cancer drug Iclusig. The company had already received at least one offer from BXLT for around $10/share (stock currently around $6). However, we think ARIA believes this significantly undervalues the company.

Our analysis suggests ARIA could be acquired for $12-13/share (or $2.4B) as a reasonable fair value assuming nobody bids higher than that. By using comparable analysis such as M&A in the last two years (our M&A chart shows average of four to five peak sales), we assume a $500 drug and 4x sales translates to $2B or $10/ share. Adding in $350M in value for a Phase II/III brigatinib gives us another $2/share, which seems possible given $200M drug but visibility is less clear given two to three competitors and not impacting revenues until 2017. One could get an even higher valuation if they used a 5x multiple or a 2-3x multiple on brigatinib.

ARIA announced new CEO Paris Panayiotopoulos, who was President of EMD Serono and as expected, is someone put in place to try to turn things around and has apparent experience deriving value and operational efficiencies. We look forward to hearing more and meeting w/ new mgmt but expect ARIA to remain range-bound as short-term investors were hoping for a takeout and Street believes there are/were ongoing strategic decisions underway to consider selling the company (consistent w prior research notes). Investors will want to meet w/ him to determine what the plan is. At around $5, it starts to trade towards $1B market cap or 3x Iclusig peak sales and brigatinib is free. And longer-term patient investors could benefit from cost-cutting, increased dialog with new leadership, and what might be a patient Board that appeared to turn down $10 offers (we said might be worth $12-13). We think new leadership could re-invigorate strategic discussions in short-term, but reality is new CEO probably going to be in place with a 3-4 quarter timeframe to show evidence of turning things around and getting stock up so they can get higher takeout price towards our $12-13 value.

ARIA has said they are actively seeking partnership opportunities for brigatinib (lung cancer drug in Phase III) but actually we think they are seeking strategic options for the whole company (Iclusig + brigatinib combined). Clearly, if they do a partnership for brigatinib, it makes it far too unlikely the company would ever be acquired anytime soon as well given partnership talks would have included talking about the whole portfolio and partnering brigatinib removes half the economics for any future acquirer.

Thoughts on guidance

With the delay of pricing and reimbursement negotiations for Iclusig in France until next year, ARIA revised 2015 guidance down to $110-115M. We believe France negotiations might conclude mid-16, and estimate $32M cumulative value of shipments through Q3:16, as $9M of Iclusig were shipped in FY15 and total shipments to date total ~ $26M.

Bear case

- Who would take on a CEO role when the board (and Street) believes it is likely trying to sell the whole company?
- Spec pharma companies may not buy this because they'll want to cut all the expenses including R&D, and ARIA believes it's worth a lot more if you finish off the head-to-head second line studies in CML.
- Big biotech is unlikely to buy it as it basically only fits AMGN, GILD, CELG and those companies have moved on to more novel drugs.
- Gleevec is still going generic so this is still a major uncertainty over the next few years, followed by Sprycel and Tasigna, also going generic, before Iclusig gets to 2nd or 1st line.
- Iclusig continues to grow only modestly (have only met or missed most quarters since launch) and visibility on $300-400M in sales is not yet assured to justify prices over $13/share
- Brigatinib for ALK+ lung cancer faces existing competition from: (1) NVS, whose drug got approved and also hits brain mets and (2) Roche, whose drug, alecensa, received accelerated approval in December 2015 for NSCLC. Chugai and others are also going after ALK+.

Exhibit 69: Expected news flow for ARIA

Time	Expected News Flow	Program
YE:15	Otuska to file NDA in Japan for CML and Ph+ALL	Iclusig
YE:15	File IND for internally discovered oncology development candidate (oral active TKI inhibitor)	AP32788
Q1:16	Complete pricing/reimbursement negotiations for France	Iclusig
Apr 2016	Present preclinical data of AP32788 at AACR annual meeting in Louisiana	AP32788
Jun 2016	Results from pivotal Phase II trial (ALTA) in ALK+ Xalkori failures	Brigatinib
H1:16	Intitate Phase III trial of brigatinib and crizotinib in 300 pts with first-line NSCLC	Brigatinib
Q3:16	NDA filing for approval of brigatinib in the U.S.	Brigatinib
YE:16	Preliminary data of the Phase II (OPTIC) trial evaluating 3 doses in patients with refractory CP-CML	Iclusig
2016	Potential resumption of the SPIRIT 3 (UK, early second-line) switch study	Iclusig
2016	Initiate Phase I/II POC trial for AP32788 (oral active TKI inhibitor)	AP32788
2017	Potential accelerated marketing approval of Brigatinib (AP26113)	Brigatinib

Source: Company reports and RBC Capital Markets.

Source: Company reports and RBC Capital Markets estimates

Exhibit 70: Income statement for ARIA

($ in millions, except per share) Fiscal Year Ends December	FY12	FY13	1Q14 Mar-14	2Q14 Jun-14	3Q14 Sep-14	4Q14 Dec-14	FY14	1Q15 Mar-15	2Q15 Jun-15	3Q15 Sep-15	4Q15E Dec-15	FY15	1Q16E Mar-16	2Q16E Jun-16	3Q16E Sep-16	4Q16E Dec-16	FY16	FY17
Revenues:																		
Ponatinib	-	45.3	8.0	11.9	14.5	21.3	55.7	23.9	27.8	27.5	33.5	112.7	36.8	42.4	82.0	60.0	221.2	255.6
Ponatinib - US	-	41.3	4.7	7.9	10.5	17.0	40.1	18.7	21.6	20.3	25.0	85.6	27.0	31.0	36.0	42.0	136.0	183.6
Ponatinib - EU/ROW	-	4.0	3.3	4.0	4.0	4.3	15.6	5.2	6.2	7.2	8.5	27.1	9.8	11.4	46.0	18.0	85.2	72.0
AP26113	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
License and collaboration revenue	-	-	3.8	0.2	0.2	45.5	49.7	0.1	1.4	1.5	1.5	4.5	1.5	1.6	1.6	1.7	6.4	8.0
Service revenue	0.6	0.1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Total revenue	**0.6**	**45.5**	**11.8**	**12.1**	**14.7**	**66.8**	**105.4**	**24.0**	**29.2**	**29.1**	**35.0**	**117.3**	**38.3**	**44.0**	**83.6**	**61.7**	**227.6**	**263.6**
Operating expenses:																		
Cost of Goods	-	9.6	1.3	2.4	0.6	0.9	5.2	0.7	0.5	0.5	0.2	1.9	0.8	0.9	1.7	1.2	4.6	5.3
Research and development	144.7	162.9	28.6	31.8	27.6	32.6	120.6	39.4	38.7	48.2	53.0	179.4	55.0	57.0	60.0	59.0	231.0	254.1
Selling, general and administrative	60.9	146.6	31.6	34.2	33.6	40.4	139.8	33.6	48.6	36.7	48.0	166.9	38.0	52.0	43.0	46.0	179.0	196.9
Total operating expenses	205.6	319.1	61.4	68.4	61.8	74.0	265.6	73.7	87.8	85.4	101.2	348.2	104.4	104.4	104.4	104.4	417.6	456.3
Income from operations	(205.1)	(273.6)	(49.7)	(56.3)	(47.1)	(7.1)	(160.2)	(49.7)	(58.6)	(56.4)	(66.2)	(230.9)	(66.1)	(60.4)	(20.8)	(42.7)	(190.0)	(192.7)
Total other income (expense), net	(15.8)	(0.2)	(0.1)	(0.5)	(2.8)	1.6	(3.4)	(2.8)	(4.2)	(4.9)	(4.8)	(16.8)	(1.8)	(1.8)	(1.8)	(1.8)	(7.1)	(28.8)
Income before taxes	(220.9)	(273.8)	(49.7)	(56.8)	(50.0)	(5.5)	(163.6)	(52.5)	(62.9)	(61.3)	(71.1)	(247.7)	(67.9)	(62.2)	(22.6)	(44.5)	(197.1)	(221.5)
Provision for income taxes	-	0.3	0.1	0.1	0.2	0.3	0.6	0.2	0.3	5.8	0.4	6.8	0.2	0.2	0.3	0.3	1.0	1.0
Net Income	**(220.9)**	**(274.1)**	**(49.8)**	**(56.9)**	**(50.1)**	**(5.8)**	**(164.2)**	**(52.7)**	**(63.2)**	**(55.5)**	**(71.5)**	**(254.5)**	**(68.1)**	**(62.4)**	**(22.9)**	**(44.8)**	**(198.1)**	**(222.5)**
Basic EPS	**($1.34)**	**($1.49)**	**($0.27)**	**($0.30)**	**($0.27)**	**($0.03)**	**($0.88)**	**($0.28)**	**($0.33)**	**($0.29)**	**($0.38)**	**($1.35)**	**($0.36)**	**($0.33)**	**($0.12)**	**($0.23)**	**($1.04)**	**($1.06)**
Diluted EPS	($1.34)	($1.49)	($0.27)	($0.30)	($0.27)	($0.03)	($0.88)	($0.28)	($0.33)	($0.29)	($0.38)	($1.35)	($0.36)	($0.33)	($0.12)	($0.23)	($1.04)	($1.06)
Shares outstanding:																		
Basic	165.0	183.5	186.3	186.8	187.0	187.2	186.8	187.8	188.6	188.9	189.3	188.7	189.8	190.2	190.6	191.0	190.4	209.5
Diluted	172.2	190.7	196.8	197.3	197.5	213.2	199.2	187.8	188.6	188.9	189.3	188.7	189.8	190.2	190.6	191.0	190.4	209.5

Summary (WW Sales)	FY12	FY13	Mar-14	Jun-14	Sep-14	Dec-14	FY14	Mar-15	Jun-15	Sep-15	Dec-15	FY15	Mar-16	Jun-16	Sep-16	Dec-16	FY16	FY17
Ponatinib	-	45.3	8.0	11.9	14.5	21.3	$56	23.9	27.8	27.5	33.5	$113	36.8	42.4	82.0	60.0	$221	$256
AP-26113	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Source: Company reports and RBC Capital Markets estimates

Valuation

Our base case of $8/share values Iclusig via assuming $350M sales in second/third-line and T315I patients, for whom Iclusig remains the only effective treatment for some CML patients. Separately, we value '113 as a $150M ALK lung cancer drug based on competitive Phase I/II data seen to date, although ALK is a more competitive therapeutic space. We do not assign valuation to ponatinib optionality in GIST or FGFR lung cancer.

Price target impediments

Modest Iclusig sales growth: Iclusig's re-launch in 2014 was rather tepid as it required regaining confidence from physicians and EU regulators who remained cautious. Sales have only met or missed most quarters since launch and visibility on $300-$400M in sales is not yet assured to justify prices over $13/share.

Brigatinib for ALK+ lung cancer faces existing competition from: (1) NVS whose drug got approved and also hits brain mets and (2) Roche whose drug alecensa received accelerated approval in December 2015 for NSCLC. Chugai and others are also going after ALK+. Positive developments from competitors could decrease briganitib's value and make potential suitors less inclined to acquire the whole company (Iclusig + brigatinib).

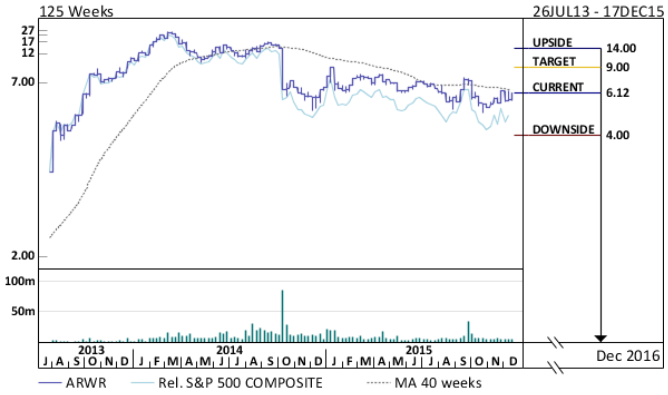
Arrowhead Research (ARWR)

Sector Perform, Speculative Risk

Price Target USD $9.00

Target/Upside/Downside Scenarios

Exhibit 71: Arrowhead Research Corp.



Source: RBC Capital Markets estimates

Target price/base case

Our $9 price target is a SOTP analysis of probability-adjusted value of the lead candidate and technology platform. 1) We assign a 5% probability for the lead program, ARC-520, in chronic hepatitis B to become a $4B+ global opportunity ($3B+ in the US alone). We discount risk-adjusted combined peak sales/ royalties of $300M in 2028 at 10% and a terminal growth rate of -15%, yielding $6/share. 2) We assign $150M EV for platform technology to deliver one or two more clinical candidates that target orphan liver indications. We apply 4x to peak risk-adjusted sales of $750M and discount back at 10%, yielding $2/share. 3) We include cash of $1/share (YE:16E).

Upside scenario

Our $14 upside scenario represents 8% assumed probability of success for the lead ARC-520 in HBV, which totals $9/share. We also assume higher $200M EV for platform technology, based on 15% probability of success as we give more credit to the scarcity of targeted RNAi delivery technologies, thereby adding $3/share of platform value to our valuation.

Downside scenario

Our $4 downside scenario represents a worst-case scenario in which ARC-520 ceases development due to unforeseen safety issues. This removes any valuation that we ascribe to ARC-520 and leaves only platform technology/ARC-AAT ($2/share) and $2/share in cash.

Investment summary

We rate ARWR shares Sector Perform, Speculative Risk because even though it is an RNAi-therapeutic platform technology company with a potential promising asset for HBV, we won't get any real answers to the key debate of whether this drug can lead to Hep B cures in the near term. We would like more data from the Phase IIb controlled multi-dose study initiated in Q4:15, which could take several months to fully enroll and take another 6-12 months of treatment. While the ARC-520 program lacks near-term catalysts, we see a few positives in ARWR: (1) recent data from ongoing Phase IIa ARC-520 program shows that the drug/platform appears to be "working" to some degree, (2) second program ARC-AAT could provide added value, and (3) ARWR is inexpensive with a valuation down to ~3x cash.

Potential catalysts for the stock

Better than expected "HBsAg knockdown" data from multi-dose Phase IIb study: ARWR's higher-dose Phase IIa data was better than prior data and got up to 1.9log peak s-knockdown in E+, nuc-naïve patients. The data was just one dose. Phase IIb will have multiple doses and a longer follow-up, and we think it could generate even better data by late 2016/ 2017.

ARC-AAT Phase I proof of concept data in mid-2016: If the Phase I data shows ~90% knockdown of AAT protein, it validates their platform and increases the potential for ARC-AAT to become a new treatment option for AATD. This program offers upside long term and isn't in consensus estimates or thinking.

Risks to our investment thesis

Failure to demonstrate causality link between reduction in HBsAg and immune de-repression: This is a central issue that determines whether ARC-520 is a novel "adjuvant" therapy to be used to lower HBsAg or a truly differentiated HBV therapy that could affect functional cures. This is an issue that will be gradually de-risked as more patients receive ARC-520, and as patients do or do not experience seroconversion.

Emergence of serious safety signal that precludes continued development of ARC-520: The development of liver, renal, or other off-target toxicities such as severe immunological reactions could result in the termination of this lead program. Tissue delivery, stability of therapeutic, and control of off-target toxicities are common challenges for RNAi-based therapy.

Competitors advancing their HBV drugs: At the end of the day, there are possibly more potent RNAi drugs from ALNY, ABUS or ASMB, and orals are coming around the corner.

2016 thoughts on ARWR

We think ARWR will remain relatively range-bound until at least Spring 2016 and until we are closer towards more information from the Phase IIb program now started. We think it will take many months before enrollment is all ramped up and enough time has passed to get any new material data (co says they don't formally plan to announce data until 6-12mos of treatment but might announce data depending if efficacy is material or remarkable earlier).

On a relative positive, recently ARWR did announce new Phase IIa data from the ongoing Phase II ARC-520 Hepatitis B program at AASLD in humans that is incrementally promising. The follow up data look better than initial data disclosed in Q3 and earlier in 2015 because:

- There was a 1-log "average" S-knockdown with just one dose in healthier HBeAg+ pts which are ~50% of the HBV population.
- This got up to 1.9log "peak" S-knockdown in E+, nuc-naive pts.
- This was just one dose and Phase IIB starting now has multiple doses and longer follow-up and likely to get even better data in '16; i.e. this could get better with longer duration of treatment.
- The drug has been very safe and tolerable so far with no SAE's or any notable adverse events.
- They have a new drug ARC-521 that addresses E- patients and this had 2-3-log knockdown in chimps, and moves into IND next year.

As a result, we do think we can draw some conclusion that the drug and platform appear to be "working" to a degree. In addition, ARWR is advancing a 2nd program ARC-AAT in Phase I and this provides some added value as another program.

Also, with valuation down to 2x cash, we believe it is relatively inexpensive. Expectations are also very low so this provides opportunity as data should read out in 2016 and stock could go up from here.

Questions still outstanding for some investors as they digest the recent data: 1) why does it work better in some groups and not others, 2) what happens with multiple doses (not just one), 3) does knocking down s-antigen with RNAi mean anything to a functional cure and does the immune system re-activate? The company will continue to focus on marketing and educating the Street. The key reason the company believes data are even stronger in E+ patients is because ARC-520 was designed against HBV from cccDNA (high in E+ patients) and as this becomes integrated DNA in E- patients, there is modification to the DNA whereby the ARC-520 triggers do not bind and thus S-antigen is still getting made and can't get knocked down

Bear case

- No evidence yet blocking S-antigen with RNAi matters towards a functional cure
- The arguments for changes in cccDNA to integrated DNA and reductions of cccDNA by nukes (which is why drug works better in nuc-naïve) goes against a lot of current HBV thinking
- Other players out there in HBV with other mechanisms and combinations.
- Company likely needs to raise capital by 2016.
- Credibility given historical bullishness for hitting 1-log but then 1-2mg data was much, much lower than expectations at 40-50% knockdown despite commentary around deep and surprising knockdown
- Toxicity may become more of an issue if they go to higher doses and as you give multiple doses.
- End of the day, there's other possibly more potent RNAi plays from ALNY and ABUS and ASMB and orals are coming around the corner.

Key questions / debates for ARWR

1. When can we see actual data on potential 'cure rates' on ARC-520?

Knocking down HBsAg is only the first step in theoretically what experts believe will lead to functional cures by reactivating the immune-system. ARWR plans to initiate a multi-dose Phase IIb study involving a 12-week dosing portion and then a long-term extension follow-up period. Consensus believes that HBsAg needs to be meaningfully suppressed for at least 3-6 months before the immune system can be reactivated. Thus for us to measure HBsAg seroconversion (sign indicating immune cells have been activated against HBsAg) and thus sign of potential 'functional cures' we don't think this data will be available until ~2017.

2. How do we see ARC-520 in the future treatment landscape for HBV?

It is too early to tell and the answer will depend on the evolving data of the drug. The primary goal of ARC-520 and other therapies in development for HBV is to achieve a 'functional cure' so that patients no longer have to take drug indefinitely, which is the current standard of care. If ARC-520 is able to achieve deep prolonged knockdown of HBsAg, it may become a critical component in the treatment paradigm for HBV. However the ultimate treatment will likely require a combination of different drugs with different mechanisms to achieve the highest cure rates. There are several oral drugs in development targeting multiple pathways of the HBV viral lifecycle and if they achieve high cure rates, their oral route of administration will provide a significant advantage over ARC-520, which is delivered intravenously.

Exhibit 72: ARWR's expected news flow

Time	Expected News Flow	Program
YE:15	File next clinical candidate ARC-F12	ARC-F12
Q1:16	Initiate Monarch study (HepArc 2008)	ARC-520
Early '16	Initiate Part B portion of Phase I to start dosing in AATD patients	ARC-AAT
mid 2016	Data from Phase I study in AATD (alpha-1 antitrypsin deficiency) patients	ARC-AAT
2016	File IND for ARC-521 (addresses E- patients)	ARC-521
late 2016-2017	Phase IIb multi-dose data in chronic HBV patients (HepArc 2002, 2003)	ARC-520

Source: Company reports and RBC Capital Markets estimates

Exhibit 73: ARWR's pipeline

Drug (Target)	Indication	Stage	Est. Completion
Clinical Stage Assets			
ARC-520	Hepatitis B	Phase II	Late 2016/ 2017
ARC-521	Hepatitis B	Pre-IND	-
ARC-AAT	Alpha-1 Antitrypsin Deficiency	Phase I	mid 2016
ARC-F12	Thrombosis and Angioedema	Pre-IND	-
ARC-HIF2	Clear cell, Renal Cell Carcinoma	Pre-IND	-
ARC-LPA	Cardiovascular Disease	Pre-Clinical	-

Source: Company reports and RBC Capital Markets estimates

Exhibit 74: ARWR's income statement

($ in millions, except per share) Fiscal Year Ends September	FYA 2012	FYA 2013	1QA Dec-13	2QA Mar-14	3QA Jun-14	4QA Sep-14	FYA 2014	1QA Dec-14	2QA Mar-15	3QA Jun-15	4QA Sep-15	FYE 2015	1QE Dec-15	2QE Mar-16	3QE Jun-16	4QE Sep-16	FYE 2016	FYE 2017
Revenues:																		
ARC-520 Sales																		
ARC-520 Royalties																		
Other Income	0.15	0.29	0.04	0.04	0.04	0.04	0.18	0.17	0.04	0.12	0.04	0.38	0.08	0.08	0.08	0.08	0.32	0.32
Total revenue	**0.15**	**0.29**	**0.04**	**0.04**	**0.04**	**0.04**	**0.18**	**0.17**	**0.04**	**0.12**	**0.04**	**0.38**	**0.08**	**0.08**	**0.08**	**0.08**	**0.32**	**0.32**
Operating expenses:																		
Cost of sales																		
Research and development	5.39	8.71	3.13	5.22	6.39	8.40	23.14	17.74	21.78	7.49	0.25	47.27	12.00	14.00	16.00	18.00	60.00	75.00
Acquired in-process research and develop	-	-	-	-	-	-	-	-	-	-	10.14	10.14	-	-	-	-	-	-
General and Administrative	6.44	3.49	0.91	1.35	1.58	2.05	5.89	3.15	1.70	1.83	1.25	7.93	1.30	1.50	1.80	2.20	6.80	10.88
Other OpEx	9.41	12.68	3.01	4.69	4.77	11.95	24.42	4.39	6.20	6.80	13.63	31.01	10.56	11.31	12.06	14.06	47.97	57.76
Total Operating Expenses	21.24	24.88	7.05	11.25	12.74	22.40	53.45	25.29	29.68	16.12	25.28	96.36	23.86	26.81	29.86	34.26	114.77	143.64
Income (loss) from operations	**(21.09)**	**(24.59)**	**(7.01)**	**(11.21)**	**(12.70)**	**(22.36)**	**(53.28)**	**(25.12)**	**(29.63)**	**(15.99)**	**(25.23)**	**(95.97)**	**(23.78)**	**(26.73)**	**(29.78)**	**(34.18)**	**(114.45)**	**(143.32)**
Total other income/expenses	(1.02)	(7.11)	(3.67)	(2.77)	1.07	(0.08)	(5.44)	2.54	0.95	0.06	0.49	4.04	-	-	-	-	-	-
Income Tax																		
Net income Attributable to ARWR	**(21.13)**	**(31.14)**	**(10.62)**	**(13.94)**	**(11.63)**	**(22.44)**	**(58.63)**	**(22.58)**	**(28.68)**	**(15.94)**	**(24.74)**	**(91.94)**	**(23.78)**	**(26.73)**	**(29.78)**	**(34.18)**	**(114.45)**	**(143.32)**
EPS (basic)	**(1.90)**	**(1.30)**	**(0.28)**	**(0.31)**	**(0.22)**	**(0.41)**	**(1.25)**	**(0.41)**	**(0.51)**	**(0.27)**	**(0.42)**	**(1.60)**	**(0.40)**	**(0.44)**	**(0.49)**	**(0.46)**	**(1.78)**	**(1.79)**
EPS (diluted)	**(1.90)**	(1.30)	(0.28)	(0.31)	(0.22)	(0.41)	(1.25)	(0.41)	(0.51)	(0.27)	(0.42)	(1.60)	(0.40)	(0.44)	(0.49)	(0.46)	(1.78)	(1.79)
Shares outstanding:																		
Basic	11.1	24.0	37.7	44.3	51.9	54.7	46.9	54.7	55.7	59.5	59.5	57.4	60.1	60.7	61.3	74.9	64.3	79.9
Diluted	11.1	25.0	52.0	58.6	57.5	60.3	57.1	54.7	55.7	59.5	59.5	57.4	60.1	60.7	61.3	74.9	64.3	79.9
Cash at end ($M)	3.4	29.8	85.5	194.7	188.5	177.3	177.3	145.4	128.4	111.6	98.8	98.8	80.7	59.7	35.6	104.9	104.9	82.1

Source: Company reports and RBC Capital Markets estimates

Valuation

Our $9 price target is a SOTP analysis of probability-adjusted value of the lead candidate and technology platform. 1) We assign a 5% probability for the lead program, ARC-520, in chronic hepatitis B to become a $4B+ global opportunity ($3B+ in the US alone). We discount risk-adjusted combined peak sales/ royalties of $300M in 2028 at 10% and a terminal growth rate of -15%, yielding $6/share. 2) We assign $150M EV for platform technology to deliver one or two more clinical candidates that target orphan liver indications. We apply 4x to peak risk-adjusted sales of $750M and discount back at 10%, yielding $2/share. 3) We include cash of $1/share (YE:16E).

Price target impediments

Our price target is primarily dependent on the clinical success of its lead candidate, ARC-520. Thus, potential impediments to our price target include: 1) failure of ARC-520 to display robust and dose-dependent knockdown of HBsAg from its Phase IIb multi-dose studies in chronic HBV patients (HepArc 2002, 2003). This would be a large setback because this is the mechanistic basis of its lead program as well as a demonstration of viability and applicability of its RNAi delivery-platform technology. 2) The emergence of a serious safety signal that precludes continued development of ARC-520. The development of liver, renal, or other off-target toxicities, such as severe immunological reactions, could result in termination of this lead program. Tissue delivery, stability of therapeutic, and control of off-target toxicities are common challenges for RNAi-based therapy. 3) At the end of the day, there are possibly more potent RNAi drugs from ALNY, ABUS or ASMB, and orals are coming around the corner.

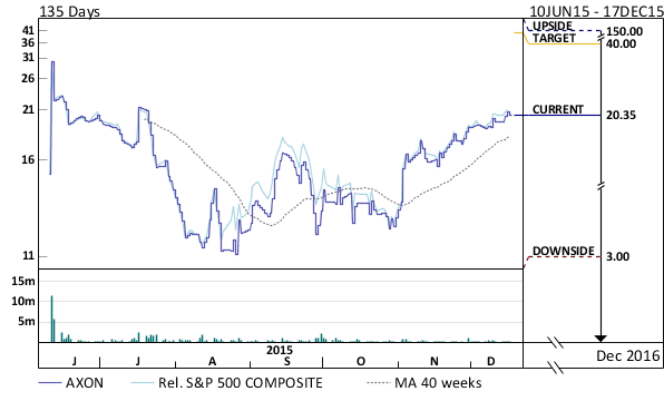
Axovant Sciences Ltd (AXON)

Outperform, Speculative Risk

Price Target USD $40.00

Target/Upside/Downside Scenarios

Exhibit 75: Axovant Sciences Ltd.



Source: RBC Capital Markets estimates

Target price/base case

Our base case of $40/share is based on a DCF analysis of RVT-101's commercial potential and applies a 65% probability of success (POS). According to our analysis, we assume RVT-101 could become a peak ~$5B drug roughly seven years after launch. This is reasonable in our view, as Aricept achieved peak $4B sales before it went generic in 2010 and we expect the Alzheimer's population to increase. For terminal value, we use -80%, as it's a small molecule that could quickly go generic, and apply a 10% discount rate. We do not include any valuation for other pipeline opportunities.

Upside scenario

Our upside scenario of $150/share reflects our best-case outcome, which would be an eventual takeout by a major pharmaceutical company post positive Phase III results. We acknowledge that it may take more than two years to get there, but if the pivotal study is convincingly positive, then based on precedent transactions, potential acquirers would likely have to pay 3–5x on peak sales estimate of $4–5B, which would be in the range of $150/share.

Downside scenario

Our downside scenario of $3/share assumes an outright failure/halt of RVT-101 development due serious unforeseen safety risks. Based on the clinical data to date, we think this outcome is unlikely, but given the high concentration on one drug, we highlight this real risk. In this scenario, the stock could trade near cash levels, which would be ~$3/share.

Investment summary

We rate Axovant Outperform, Speculative Risk, as we believe, based on its de-risked Phase II data and current valuation, AXON stock has one of the most upside potential (binary) opportunities within our coverage over the next two to three years when Phase III data reads outs. Our call over the near term is the stock is likely to trade up from: 1) time value of the significant potential upside call option as the Phase III study gets closer and more de-risked; 2) AXON additional neuro drug nelotanserin could add value soon; and 3) Phase II/III data from additional dementia indications could come H2:16-2017, which could be upside to models. Lastly, an inexpensive call option on competitor Lundbeck's similar drug with Phase III data possibly early '17 although we believe this drug has only a very low 25–30% probability of positive data given new lower doses.

Potential catalysts for the stock

Positive Phase III data readout for Lundbeck's idalopirdine (Q1:17): RVT-101 showed better efficacy and safety than idalopirdine in their respective Phase II results. We think the POS of Phase III resulting in positive data in 50%.

Phase II nelotanserin could be better than ACAD's drug, now on file to FDA: ACAD will have important new data for their drug in mid-16 and this is now a big potential derivative catalyst for AXON. Furthermore, ACAD trades at around a $3.5B market cap which is 3x bigger than AXON's valuation.

Risks to our investment thesis

Failure to develop RVT-101 into safe and efficacious drug. Our thesis is predicated on RVT-101 succeeding Phase III pivotal study and launching commercially thereafter. Another risk to our investment thesis is that the pipeline is relatively concentrated on a single drug that has a long estimated timeline of two years until data readout. AXON launched a Phase III trial H2:15, with results expected in H2:17. The Phase IIb adjunct therapy success seen so far may not translate to that seen in the Phase III study.

RVT-101 may face unknown safety risks. Patients have only been treated with RVT-101 for 48 weeks. While RVT-101's safety and tolerability profile appears favourable so far, its MOA may be associated with glutamate toxicity, and AD drugs generally have been associated with liver toxicity. Long-term studies will be needed to demonstrate the safety of RVT-101.

Lundbeck, whose 5HT6 antagonist Lu AE58054 (idalopirdine) is a drug with similar MOA targeting the same indication. Lundbeck could announce Phase III data in early 2017 that could cause headline risk. Also, delayed timelines, increased competition, regulatory setbacks, or other limitations in the potential for AD therapies could impact AXON's valuation.

2016-2017 thoughts on AXON

This stock has the most upside potential in our coverage universe – over +500% upside potential is possible in our bull case if the Phase III Alzheimer's study reads out positively in 2017. We think probability of success of the Phase III resulting in positive data is at least 50%. There are reasons it could be higher than this, realizing most investors will not want to ascribe more than this for any Phase III Alzheimer's drug.

Reasons Phase III could be positive: (1) positive Phase II data in large randomized study with a 2-pt ADAS-cog benefit stat sig on top of Aricept (combo), (2) clear dose response, (3) Lundbeck has similar drug and reported similar efficacy in their own separate Phase II combination trial.

New in-licensed second drug program (nelotanserin) based on 5HT2 inverse agonism in Phase II. This drug is nearly identical but could be more potent and better safety (less/no QTC prolongation) than ACAD pimavansein, which supports their $3B+ market cap and is clearly validated and has positive Phase III data in Parkinson's psychosis and is up for FDA approval mid-16. (1) ACAD has Phase II Alzheimer's pscyhosis data in Q3:16, which could expand the opportunity much further. (2) If ACAD is approved and/or acquired, then this would validate/prove the potential value and set a future comp for AXON.

We would caution that in early 2017 Lundbeck could announce Phase III data for their own 5HT6 antagonist and that data is 75% likely to be negative (due to much lower dose due to liver tox in Phase II and the higher doses were needed for efficacy). AXON investors need to know this could cause some headline risk to AXON but we/many people know the competitor drug should fail. If it was surprisingly positive (25% chance or less), then AXON would be up significantly given RVT-101 looks much better.

Bear case

- Another Phase III Alzheimer's program based on some Phase II dataset and will fail when expanded into a huge randomized Phase III study around the world. RVT-101 is just like all the others that came before it in Phase III and a ton of other Alzheimer's programs that failed before they got to Phase II/III.
- AXON got RVT-101 for $5M upfront and 12% royalties from GSK just a year or so ago. If it was so good then why would GSK give it up and why didn't anyone else buy this drug and pay $5M? AXON has a $1-2B market cap, which seems like market dislocation.
- RVT-101 failed and showed no signals in monotherapy use and only worked when it was combined with Aricept. If there are cognitive benefits you should see some of this in monotherapy too.
- The new program also cost only $5M – this time from ARNA. Why are all these drugs on fire sale and picked off for $5M? Why didn't ARNA continue development or sell it for higher than $5M? This was all after ACAD had reported positive Phase III data too.

Key questions / debates for AXON

1. What are the economics from GSK, and why would GSK give up RVT-101?

AXON acquired global rights to RVT-101 from GSK in December 2014 for $5M upfront, up to $160M in milestone payments, and a fixed 12.5% royalty on future net sales. Before the positive Phase IIb adjunct therapy trial completed in 2011, GSK had already announced de-investment in neurosciences and a shift from small molecules to biological drugs. There are many other examples where big pharma has given up prior drugs that ultimately turned out to be successful, e.g., PFE gave up PBYI's neratinib and ESPR's ETC-1002; Pharmion licensed Vidaza from Upjohn for zero upfront and CELG acquired Pharmion for $2.9B.

2. What is AXON's plan for Phase III development, and will that be sufficient for regulatory approval?

The Phase III study will be designed similarly as the Phase IIb adjunct study, but will be larger and better powered with 1,000 patients receiving placebo or 35 mg once-daily RVT-101. There is no need to dose above 35 mg, as PET imaging shows full receptor occupancy at this dose. The FDA has previously granted approval to Alzheimer's disease (AD) drugs based on two successful studies that demonstrate efficacy in cognition and function. At a meeting in March, the FDA confirmed that one final Phase III study should be sufficient for regulatory filing, as the data could be evaluated with the positive Phase IIb adjunct trial data.

3. How is RVT-101 differentiated from Lundbeck's idalopirdine, which is ahead in development?

Both RVT-101 and idalopirdine belong to a newer class of AD drugs under development called 5HT6 antagonists. While Lundbeck is running three Phase III studies with data by 2017 and could receive approval by late 2017 (versus our estimate of 2018 for RVT-101), Phase II studies demonstrate that RVT-101 has better safety and tolerability profile: RVT-101 resulted in lower discontinuation rates, less liver toxicity, less serious adverse events, and even better efficacy—hit on both cognition (ADAS-cog) and function (ADCS-ADL). In fact, Lundbeck is dosing down in Phase III program due to toxicity concerns, and thus, we think idalopirdine may only have a low 25–35% POS. If idalopirdine does not work, then RVT-101 could become the first 5HT6 antagonist to be approved, presenting a new drug with a new MOA for mild/moderate AD; if idalopirdine Phase III works, then it is a potentially significant upside catalyst in 2016 for AXON, as RVT-101 has shown better efficacy and safety than idalopirdine in Phase II comparisons.

4. Why did three Phase II monotherapy studies fail? RVT-101 did not meet the other primary endpoint of CDR-SB—do not all Alzheimer's drugs fail?

Donepezil (Aricept) did not meet statistical significance in one Phase II monotherapy trial, suggesting that the study may have been underpowered. Furthermore, AXON intends to advance RVT-101 as adjunct therapy only, where preclinicial and clinical data support its potential to enhance standard of care acetylcholinesterase inhibitors synergistically. RVT- 101 has presented a very good safety and tolerability profile so far (better than Aricept alone or idalopirdine) and has been tested in over 2,000 patients and healthy adults. Based on previous approvals, meeting one cognition and one function endpoint may be sufficient for FDA approval for AD. Most AD drugs have failed, especially a-beta antibodies (PFE & JNJ bapineuzumab), but they were based on small studies or retrospective analyses (ELN & MYGN), or limited sites (MDVN). Unlike a-beta antibodies, RVT-101 does not require amyloid imaging and does not cause ARIA side effects, which could inadvertently unblind ongoing trials and skew study results. With a different MOA, RVT- 101 could present a novel, safer, more efficacious treatment for mild/moderate AD.

Exhibit 76: AXON's expected news flow

Time	Expected News Flow	Program
Feb/Mar 2016	AdCom panel for pimavanserin in Parkinson's Disease Psyochosis	ACAD (competitor)
Q1:16	Initiate Phase IIb in DLB	RVT-101
Q1:16	Initiate Phase II studies in LBD and RBD/DLB	Nelotanserin
May 2016	PDUFA date for Parkinson's Disease Psychosis	ACAD (competitor)
Q3:16	Phase II results for pimavanserin in ADP	ACAD (competitor)
H2:16	Potential Phase II results for LBD	Nelotanserin
YE:16	Potential Phase IIa data for SYN120 in PDD	BITI (competitor)
Q1:17	Potential Phase III data for idalopirdine	Lundbeck (Competitior)
H1:17	Potential Phase II results for RBD/DLB	Nelotanserin
H2:17	Potential Phase III results in Alzheimer's disease	RVT-101
2017	Potential Phase IIb results in DLB	RVT-101
YE:17-early '18	Potential filing of NDA and MAA in Alzheimer's disease	RVT-101
2018	Potential regulatory approval(s) from FDA/EMA	RVT-101

*Note: Highlighted in blue indicates events of high significance

LBD: Lewy Body Dementia; **DLB:** Dementia with Lewy Bodies; **PDD:** Parkinson's Disease Dementia

LBD = DLB + PDD

RBD: REM Behavior Disorder

ADP: Alzheimer's Disease Psychosis

Source: Company reports and RBC Capital Markets estimates

Exhibit 77: AXON's income statement

($ in millions, except per share) Fiscal Year Ends March	FYA 2014A	1QA Jun-15	2QA Sep-15	3QE Dec-15	4QE Mar-16	FYE 2015E	1QE Jun-16	2QE Sep-16	3QE Dec-16	4QE Mar-17	FYE 2016	FYE 2017E	FYE 2018E	FYE 2019E	FYE 2020E
Revenues:															
RVT-101 WW	-	-	-	-	-	-	-	-	-	-	-	-	-	221.3	797.7
US	-	-	-	-	-	-	-	-	-	-	-	-	-	221.3	625.3
ex-US	-	-	-	-	-	-	-	-	-	-	-	-	-	-	172.4
Total Revenues, net	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**221.3**	**797.7**
Costs and expenses:															
Cost of product sales	-	-	-	-	-	-	-	-	-	-	-	-	-	26.6	95.7
Research and development	14.3	10.6	8.3	12.0	14.0	44.9	16.5	18.0	19.0	20.0	73.5	95.6	124.2	161.5	209.9
- Milestones due to GSK				-	-	-			-	-	5.0	4.0	35.0	25.0	95.0
- Royalties due to GSK						-					-	-	-	42.6	153.4
Selling, general and administrative	6.7	17.4	3.8	5.0	6.5	32.6	7.5	9.0	11.0	13.0	40.5	50.0	65.0	78.0	93.6
Total operating costs and expenses	21.0	28.0	12.0	17.0	20.5	77.5	29.0	27.0	30.0	33.0	119.0	149.6	224.2	333.6	647.6
Income (loss) from operations	(21.0)	(28.0)	(12.0)	(17.0)	(20.5)	(77.5)	(29.0)	(27.0)	(30.0)	(33.0)	(119.0)	(149.6)	(224.2)	(112.3)	150.0
Interest expense	(0.0)	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Total interest and other, net	(0.0)	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Income (loss) before income taxes	(36.4)	(12.2)	(13.3)	(15.2)	(15.2)	(77.5)	(12.2)	(13.3)	(15.2)	(15.2)	(119.0)	(149.6)	(224.2)	(112.3)	150.0
Provision for Income Tax	-	(0.1)	(0.0)	-	-	-	-	-	-	-	-	-	-	-	45.0
Net income (loss)	**(21.0)**	**(28.1)**	**(12.1)**	**(17.0)**	**(20.5)**	**(77.5)**	**(29.0)**	**(27.0)**	**(30.0)**	**(33.0)**	**(119.0)**	**(149.6)**	**(224.2)**	**(112.3)**	**195.0**
EPS (basic)	($1.32)	($0.35)	($0.12)	($0.17)	($0.20)	($0.81)	($0.28)	($0.26)	($0.29)	($0.31)	($1.15)	($1.41)	($1.99)	($0.98)	$1.66
EPS (diluted)	($1.32)	($0.35)	($0.12)	($0.17)	($0.20)	($0.81)	($0.28)	($0.26)	($0.29)	($0.31)	($1.15)	($1.41)	($1.99)	($0.98)	$1.61
Shares outstanding:															
Basic	16.0	80.3	99.2	100.1	101.1	95.2	102.2	103.2	104.2	105.2	103.7	105.8	112.9	115.1	117.4
Diluted	16.0	84.3	103.2	104.2	105.2	99.2	106.2	107.2	108.2	109.3	107.7	109.8	116.9	119.1	121.4
Cash at end		331.1	320.2	315.2	308.7	308.7	290.2	278.7	269.2	261.7	261.7	197.2	213.2	216.0	544.4

*Basic shares used to calculate diluted EPS when earnings are negative

Source: Company reports and RBC Capital Markets estimates

Valuation

Our base case of $40/share is based on a DCF analysis of RVT-101's commercial potential in the US and EU and applying a 65% POS. According to our analysis, we assume RVT-101 could become a peak ~$5B drug roughly seven years after launch. This is reasonable in our view, as Aricept achieved peak $4B sales before it went generic in 2010, and the Alzheimer's population is only expected to increase. We assume that about two-thirds of sales will be

from the US and we also incorporate the 12.5% royalty due to GSK. For terminal value, we use -80%, as it is a small molecule that could quickly go generic, and apply a 10% discount rate. We do not include any valuation for other pipeline opportunities, as data are absent.

Price target impediments

Our price target is primarily dependent on the successful development of RVT-101 through its Phase III pivotal study and commercial launch thereafter. One of the greater risks to our investment thesis is that the pipeline is relatively concentrated on one drug that has a long estimated timeline of two years until data readout. Before the readout of this key catalyst, the stock may be volatile based on events from competitors such as Lundbeck's Lu AE58054, which is a drug with similar MOA targeting the same indication that is ahead of Axovant's RVT-101. Any delayed timelines, increased competition, regulatory setbacks, or other limitations to the market potential of AD therapies could negatively affect our valuation.

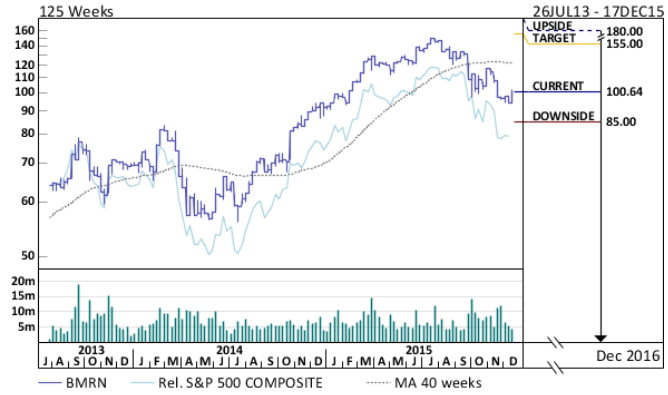
BioMarin Pharmaceutical (BMRN)

Outperform

Price Target USD $155.00

Target/Upside/Downside Scenarios

Exhibit 78: BioMarin Pharmaceutical



Source: RBC Capital Markets estimates

Target price/base case

Our base case of $155/share assumes stable base business growth (3%-9% y/y), Vimizim to grow to $600M franchise by 2020, PEG-PAL a $300M franchise by 2022 (80% prob), BMN-701 as $450M franchise by 2020 (80% prob.), and $17/share for remaining pipeline (BMN-190, BMN-270). We add $26/share for BMN-111 Achondroplasia assuming 65% prob on peak $2B drug and $25/share for drisapersen in Duchenne muscular dystrophy (DMD) based on $1000M peak sales (65% prob.) We use 9% discount rate and blended tax rates ranging from 18% to 25%, depending on projected product/geographical mix in our DCF valuation.

Upside scenario

Our upside scenario of $180 takes into account same assumptions as our base case but incorporates more positive scenarios on four key events: 1) Drisapersen is approved by the FDA in 2015, increasing our probability to 100%; 2) BMN-111 also works in pivotal study for achondroplasia; 3) BMN-190 shows positive efficacy trends for Batten's disease; and 4) BMN-270 shows POC in Hemophilia A. The latter three events would increase our probability on the early-stage pipeline. Collectively, this increases our SOTP to $180/share.

Downside scenario

Our downside scenario of $85 assumes no DMD approval and less robust growth in base business and slightly less promising Vimizim prospects. We assume lower probability of success across pipeline programs, such as PEG-PAL and BMN-701.

Investment summary

We rate BioMarin as Outperform and think the stock will trend higher from a rich line-up of catalysts in the next 12-24 months. Following BMRN's release of positive Phase II data on dwarfism in June, we have further conviction that the company's other "big" catalyst (DMD approval) could occur early '16. DMD is not really in consensus models since its approval is a bit binary. Our longer-term Bull thesis is an evolution of revenue growth and continued successful development of numerous Orphan drug programs that could lead to BMRN being acquired. The $2-3B+ potential revenues and the profitability of this revenue base would be too scarce to pass up. We'd be continued buyers for 2016 and believe the stock should play out well. Additional opportunities that have big upside and good risk/reward: 1) Phase I Batten's data YE:15 and 2) Phase I hemophilia gene therapy – which theoretically eliminates the need for recombinant Factor VIII.

Potential catalysts for the stock

Accelerated approval of drisapersen for DMD in the US and/or EU: BMRN acquired Prosensa primarily for its DMD asset, drisapersen. The drug/company has had a bumpy development path as the final Phase III did not meet its primary endpoint. However, BMRN believes the drug could be approved based on positive analysis in the younger subgroup and the unmet medical need for DMD. Although the November 2015 AdCom panel left several confused as it was not overly positive, we think unmet need is key and there is enough safety data to let patients decide on using it.

Positive data in 2016 from early-stage higher-risk/higher-reward drug candidates: BMN-190 for Batten's disease is a high-risk challenging indication, but the opportunity could be $300– 500M+ if BMRN reports positive Phase I/II results in Q1:16. Peg-Pal will have top-line results from its Phase III trial for treatment of PKU in March/April 2016. In April 2016, BMRN will also provide updates BMN-270 (Hemophilia A) and Phase III plans of BMN-111 (as well as share 12- month results).

Risks to our investment thesis

Delay in pipeline: Given that BMRN is not yet profitable and is still a pipeline-driven story, frequent delays in other pipeline candidates could decrease investor interest in the stock. Drisapersen rejection by FDA/EMA would delay its timeline by a few years. Also, Peg-Pal could require head-to-head EU studies, take 1-2 more years and present a risk for EU pricing.

Kuvan IP: Kuvan has IP settlement for 2020 in the US, but it's unclear how erosion looks for an oral like this.

Other risks include: Ongoing clinical risk with pipeline programs, uncertainty on DMD approval given failed Phase III and mixed AdCom commentary in November 2015, and the company (still) being unprofitable.

2016 thoughts on BMRN

We think BMRN is a solid long-term biotech holding due to its leading core orphan drug franchise and numerous pipeline products in development that could lead to further upside. We are buyers of BMRN because we think the Street nearly fully assumes that drisapersen for DMD will NOT get approved by the PDUFA of early January '16 and the stock will recover back higher after this event is out of the way for more pipeline events later in 2016. If surprisingly approved, it would be +10-20% upside and minimal approximately -5% downside if not approved.

We'd be buyers if stock is weak on DMD rejection and our long-term positive thesis on big pipeline value is intact. We previously had a 60% confidence on FDA approval and we are now in the 25% range post the panel. While panel questions and vote results were not overly positive and were mixed (no clear consensus), we think the needle still pointed to 1) high unmet need, 2) safety is sufficient to give patients a choice, and 3) efficacy has "signals" and "there are some patients that clearly benefit".

Note that if BMRN gets rejected – we would want SRPT to get approved as BMRN could extract a royalty (e.g. 10% from SRPT and this in itself could end up paying for the $600M they paid for Prosensa), thereby getting their capital back. For example a 10% royalty on $600M peak sales is $60M x 10 multiple = $600M.

We think stock could recover by the spring and into the April 2016 R&D day. Here we should get updated on Batten's data, which BMRN may file to FDA, and an update on gene therapy hemophilia, and Phase III Peg-PAL data.

We continue to think BMRN remains an attractive takeout target in the long-run and more so now that DMD could be out of the way. On pharma earnings calls for Q3, we were surprised how open and transparent more companies were looking at general M&A ideas right now (SNY, AMGN, JNJ, Shire, etc.).

Bear case

- Management credibility suffered after the DMD panel and documents.
- DMD will not get approved and management was so confident all year. They disparaged SRPT earlier in the year and then explained all the ways their data looked great and FDA dialog was going very well. The panel ended up being quite negative and didn't appear that FDA was on board with BMRN at all.
- BMN-709 (Pompe's) will not look good – uses odd MIP/MEP endpoint that they used only because 6MWD did not look good. Not clear this will support regulatory filing and approval.
- Peg-Pal will probably fail again. This has been an iteration for years now. Plus, they could also need head-to-head studies for EU and could take 1-2 years and it presents risk for pricing in EU (drug is better than Kuvan though).
- Batten's disease will be another high-risk situation going to the FDA on only Phase I data – plus Spark Therapeutics could be a competitor as they are going after same concept but using gene therapy instead.
- Kuvan USA has IP settlement for 2020 but not clear how erosion looks on an oral like this.
- Will they ever be profitable? The company continues to increase expenses and will likely not be profitable within the next few years now that DMD could be out of the picture.
- Gene therapy hemophilia is extremely high risk and unlikely to be successful on the first iteration.
- M&A is not highly likely due to the high valuation of BMRN on only $1B+ of sales next year, making it trade at 15x forward revenues.

Exhibit 79: Expected news flow for BMRN

Time	Expected News Flow	Program
Q4:15	Interim results from single arm of II/III trial for the treatment of Pompe disease	BMN-701 (Pompe)
Q4:15	Initiate Phase I/II in MPS IIIB	BMN-250 (MPS IIIB)
Early Jan 2016	Potential FDA approval for drisapersen (DMD) on December 27, 2015	drisapersen 'Kyndrisa' (DMD)
Jan 22, 2016	FDA advisory panel to discuss eteplirsen	eteplirsen (DMD)
Feb 26, 2016	Potential FDA approval for SRPT's eteplirsen	eteplirsen (DMD)
Q1:16	Results from Phase 1/2 of BMN-190 in Batten's disease (study concluded YE:15)	BMN-190 (Battens)
Mar/Apr, 2016	Top-line results from pivotal Phase 3 trial with PEG PAL for the treatment of PKU	PEG-PAL (PKU)
Apr 20 2016	Host R&D Day to provide program update on BMN-270 Hemophilia A, and to share Phase III plans of BMN-111 and its 12-mo Phase II results	BMN-270 (Hemophilia A) BMN-111 (achondroplasia)
H1:16	Potential CHMP opinion	drisapersen 'Kyndrisa' (DMD)
H2:16	Submission of PEG PAL BLA to the FDA for the treatment of PKU	PEG-PAL (PKU)
H2:16	Potential EMA approval for drisapersen for DMD by Q3:16	drisapersen 'Kyndrisa' (DMD)

Source: Company reports and RBC Capital Markets estimates

Exhibit 80: Exon 51 Market Model

Kyndrisa (Drisapersen) EXON-51 APP

Dates refer to calendar years

Price of therapy in US ($/yr)	$350,000
Price Growth	2.0%
Gross to Net	18.0%
Price of therapy in EU ($/yr)	$250,000
Price Growth	0.0%
Gross to Net	0.0%
Price of therapy in ROW ($/yr)	$150,000
Price Growth	0.0%
Gross to Net	0.0%

DCF -- Drisapersen	
Terminal Growth	-8%
Discount Rate	9%
NPV Sum ($M)	$2,141.7
Share Count	164.4
Prob. Of Success (POS)	25%
Prob. Adjusted NPV Sum ($M)	$535.4
Prob. Adj NPV/Share	**$3**

Quick Peak Sales Multiple Estimator	
Peak sales	$134
Peak year	2026
Sales multiple	9.0 x
Discount rate	9%
Prob. Adj NPV ($M)	$468
Prob. Adj NPV/Share ($M)	$3

Prob. Adjusted Revenue ($M)	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E
US Revenue	-	$9.6	$21.4	$29.6	$30.9	$32.1	$35.2	$36.6	$38.1	$40.6	$43.3	$46.1
EU Revenue	-	0.9	3.5	6.2	27.8	29.2	31.5	31.9	32.4	32.9	33.4	33.9
ROW Revenue	-	-	2.1	8.5	27.1	38.5	44.6	51.0	51.7	52.5	53.3	54.2
Total Prob. Adjusted Revenue	**-**	**$10.4**	**$26.9**	**$44.4**	**$85.7**	**$99.8**	**$111.2**	**$119.5**	**$122.3**	**$126.1**	**$130.1**	**$134.2**
Total Number of Patients on Therapy	**-**	**147**	**347**	**496**	**851**	**881**	**947**	**964**	**981**	**1,010**	**1,040**	**1,070**

Drisapersen Revenue Model													
US Market	**Assumptions**	**2015E**	**2016E**	**2017E**	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**
Males w/ DMD (Prevalence)	14,353	14,353	14,654	14,961	15,274	15,594	15,921	16,254	16,594	16,942	17,297	17,659	18,029
Growth rate (Incidence - Death Rate)	2.1%												
Potentially Treatable Patients (Exon 51)	13.0%	1,866	1,905	1,945	1,986	2,027	2,070	2,113	2,157	2,202	2,249	2,296	2,344
% Ambulatory Patients (Exon 51)		50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%
Ambulatory Patient Penetration (Exon 51)		**0%**	**14%**	**30%**	**40%**	**40%**	**40%**	**42%**	**42%**	**42%**	**43%**	**44%**	**45%**
Patients Treated		-	133	292	397	405	414	444	453	463	483	505	527
Net Price per Year	$287,000		$287,000	$292,740	$298,595	$304,567	$310,658	$316,871	$323,209	$329,673	$336,266	$342,992	$349,851
Price increase	2.0%			2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%
Total Revenue - US ($M)		**-**	**$38.3**	**$85.4**	**$118.6**	**$123.5**	**$128.6**	**$140.6**	**$146.4**	**$152.5**	**$162.6**	**$173.2**	**$184.5**
EU Market	**Assumptions**	**2015E**	**2016E**	**2017E**	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**
Males w/ DMD (Prevalence)	20,791	20,791	21,109	21,432	21,760	22,093	22,431	22,775	23,123	23,477	23,836	24,201	24,572
Growth rate (Incidence - Death Rate)	1.5%												
Potentially Treatable Patients (Exon 51)	13.0%	2,703	2,744	2,786	2,829	2,872	2,916	2,961	3,006	3,052	3,099	3,146	3,194
% Ambulatory Patients (Exon 51)		50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%
Ambulatory Patient Penetration (Exon 51)		**0%**	**1%**	**4%**	**7%**	**31%**	**32%**	**34%**	**34%**	**34%**	**34%**	**34%**	**34%**
Patients Treated		-	14	56	99	445	467	503	511	519	527	535	543
Net Price per Year	$250,000		$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000
Price increase	0.0%			0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Total Revenue - EU ($M)		**-**	**$3.4**	**$13.9**	**$24.8**	**$111.3**	**$116.6**	**$125.8**	**$127.8**	**$129.7**	**$131.7**	**$133.7**	**$135.8**
ROW Market	**Assumptions**	**2015E**	**2016E**	**2017E**	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**
Males w/ DMD (Prevalence)		41,779	42,418	43,067	43,726	44,396	45,075	45,765	46,465	47,176	47,898	48,631	49,376
Growth rate	1.5%												
Potentially Treatable Patients (Exon 51)	13.0%	5,431	5,514	5,599	5,684	5,771	5,860	5,949	6,040	6,133	6,227	6,322	6,419
% Ambulatory Patients (Exon 51)		50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%
Ambulatory Patient Penetration (Exon 51)		**0%**	**0%**	**2%**	**8%**	**25%**	**35%**	**40%**	**45%**	**45%**	**45%**	**45%**	**45%**
Patients Treated		-	-	56	227	721	1,025	1,190	1,359	1,380	1,401	1,422	1,444
Net Price per Year	$150,000		$150,000	$150,000	$150,000	$150,000	$150,000	$150,000	$150,000	$150,000	$150,000	$150,000	$150,000
Price increase	0.0%			0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Total Revenue - ROW ($M)		**-**	**-**	**$8.4**	**$34.1**	**$108.2**	**$153.8**	**$178.5**	**$203.9**	**$207.0**	**$210.2**	**$213.4**	**$216.6**

Source: RBC Capital Markets estimates

Exhibit 81: BMRN pipeline

Drug	Indication	Stage: Pre-clinical	Phase I	Phase II	Phase III	BLA/NDA/MAA
Drisapersen	Duchenne muscular dystrophy (Exon 51)					
Pegvaliase (Peg-Pal)	PKU					
Reveglucosidase alfa (BMN 701) - GILT GAA	Pompe disease					
BMN 111 Analog of CNP	Achondroplasia					
BMN 044	Duchenne muscular dystrophy (Exon 44)					
BMN 045	Duchenne muscular dystrophy (Exon 45)					
BMN 053	Duchenne muscular dystrophy (Exon 53)					
Cerliponase Alfa (BMN 190) - TPP1	CLN2 disease					
BMN 270 AAV-Factor VIII Vector	Hemophilia A					
BMN 250 Gilt rhNAGLU	Sanfilippo syndrome / MPS IIIB					

Source: Company reports and RBC Capital Markets estimates

Exhibit 82: BMRN's income statement

Fiscal Year (Ending in December) ($ figures in MM, except per share)	FY12	FY13	FY14	1Q15 Mar-15	2Q15 Jun-15	3Q15 Sep-15	4Q15E Dec-15	FY15E	1Q16E Mar-16	2Q16E Jun-16	3Q16E Sep-16	4Q16E Dec-16	FY16E	FY17E
Net product revenues	**$496.5**	**$538.3**	**$738.5**	**$201.3**	**$249.0**	**$207.8**	**$224.0**	**$882.1**	**$249.5**	**$288.9**	**$264.8**	**$306.4**	**$1,109.6**	**$1,339.5**
Naglazyme	257.0	271.2	334.4	78.2	111.1	54.1	64.0	307.4	80.0	100.0	60.0	71.0	311.0	317.2
Aldurazyme	82.3	83.5	105.7	18.2	20.2	20.6	28.0	87.0	18.0	20.0	19.0	27.0	84.0	79.8
Kuvan	143.1	167.4	202.9	50.2	60.1	64.2	67.0	241.5	74.0	81.0	88.0	96.7	339.7	407.6
Firdapse	14.2	16.1	18.1	4.1	3.7	3.8	4.0	15.6	4.0	3.9	3.8	3.7	15.4	13.9
Vimizim (GALNS)	-	0.1	77.4	50.6	53.9	65.1	61.0	230.6	70.0	76.0	79.0	83.0	308.0	371.0
Drisapersen	-	-	-	-	-	-	-	-	3.5	8.0	15.0	25.0	51.5	150.0
Collaborative agreement revenues	**$2.0**	**$3.9**	**$1.6**	**$0.4**	**$0.3**	**$0.1**	**$0.3**	**$1.1**	**$0.3**	**$0.3**	**$0.3**	**$0.3**	**$1.2**	**$1.2**
Royalty and license revenues	**$2.3**	**$6.3**	**$11.0**	**$1.6**	**$1.2**	**$1.0**	**$0.9**	**$4.7**	**$0.8**	**$0.7**	**$0.6**	**$0.5**	**$2.6**	**$2.5**
Total revenue	**$500.7**	**$548.5**	**$751.1**	**$203.3**	**$250.5**	**$208.9**	**$225.2**	**$887.9**	**$250.6**	**$289.9**	**$265.7**	**$307.2**	**$1,113.4**	**$1,343.2**
Total expenses	610.9	704.5	843.9	269.1	314.8	290.8	(73.7)	800.9	353.4	382.7	335.3	366.2	1,437.6	1,599.8
Cost of sales	91.8	95.7	129.8	32.8	39.9	36.7	44.8	154.2	42.4	49.1	46.3	53.6	191.5	241.1
Research and development	302.2	354.8	461.6	142.1	157.9	158.7	170.2	628.9	174.7	182.0	153.6	162.4	672.6	709.9
Selling, General and administrative	198.2	235.4	302.5	92.8	101.5	94.0	118.7	407.1	114.8	130.0	113.9	128.7	487.3	562.6
Operating income	**($110.2)**	**($156.0)**	**($92.8)**	**($65.9)**	**($64.2)**	**($81.9)**	**$298.9**	**$87.0**	**($102.8)**	**($92.8)**	**($69.6)**	**($59.0)**	**($324.2)**	**($256.6)**
Total other income	(7.9)	(20.1)	(32.0)	(8.8)	(18.3)	(8.6)	(9.2)	(44.9)	(9.8)	(9.8)	(9.8)	(9.8)	(39.1)	(39.1)
Equity in the loss of BioMarin/Genzyme	(1.2)	(1.1)	(0.9)	(0.2)	(0.2)	(0.2)	(0.5)	(1.0)	(0.9)	(0.9)	(0.9)	(0.9)	(3.5)	(3.5)
Interest income	2.7	3.2	6.3	0.7	1.0	1.3	1.3	4.4	1.1	1.1	1.1	1.1	4.4	4.4
Interest expense	(7.6)	(11.8)	(36.6)	(9.5)	(10.0)	(9.4)	(10.0)	(38.9)	(10.0)	(10.0)	(10.0)	(10.0)	(40.0)	(40.0)
Impairment loss on equity investments	-	0.3	(0.1)	0.2	(9.1)	(0.3)	-	(9.2)	-	-	-	-	-	-
Debt conversion expense	(1.8)	(13.0)	(0.7)	(0.2)	-	-	-	(0.2)	-	-	-	-	-	-
Pretax income	**(118.1)**	**(176.1)**	**(124.8)**	**(74.7)**	**(82.5)**	**(90.4)**	**289.7**	**42.1**	**(112.6)**	**(102.5)**	**(79.4)**	**(68.8)**	**(363.3)**	**(295.7)**
Provision for income taxes	(3.5)	(0.2)	9.1	(7.2)	(0.6)	0.5	143.5	136.2	3.0	3.0	3.0	3.0	12.0	15.0
Net Income	**($114.6)**	**($176.0)**	**($133.9)**	**($67.5)**	**($82.0)**	**($90.9)**	**$146.2**	**($94.2)**	**($115.6)**	**($105.5)**	**($82.4)**	**($71.8)**	**($375.3)**	**($310.7)**
Basic EPS	($0.95)	($1.28)	($0.92)	($0.43)	($0.51)	($0.57)	$0.90	($0.60)	($0.71)	($0.64)	($0.50)	($0.43)	($2.29)	($1.85)
Diluted EPS	**($0.95)**	**($1.28)**	**($0.92)**	**($0.43)**	**($0.51)**	**($0.60)**	**$0.90**	**($0.64)**	**($0.71)**	**($0.64)**	**($0.50)**	**($0.43)**	**($2.29)**	**($1.85)**
Shares outstanding - Basic	120.2	137.7	146.3	157.6	160.4	160.9	162.3	160.3	163.1	164.0	164.8	165.6	164.4	167.7
Shares outstanding - Diluted	**120.2**	**137.7**	**146.3**	**157.6**	**160.4**	**161.1**	**162.3**	**160.4**	**163.1**	**164.0**	**164.8**	**165.6**	**164.4**	**167.7**

Source: Company reports and RBC Capital Markets estimates

Valuation

Our base case of $155/share assumes stable base business growth, Vimizim to grow to $600M franchise by 2020, PEG-PAL a $300M franchise by 2022 (80% probability), BMN-701 a $450M franchise by 2020 (80% probability), and $17/share for remaining pipeline (BMN-190, BMN-270). We add $26/share for BMN-111 achondroplasia assuming 65% probability on peak $2B drug and $25/ share for drisapersen in DMD based on $1000M peak sales (65% prob.) We use 9% discount rate and blended tax rates ranging from 18% to 25%, depending on projected product/ geographical mix in our DCF valuation.

Price target impediments

Our price target is primarily dependent on prospects of the base business continuing to grow modestly as well as pipeline clinical, regulatory, and commercial success of Vimizim, Peg-Pal, and other pipeline products such as BMN-701 and drisapersen. If pipeline programs fail or the current base business has disappointing sales relative to consensus expectations, the stock would be unlikely to meet our price target. Also, while management has been fairly confident on getting drisapersen approved, the AdCom panel ended up being mixed after reviewing the documents. A potential rejection of drisapersen could decrease management's credibility and cause investors to have less conviction on BMRN's other pipeline products, including the high-risk Batten's program.

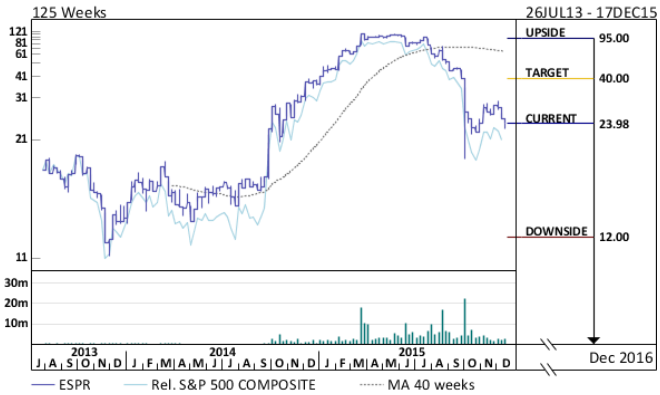
Esperion Therapeutics (ESPR)

Outperform, Speculative Risk

Price Target USD $40.00

Target/Upside/Downside Scenarios

Exhibit 83: Esperion Therapeutics.



Source: RBC Capital Markets estimates

Target price/base case

Our base case of $40/share is based on assigning ETC-1002 a 20% probability to market (down from 25-35% previously). We reduced the probability of success of ECT-1002's approval for conservatism. We estimate ETC-1002 could become a $2B+ US drug (peak sales) by 2025; we also estimate 15% ex-US royalty and use a 9% discount rate.

Upside scenario

Our upside scenario assumes a higher probability of success of 40% (lowered from 75%) for ETC-1002, yielding $95/share. We reduced the probability of success of ECT-1002's approval for conservatism. We assume no CVOT trial will need to be completed prior to FDA approval. We lowered the probability of success of ECT-1002's regulatory approval from 75% to 40% for conservatism.

Downside scenario

Our downside scenario of $12 assumes a lower probability of success for ETC-1002 (reduced to 10% from 15% previously). We reduced the probability of success of ECT-1002's approval for conservatism. Our downside valuation is predicated on whether long-term safety issues arise and/or a large outcomes study needs to be completed for approval.

Investment summary

We believe ESPR represents an attractive long-term opportunity, as its lead drug candidate ETC-1002 is fairly de-risked with multiple Phase II studies and clear efficacy. ETC-1002 is a novel, first-in-class, once-daily pill that shows a solid 25–30% reduction in LDL cholesterol. We think ETC-1002 can be a multi-billion dollar blockbuster drug, with potential $2–3B peak US sales. While we think it will take some time through 2016-17 for ESPR to play out as Phase III data won't come until 2017, we think the stock looks very cheap for a Phase III billion-dollar potential asset that is wholly-owned, somewhat de-risked and likely to work.

Potential catalysts for the stock

Phase II "high dose statin" data with ETC-1002 in mid-2016: The ECT1002-035 study is evaluating ECT-1002 combo therapy with "high dose statins" to prove the drug works even with high dose statin background and ETC efficacy is not diminished.

Landing a major global partnership or getting acquired: ESPR owns exclusive worldwide rights to ETC-1002. We think that ESPR sets up well to land a global pharma partnership or get acquired, given tuck-in synergy with commercial salesforces from big pharma who already hit the key CV/diabetes markets.

AMGN Repatha CVOT and IVUS imaging data: If positive (we're confident), these data could not only bolster the PCSK9 class but also raise confidence in other LDL-lowering drugs like ESPR's ETC-1002.

Risks to our investment thesis

Failure to develop ETC-1002 into safe and efficacious drug for hypercholesterolemia. ESPR is planning to launch a Phase III program next. Its Phase II success seen so far may not translate to its future Phase III studies.

ETC-1002 may face unknown safety risks. The FDA had previously put ETC-1002 on 2 partial clinical holds, due to its structural similarity to PPAR alpha drugs and toxicities seen in monkeys. ETC-1002 showed clean results in two-year rat and mouse carcinogenicity studies, and the FDA lifted the PPAR partial clinical hold in record time. Still, long-term studies will be needed to demonstrate the safety of ETC-1002.

High dose statins could already max out the pathway, making ETC-1002 less relevant and less efficacious.

ESPR may face additional risks from other LDL-C lowering therapies. PCSK9 inhibitors are gaining sales traction, and MRK's CETP inhibitor (oral) could enter the market within the next couple of years.

2016 thoughts on ESPR

We think ESPR has a drug on its hands but it will take some time through 2016-17 to play out as the key Phase III data won't come until well into 2017. We do think the stock could trade up into the mid-16 "high dose statin" data but there is a lot of debate around this and even if it's positive it will help but not fully solve a lot of the other uncertainties investors have right now (full data, safety, regulatory decision without CV outcomes data). Thus, we're not very high conviction on the stock in 2016 as the key debates and answers will take some time.

FDA cardiovascular Adcom panel vote against MRK's Zetia label expansion in December 2015 makes confidence in the clinical and regulatory path for ESPR murkier. There are lots of questions that need to be answered and we won't have these answers for a while, so we believe the stock is likely to be range bound. (1) Will the drug work on high dose statins? Data mid-16 could be a catalyst but even if positive and stock goes up, there are still other questions that need to be answered. (2) Will the drug be safe? Full Phase III data are far away in 2017). (3) Will they get approved on just an LDL reduction of 20-30%? Won't know this until filed and Adcom in 2018-19. A year ago it was simply "LDL is the best surrogate" and drugs that lower cholesterol can get FDA approved, but this is simply not known today and thus we believe only investors with a long-term horizon should buy the stock.

On a positive, bigger picture, ESPR looks very cheap for a Phase III billion-dollar potential asset that is wholly-owned, somewhat de-risked, and is a drug that probably works. So with a longer-term time horizon, investors with patience could be rewarded. But it is just a question of when we get the Phase III data and when does it get rewarded for it as Phase III won't start until mid-16 (been pushed out 1-2x as original was starting by YE:15) and data is not until 2017. As such this will require patience. There is important Phase II "high dose statin" data with ETC-1002 mid-16 that should move the stock, but otherwise not many catalysts other than a partnership, which we don't see anytime soon.

What are the next steps? After their analyst event at AHA (11/10), ESPR will be initiating two further studies of ETC1002 — a Phase II study in combo with "high dose statins" which is important to prove that the drug works even with high dose statin background and ETC efficacy is not diminished (data mid-16); and a Phase III long-term safety study on statin background. Investors are looking for clean safety profile here—no liver toxicity, no increase in systemic statin levels, no further muscle toxicity, etc. Also, ESPR plans to finalize the design of their global Phase III pivotal study by mid-16 for initiation thereafter, and also initiate a CVOT study in H2:16.

While pivotal Phase III data won't be available near-term and ETC-1002 may not get approved until late 2018, investors may derive further comfort from AMGN Repatha CVOT and IVUS imaging data next year. If positive (we're confident), these data could not just bolster the PCSK9 class, but also raise confidence in other LDL-lowering drugs like ESPR's ETC1002 to FDA and thus is a catalyst for ESPR. Note the MRK CETP Phase III data are also coming, which is a major competitive threat, but the likelihood of positive data is very low.

Bear case

- Lack of catalysts in 2016.
- Limited long-term safety, 4 monkeys died, limited chronic dosing beyond 3 months, drug has had 2 partial clinical holds.

- Controversy on high-dose statin results (we don't think this is a big issue) and whether high dose statins will already max out the pathway and thus make ETC-1002 less relevant and less efficacious.
- CVOT study will be needed. Regarding CVOTs, it bears to note two issues. (1) Will ESPR be required to complete CVOT study for FDA approval? Management seems to have backed away from a confident 'no'. (2) Will CVOT be powered to work period? Management said they were modeling LLY's shorter trial design, but given LLY evacetrapib failure, does that mean ESPR now needs a larger, longer, more expensive CVOT now?
- How do you know they don't have to run CV outcomes studies pre-approval? It's a different mechanism than statins and PCSK9 is pretty clear how that works. ESPR, how do you know for sure? Management seems to have backed away from a confident 'no'.
- Have to worry about PCSK9 competition and then I have to worry about CETP data coming – too many things to have to worry about.
- Can ETC-1002 compete initially against PCSK9's CVOT data while it has no CVOT data on label? Pricing will be a major issue without outcomes studies and vs CETP, which will have outcomes data.
- Nobody will partner or acquire the drug until we know what happens with MRK's CETP in 2016, and FDA cardiovascular Adcom panel vote against MRK's Zetia label expansion in December 2015 makes confidence in the clinical and regulatory path for ESPR murkier.

Exhibit 84: ESPR's expected news flow

Time	Expected News Flow	Program
ETC1002		
Dec 14, 2015	Anticipated Adcom panel for Merck's Improve-IT	-
Dec 2015	Initiate Phase II study ETC1002-035 to evaluate '1002 in combination with high-dose statins	ETC1002
Dec 2015	Initiate Phase III study ETC1002-040 long-term safety study on background statin therapy	ETC1002
H1:16	File IND for fixed dose combination of ETC1002 and ezetimibe	ETC1002
mid '16	Potential results of the Phase II study ETC1002-035 of '1002 in combination with high-dose statins	ETC1002
mid '16	Initiate global Phase III efficacy study in patients with statin intolerance	ETC1002
H2:16	Initiate Phase III CVOT study	ETC1002
H1:17	Potential data from Phase III long-term safety study (ECT1002-040) on background statin therapy	ETC1002
2018	Potentially submit for regulatory approval in EU and USA	ETC1002
YE:18-2019	Potential FDA approval for lowering LDL-C	ETC1002
Preclinical Programs		
TBD	Initiate Phase I	ESP41091
TBD	Initiate Phase I	4WF

*Note: Highlighted in blue indicates events of high significance

Source: Company reports and RBC Capital Markets estimates

Exhibit 85: ESPR's income statement

($ in millions, except per share) Fiscal Year Ends December	FYE 2014A	1QA Mar-15	2QA Jun-15	3QA Sep-15	4QE Dec-15	FYE 2015E	1QE Mar-16	2QE Jun-16	3QE Sep-16	4QE Dec-16	FYE 2016E	FYE 2017E	FYE 2018E	FYE 2019E
Revenues:														
ETC1002													8.9	222.2
ETC1002 ex-US royalty													-	40.6
Grant income	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Total Revenues, net	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**8.9**	**262.8**
Costs and expenses:														
Cost of product sales													1.8	21.8
Research and development	25.3	7.4	7.2	7.2	8.0	29.8	9.0	10.0	11.0	12.0	42.0	50.4	60.5	72.6
General and administrative	10.9	4.0	5.3	5.7	6.0	21.0	6.5	7.0	7.5	8.0	29.0	34.8	43.5	54.4
Total operating costs and expenses	36.2	11.4	12.5	12.9	14.0	50.8	15.5	17.0	18.5	20.0	71.0	85.2	105.8	148.8
Income (loss) from operations	**(36.2)**	**(11.4)**	**(12.5)**	**(12.9)**	**(14.0)**	**(50.8)**	**(15.5)**	**(17.0)**	**(18.5)**	**(20.0)**	**(71.0)**	**(85.2)**	**(96.8)**	**114.0**
Interest expense	(0.3)	(0.1)	(0.1)	(0.1)	(0.1)	(0.5)	(0.1)	(0.1)	(0.1)	(0.1)	(0.4)	(0.4)	(0.4)	(0.4)
Change in fair value of warrant liability	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Other income (expense), net	0.1	0.1	0.2	0.2	0.2	0.8	0.2	0.2	0.2	0.2	0.8	0.8	0.8	0.8
Total interest and other, net	(0.2)	(0.0)	0.1	0.1	0.1	0.3	0.1	0.1	0.1	0.1	0.4	0.4	0.4	0.4
Income (loss) before income taxes	(36.4)	(11.5)	(12.4)	(12.8)	(13.9)	(50.5)	(15.4)	(16.9)	(18.4)	(19.9)	(70.6)	(84.8)	(96.4)	114.4
Provision for Income Tax	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Net income (loss)	**(36.4)**	**(11.5)**	**(12.4)**	**(12.8)**	**(13.9)**	**(50.5)**	**(15.4)**	**(16.9)**	**(18.4)**	**(19.9)**	**(70.6)**	**(84.8)**	**(96.4)**	**114.4**
EPS (basic)	(2.22)	(0.56)	(0.55)	(0.57)	(0.58)	(2.26)	(0.61)	(0.63)	(0.65)	(0.66)	(2.55)	(2.95)	(3.23)	3.68
EPS (diluted)	(2.22)	(0.56)	(0.55)	(0.57)	(0.58)	(2.26)	(0.61)	(0.63)	(0.65)	(0.66)	(2.55)	(2.95)	(3.23)	3.41
Shares outstanding:														
Basic	16.4	20.6	22.5	22.5	23.8	22.3	25.3	26.8	28.4	30.1	27.6	28.7	29.9	31.1
Diluted	16.4	23.1	25.0	25.0	26.3	24.8	27.8	29.3	30.9	32.6	30.1	31.2	32.4	33.6

Source: Company reports and RBC Capital Markets Estimates

Exhibit 86: ESPR's product pipeline

Drug	Mechanim of action	Indication	Stage: Pre-clinical	Phase I	Phase II	Phase III	Est time to market
ETC1002	inhibits ACL and activates AMPK	LDL-C lowering (hypercholesterolemia, hypertension)	→	→	→		2018
ESP41091	small molecule	cardiometabolic risk factors (T2DM, obesity)	→				2019+
4WF	ApoA-I mimetic	acute coronary syndrome (atherosclerosis)	→				2019+

Source: Company reports and RBC Capital Markets estimates

Valuation

Our base case of $40/share is based on assigning ETC-1002 a 20% probability to market. We reduced the probability of success of ECT-1002's approval for conservatism. We estimate ETC-1002 could become a $2B+ US drug (peak sales) by 2025; we also estimate 15% ex-US royalty and use a 9% discount rate.

Price target impediments

Failure to develop ETC-1002 into safe and efficacious drug for hypercholesterolemia. ESPR is planning to launch a Phase III program next. Its Phase II success seen so far may not translate to its future Phase III studies.

ETC-1002 may face unknown safety risks. The FDA had previously put ETC-1002 on two partial clinical holds due to its structural similarity to PPAR alpha drugs and toxicities seen in monkeys. However, ETC-1002 showed clean results in two-year rat and mouse carcinogenicity studies, and the FDA lifted the PPAR partial clinical hold in record time. The high-dose toxicity seen in a few monkeys may have been due to a one-time, incorrect dosing

error, as toxicity side effects were absent from other preclinical studies. Still, long-term studies will be needed to demonstrate the safety of ETC-1002

High dose statins could already max out the pathway, making ETC-1002 less relevant and less efficacious.

ESPR may face additional risks from other LDL-C lowering therapies. PCSK9 inhibitors are gaining sales traction, and MRK's CETP inhibitor (oral) could enter the market within the next couple of years.

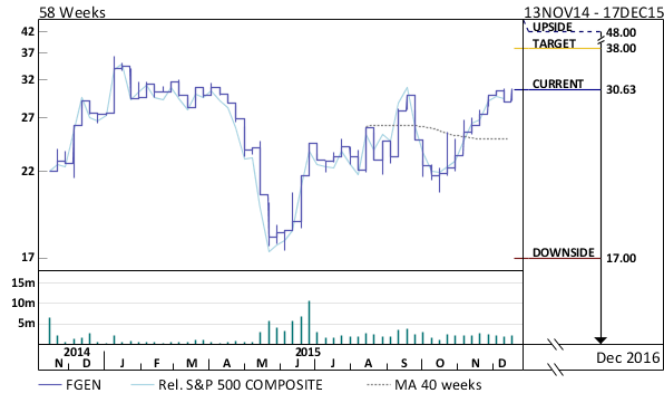
FibroGen, Inc. (FGEN)

Outperform, Speculative Risk

Price Target USD $38.00

Target/Upside/Downside Scenarios

Exhibit 87: FibroGen, Inc.



Source: RBC Capital Markets estimates

Target price/base case

Our base case of $38/share is a SOTP of 1) Roxadustat successfully penetrating the anemia market (both dialysis and non-dialysis) as a safe first-in-class oral drug and achieving $3B+ peak WW sales. We apply conservative ~45% prob. to market; 2) FG-3019 is developed for (idiopathic pulmonary fibrosis) IPF and becomes a $1.5B + WW drug by 2024 and applying 25-30% probability; and 3) small credit to FG-3019's potential opportunity in other indications such as pancreatic cancer with additional peak sales ~$500M, 4x peak sales and 15% prob. discounted back yields ~$2/share. We use a 10% discount rate consistently across the three SOTP components.

Upside scenario

Our upside scenario of $48 assumes 1) higher probability of success of 60% for Roxadustat, 2) higher prob. for FG-3019 in IPF, yielding ~$10/share, 3) maintain same $2/share for FG-3019's potential in pancreatic cancer, and 4) small credit to its fourth pipeline drug, FG-5200 in development for corneal blindness, which if it works in China could become a peak $300M drug, adding $2/share at 20% probability.

Downside scenario

Our downside scenario of $17 assumes 1) lower 20% probability to market for Roxadustat taking into consideration the great risk remaining in running a long and large phase III and the high bar on safety with new agents for anemia post removal of Omontys from the market in 2013. We do not include any valuation for other pipeline drugs such as FG-3019 and FG-5200 given the early stage of development or lack of controlled data.

Investment summary

We believe FibroGen (Outperform, Speculative Risk) represents an attractive long-term opportunity with multiple shots-on-goal in blockbuster indications like anemia, fibrosis and cancer. Lead candidate Roxadustat is in a Phase III program for anemia that could be a significant competitor as the only oral drug in a $6B+ class of EPO drugs. It is already partnered with AstraZeneca and Astellas through one of the largest pharma/biotech deals we have seen for any biotech product. FGEN's second drug, FG-3019, is in a Phase II anti-fibrosis antibody program for IPF, pancreatic cancer, DMD, and liver fibrosis (NASH, Hepatitis C). We think FGEN should climb higher as Phase III anemia continues to be de-risked through 2016 and as we approach: (1) major data across multiple Phase III anemia programs in 2017 and (2) under-the-radar fibrosis program begins to show positive Phase II data.

Potential catalysts for the stock

Pipeline advancement in 2016 should trigger a portion of the $1.7B remaining milestone payments from Astellas and Astrazeneca: FGEN is initiating Phase III studies in dialysis and non-dialysis settings for China, further advancing their global development program for anemia. Phase III data are expected in H2:16. We expect interim Phase II data for FG-3019 on top of abraxane + gemcitabine in pancreatic cancer (in January 2016), IND filing for Phase II trial in subjects with liver fibrosis (in Q1:16), and enrollment completion of Phase IIb randomized controlled study in mild-moderate IPF (in H1:16).

Risks to our investment thesis

Failure to develop Roxadustat into safe and efficacious drug for anemia: FGEN is currently launching an extensive, global Phase III program that will include almost 8,000 CKD patients with either incident dialysis, stable dialysis or no dialysis. Phase II data to date look clean, but there is no guarantee that this will be replicated in the larger, global Phase III program.

Failure to develop FG-3019 for IPF, pancreatic cancer and other fibrotic diseases: By 2017, FGEN will have started Phase II studies on liver fibrosis, DMD and IPF. While data has shown promising signs of reversal of fibrosis and promising efficacy in pancreatic cancer, and there is growing interest in anti-fibrosis antibodies, there is the risk that further clinical development could fail.

Lack of major near-term catalysts: Emerging biotech stocks with no commercial products primarily trade based on newsflow or catalysts regarding its pipeline drugs. Fibrogen's two major pipeline assets are in mid- to late-stage trials with key top-line data not expected until mid-2016 and later. This may not create the urgency for investors to buy Fibrogen stock in the near term given the opportunity cost analysis.

2016 thoughts on FGEN

We continue to like FGEN because: 1) they have multiple programs in Phase II/III and data has been very promising so far for blockbuster indications, 2) valuation is reasonable (25% of market cap is cash and the anaemia program is fully funded and partnered with AZN and Astellas), and 3) the other half of the company is starting to play out - Phase II fibrosis antibody FG-3019 is starting to report out positive data in pancreatic cancer.

We think key value driver (oral) Roxadustat for anemia has significant upside potential when Phase III data comes by 2017. While the key question is mostly safety – we think safety will be likely fine when data comes because 1) thousands of patients have been enrolling in Phase III and there have been 4+ DSMB analyses that have occurred with no modification or changes, 2) preclinical data is clean including a 2-year animal carcinogenicity study, 3) there was significant diligence done by many pharma companies and AZN and Astellas partnered it and put up significant upfront payments (hundreds of millions).

Two major global pharma partnerships with AstraZeneca (US, China) and Astellas (EU, Japan) provide major resources via one of the largest pharma/biotech deals we've seen, validating and funding this blockbuster program all the way through. In essence, FibroGen is eligible for ~20%-25% royalties and over $1.5B in clinical and commercial milestones – including $762M in upfronts combined. We model $3.5B peak sales for Roxadustat WW with conservative 40%-70% probability of success. Of note, FibroGen's management is also working closely with regulatory authorities to bring Roxadustat to China where the oral administration provides significant logistical advantages (estimate $500M+ potential sales in 2020), and where the Street is likely to undervalue this opportunity.

Separately, we will be keenly watching Phase II FG-3019 for fibrotic diseases. This is a separate, wholly owned anti-fibrotic antibody with a differentiated MOA (anti-CTGF). It is in a randomized controlled Phase IIb for treating orphan lung disease IPF; Phase IIa data showed signs of reversal of fibrosis, and a separate Phase II has shown promising efficacy in pancreatic cancer. The $8B acquisition of ITMN by Roche for IPF, and high interest in GILD's simtuzumab antibody for IPF and NASH supports what we think will be growing interest in FibroGen's off-the-radar fibrosis antibody.

Flush with cash: Management guided to ending YE:16 with $295-300M in cash, which does not account for the $1B+ in pre-commercial milestone payments FGEN could receive over the next two to three years. $1B in payments would translate to *one of the biggest balance sheets across SMID-cap biotech companies*.

Bear case

- Skeptics say HIF-1 is associated with immune surveillance (via Von Hippel-Lindau tumor suppression) and could lead to renal cell carcinoma.
- No major catalysts in 2016 with the exception of Phase III anemia data in H2:16 from China (e.g. USA/EU is in 2017-2018).
- There is always safety risk if FGEN is enrolling thousands of patients. Then only announcement can be a negative one, which is a safety issue during the study.
- There has been a history of some safety issues with Roxadustat and FGEN previously received a prior clinical hold, although FDA released it.
- IPF Phase II data was based on an open-label study with no placebo so difficult to interpret what's going on with efficacy given no comparator and fairly heterogeneous disease.
- Akebia (AKBA) comp trades at a fraction of FGEN and its oral anemia drug AKB-6548 is unpartnered. AKBA still needs to be watched.

- GSK reported Phase IIb data for daprodustat (GSK1278863) back in November 2015. The company will initiate Phase III in 2016 for treatment of anemia of CKD in subjects on dialysis and not yet on dialysis (filing 2019 Japan, 2021 US/ ROW).

Key questions and debates for FGEN

1. What advantages could FGEN bring to the anemia market?	**With a de-risked and well-funded Phase III program, FGEN's Roxadustat/FG-4592 is a serious competitive threat to AMGN's IV/subQ drugs**: 1) Roxadustat is an attractive oral anemia pill that does not require IV iron supplementation, 2) unlike ESAs, Roxadustat does not seem to pose CV risk (which led to declined ESA utilization), and 3) besides taking meaningful share from erythropoiesis-stimulating agents (ESAs), Roxadustat can further expand the current anemia market via treating pre-dialysis CKD and other undertreated anemia patients (e.g., cancer, inflammation).
2. Are there cardiovascular risks associated with Roxadustat or other safety concerns such as carcinogenesis?	**In contrast to ESAs, Roxadustat has not been associated with increased CV events, new and/or worsening hypertension, increased platelet counts, prolonged QT interval, or thrombosis that could lead to stroke.** In fact, Phase II studies have suggested that Roxadustat may help lower total cholesterol, improve the average HDL/LDL ratio, and even reduce the need for concomitant medications such as statins. Furthermore, Roxadustat treatment did not increase EPO beyond physiologic levels, and liver enzyme tests did not show any hepatotoxicity. Despite the association between HIF activity and angiogenesis, Roxadustat did not increase cancer risk (via tumor initiation, development, or metastasis) or otherwise adversely affect rodent mortality in 12 carcinogenicity studies conducted so far.
3. What is the commercial opportunity in China, and what regulatory path will FGEN pursue in China?	**FGEN is planning its first global launch in China, as a drug intended antihypertension, ESA, and IV iron**. With a large, undertreated population, China represents a large unmet opportunity. FGEN is pursuing a domestic regulatory approval pathway via FibroGen China, launching two Phase II studies in December 2015 and targeting potential approval in H2:17; AZN would be responsible for commercialization and distribution. The Chinese government's growing interest in addressing CKD (expanded reimbursement programs and dialysis facility build-outs) and in recombinant collagen for corneal blindness (FG-5200 tied to anemia pursuits) may help with regulatory approval in China. A post-marketing observational study would be required, and reimbursement delays may last six to 12+ months.
4. Are there other anemia opportunities for Roxadustat to target beyond CKD-related indications?	**The prevalence of anemia rises as CKD progresses**. However, anemia may also be brought on by other conditions, such as liver disease, cancers (myelodysplastic syndrome MDS), chemotherapy, chronic inflammation (lupus and rheumatic arthritis), genetic conditions (sickle cell anemia and enzyme deficiencies), or iron, vitamin B12, or folic acid deficiencies. These represent further upside options for Roxadustat, e.g., ESAs do not work in patients with inflammatory diseases such as Crohn's or lupus.
5. How is FibroGen's Roxadustat differentiated from Akebia's AKB-6548, which is also an oral HIF-inhibitor?	**While FGEN's Roxadustat is not the only HIF-PH inhibitor under development for treating anemia, it is the most advanced (FGEN is running extensive, global Phase III program).** It may also be more effective than AKB-6548 at treating patients with severe anemia by primarily targeting HIF-1 instead of HIF-2. In addition, Roxadustat may be safer than AKB-6548, as three patients under AKB-6548 treatment died during the Phase IIb study (n=138)—including one "possibly related" death from ischemic heart disease. While many of the patients were quite sick with cardiovascular and other co-morbidities, these deaths raise questions about AKB-6548's safety, especially in light of the increased CV risk associated with ESAs.

FG-3019: Plenty of upside opportunities with this interesting anti-fibrotic antibody

FGEN's second drug candidate, FG-3019, is a monoclonal antibody in Phase II development for treatment of fibrotic cancer and fibrotic diseases, including idiopathic pulmonary fibrosis (IPF), Duchenne muscular dystrophy (DMD) and nonalcoholic steatohepatitis (NASH). The drug ties back to the original foundation of the company, which was to discover drugs targeting fibrotic diseases and hence the name "FibroGen". FG-3019 inhibits the activity of Connective Tissue Growth Factor (CTGF), shown to be a central mediator of fiborisis and a contributor of tumor growth and metastasis. CTGF has been found to be elevated in multiple fibrotic tissue and organs. In a preclinical study in radiation-induced fibrosis in mice, treatment with FG-3019 showed statistically significant improvement in fibrosis as measured by HRCT.

FGEN is using FG-3019 to treat four main indications:

- **Pancreatic cancer:** FGEN is running an open label, placebo-controlled Phase II trial of FG-3019/abraxane/gemcitabine combo in patients with inoperable pancreatic cancer**.** A published surgery review showed that treated patients had median survival of 21 months vs. 9 months for patients whose tumors could not be fully removed. Twelve subjects are currently enrolled in the study, 7 of whom have finished. FGEN plans to enroll up to 40 subjects in the study, although management does not foresee enrolling all 40 subjects if data readouts continue to show efficacy. The company could theoretically elect to move forward before they finish enrolling all 40 patients, although management noted that the numbers are "still too small" to be convincing. Preliminary data will be presented at the ASCO GI Meeting in January 2016.
- **IPF:** FGEN has completed a dose-finding, single-arm open-label trial in subjects with moderate IPF. Results showed that 35% of subjects had stable or improved lung fibrosis after 48-week treatment. To management's knowledge, no IPF clinical trial has shown improvement in lung fibrosis – including trials of approved drugs Pirfenidone and nintedanib. FGEN is running Study 067, a randomized, double-blind, placebo-controlled trial as a first-line therapy for patients with mild to moderate IPF. Accrual has slowed due to the US launch of pirfenidone and nintedanib. Ability to complete the trial depends on opening sites in countries where pirfenidone and nintedanib are not prevalent. FGEN is activating 23 new sites in Canada, New Zealand, India, and South Africa, and an additional 9 sites in Australia, Bulgaria and Romania. Management expects enrollment to complete in H1:16, with topline data slated for H1:17. FGEN is also evaluating a trial that combines FG-3019 with an approved therapy.
- **DMD:** FGEN views DMD as high-priority program, as FG-1303 could potentially treat all subjects with DMD, regardless of the underlying genetic defect. As such, FG-1303 appears to be differentiated from the current drugs in development that target specific genetic defects. The company received FDA clearance in July 2015 for Investigational New Drug (IND) application to treat non-ambulatory patients with DMD. Endpoints include changes in lung function, arm function, and MRI assessment of cardiac and arm muscle fibrosis. The company is starting to screen subjects for enrollment in this trial. In 2016, the company intends to meet with the FDA to discuss plans for running trials in ambulatory patients.
- **Liver fibrosis (NASH, Hepatitis C):** In October 2015, FGEN met with the FDA to discuss the treatment of liver fibrosis due to NASH or Hepatitis C. FGEN is working with an FDA reviewer to finalize plans for a Phase II trial for NASH, and the company plans to file an IND in Q1:16. The NASH study will be a placebo-controlled trial, and management anticipates endpoints to include changes in fibrosis and liver function.

Exhibit 88: FGEN's expected news flow

Time	Expected News Flow	Program
Roxadustat (Anemia, Cancer)		
Dec 2015	Initiate enrollment of two Phase III studies in dialysis and non-dialysis settings in China	Roxadustat (China)
Q4:15/H1:16	Cornea green pass (Expedited review submission)	Roxadustat (China)
YE:15/Q1:16	Complete enrollment in non-dialysis setting (ANDES)	Roxadustat (US/ ROW)
YE:15/Q1:16	Complete enrollment in global incident dialysis study (HIMALAYS)	Roxadustat (US/ ROW)
YE:15/Q1:16	Complete enrollment in FibroGen stable dialysis study (SIERRAS)	Roxadustat (US/ ROW)
H1:16	File clinical application trials in myelodysplastic syndromes (MDS) and chemo-induced anemia (CIA)	Roxadustat (China)
H2:16	Data readout from two Phase III studies in dialysis and non-dialysis settings in China	Roxadustat (China)
2016	Submit for regulatory approval in China	Roxadustat (China)
H1:17	Data readout from initial Phase III studies in non-dialysis setting	Roxadustat (US)
H2:17	NDA approval in China	Roxadustat (China)
2017	Final Phase III data from non-dialysis and dialysis setting	Roxadustat (US/EU)
2018	Submit for regulatory approval in EU and USA	Roxadustat (US/EU)
FG-3019 (IPF, Pancreatic cancer, other fibrotic diseases)		
Q4:15/early'16	Efficacy data from Phase II study in liver fibrosis associated with HBV in Hong Kong	FG-3019 (liver fibrosis)
YE:15	Initiate non-ambulatory patient enrollment in Phase II study of DMD	FG-3019 (DMD)
Jan 2016	Preliminary Phase II data on FG-3019/abraxane/gemcitabine combo at ASCO GI Meeting (Study 069)	FG-3019 (pancreatic)
H1:16	Complete enrollment of Phase IIb randomized controlled study in mild-moderate IPF (Study 067)	FG-3019 (IPF)
Q1:16	File IND for Phase II trial in subjects with liver fibrosis due to NASH	FG-3019 (liver fibrosis)
2016	Initiate stage 4 Phase II study in pancreatic cancer	FG-3019 (pancreatic)
2016	Discussions with FDA to extend to ambulatory patients with DMD	FG-3019 (DMD)
H1:17	Topline data from Phase IIb randomized controlled study in mild-moderate IPF	FG-3019 (IPF)
FG-5200 (Corneal Implant)		
Q1:16	Start local production of corneal implant materials in China	FG-5200 (China)
Q3:16	Start required chronic toxicity study in China	FG-5200 (China)

Source: Company reports and RBC Capital Markets estimates

Exhibit 89: FGEN's product pipeline

Drug	Mechanim of action	Indication	Stage: Pre-clinical / Phase I / Phase II / Phase III	Est time to market
			HIF Platform	
roxadustat (FG-4592)	HIF-PH inhibitor	Anemia (DD- and NDD-CKD)	**US:**	2019
			EU:	2018
			China:	2H:17
			Japan:	2019+
FG-6874	HIF-PH inhibitor	Stem Cell Mobilization		2019+
FG-8205	HIF-PH inhibitor	Heart Failure after Myocardial Infarction		2019+
			Fibrotic Diseases	
FG-3019	anti-CTGF antibody	Pancreatic Cancer		2019
		Idiopathic Pulmonary Fibrosis		2019
		Liver Fibrosis (HBV, HCV, NASH)		2019
		Duchenne Muscular Dystrophy		2019+
			rhCOLLAGEN III Scaffold	
			Pilot / Pivotal	
FG-5200	corneal implant	Corneal Blindness		2017+

Partnered Wholly-owned

Source: Company reports and RBC Capital Markets estimates

Exhibit 90: FGEN's income statement

($ in millions, except per share) Fiscal Year Ends December	FYA 2014A	1QA Mar-15	2QA Jun-15	3QA Sep-15	4QE Dec-15	FYE 2015E	1QE Mar-16	2QE Jun-16	3QE Sep-16	4QE Dec-16	FYE 2016E	FYE 2017E	FYE 2018E	FYE 2019E
Revenues:														
Roxadustat Sales (China)													3.7	42.8
Roxadustat Royalties (US, ROW ex-China)													6.8	50.2
FG-3019 Sales													-	46.1
License and milestone revenue	117.2	11.5	106.9	13.0	20.0	151.4	10.0	62.0	10.0	30.0	112.0	150.0	100.0	50.0
Collaboration services and other revenue	20.4	4.8	13.7	6.5	9.0	34.0	10.0	11.0	12.0	13.0	46.0	55.0	56.1	57.2
Total Revenues, net	**137.6**	**16.3**	**120.6**	**19.5**	**29.0**	**185.4**	**20.0**	**73.0**	**22.0**	**43.0**	**158.0**	**205.0**	**166.6**	**246.2**
Costs and expenses:														
Cost of product sales													0.8	11.1
Research and development	150.8	50.5	51.6	52.1	45.0	199.2	37.0	39.0	41.0	43.0	160.0	184.0	202.4	212.5
Selling, general and administrative	36.9	10.5	9.7	11.2	12.0	43.4	10.0	8.0	9.0	10.0	37.0	40.7	44.8	56.0
Total operating costs and expenses	187.7	61.0	61.2	63.3	57.0	242.6	47.0	47.0	50.0	53.0	197.0	224.7	248.0	279.6
Income (loss) from operations	**(50.1)**	**(44.7)**	**59.3**	**(43.8)**	**(28.0)**	**(57.2)**	**(27.0)**	**26.0**	**(28.0)**	**(10.0)**	**(39.0)**	**(19.7)**	**(81.4)**	**(33.4)**
Toal interest and other, net	(9.4)	(1.9)	(2.1)	(1.3)	(2.0)	(7.3)	(2.0)	(2.0)	(2.0)	(2.0)	(11.0)	(11.0)	(11.0)	(11.0)
Income (loss) before income taxes	(59.5)	(46.6)	57.3	(45.1)	(30.0)	(64.4)	(29.0)	24.0	(30.0)	(12.0)	(47.0)	(30.7)	(92.4)	(44.4)
Provision for Income Tax	-	0.3	(0.2)	0.0	-	0.1	-	-	-	-	-	-	-	-
Net income (loss)	**(59.5)**	**(46.4)**	**57.1**	**(45.0)**	**(30.0)**	**(64.4)**	**(29.0)**	**24.0**	**(30.0)**	**(12.0)**	**(47.0)**	**(30.7)**	**(92.4)**	**(44.4)**
EPS (basic)	($3.17)	($0.78)	$0.95	($0.74)	($0.49)	($1.07)	($0.47)	$0.39	($0.49)	($0.19)	($0.76)	($0.49)	($1.41)	($0.65)
EPS (diluted)	($3.17)	($0.78)	$0.83	($0.74)	($0.49)	($1.07)	($0.47)	$0.39	($0.49)	($0.19)	($0.76)	($0.49)	($1.41)	($0.65)
Shares outstanding:														
Basic	18.8	59.2	59.8	60.8	61.0	60.2	61.3	61.5	61.7	62.0	61.6	62.9	65.4	68.0
Diluted	18.8	59.2	68.8	60.8	61.0	62.4	61.3	61.5	61.7	62.0	61.6	62.9	65.4	68.0

Source: Company reports and RBC Capital Markets Estimates

Valuation

Our base case of $38/share is a SOTP of 1) Roxadustat successfully penetrating the anemia market (both dialysis and non-dialysis) as a safe first-in-class oral drug and achieving $3B+ peak WW sales. We apply conservative ~45% prob. to market; 2) FG-3019 is developed for IPF and becomes a $1.5B+ WW drug by 2024 and applying 25-30% probability; and 3) small credit to FG-3019's potential opportunity in other indications such as pancreatic cancer with additional peak sales ~$500M, 4x peak sales and 15% prob. discounted back yields ~$2/share. We use a 10% discount rate consistently across the three SOTP components.

Price target impediments

Failure to develop Roxadustat into safe and efficacious drug for anemia: FGEN is currently launching an extensive, global Phase III program that will include almost 8,000 CKD patients with either incident dialysis, stable dialysis or no dialysis. Phase II data to date look clean, but there is no guarantee that this will be replicated in the larger, global Phase III program.

Failure to develop FG-3019 for IPF, pancreatic cancer and other fibrotic diseases: By 2017, FGEN will have started Phase II studies on liver fibrosis, DMD and IPF. While data has shown promising signs of reversal of fibrosis and promising efficacy in pancreatic cancer, and there is growing interest in anti-fibrosis antibodies, there is the risk that further clinical development could fail.

Lack of major near-term catalysts: Emerging biotech stocks with no commercial products primarily trade based on newsflow or catalysts regarding its pipeline drugs. Fibrogen's two major pipeline assets are in mid- to late-stage trials with key top-line data not expected until mid-2016 and later. This may not create the urgency for investors to buy Fibrogen stock in the near term given the opportunity cost analysis.

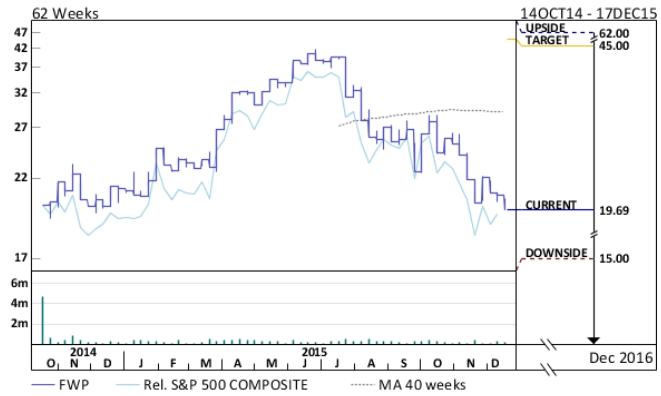
Forward Pharma (FWP)

Outperform, Speculative Risk

Price Target USD $45.00

Target/Upside/Downside Scenarios

Exhibit 91: Forward Pharma



Source: RBC Capital Markets estimates

Target price/base case

Our base case of $45/share is a sum-of-the-parts (SOTP) analysis of the following assumptions: 1) FWP wins the intellectual property (IP) interference vs. BIIB's Tecfidera and earns 10% royalty on Tecfidera net sales, with 55% weight; 2) FWP wins a 50% profit-share scenario with 35% weight, 3) FP187 developed as a wholly owned oral Multiple Sclerosis (MS) drug with peak sales ~$1B and 10% weight; and 4) FP187 developed as a wholly owned oral psoriasis drug with peak sales ~$500M. We use a 10% discount rate consistently across the three SOTP methods.

Upside scenario

Our upside scenario of $62/share assumes more weight on the profit-share scenario and less weight for the pure royalty scenario. For FWP187's opportunity in psoriasis, we assume a higher 75% probability of success, which yields $12/share. We expect FP187 to discontinue developing FP187 for MS and focus its efforts for psoriasis.

Downside scenario

Our downside scenario of $15/share assumes the IP interference does not go in FWP's favor. In this case, FWP would not earn any royalty from BIIB and would need to develop FP187 as a drug for MS and psoriasis. Downside would be from a 50% probability of success of FP187 becoming a $500M+ psoriasis and ~25% probability of success of FP187 becoming a $1B MS drug, which they still have and is in Phase III stages.

Investment summary

We rate Forward Pharma Outperform, Speculative Risk, because we think it has an attractive, low-risk Phase III MS drug with call option royalties on Tecfidera. We think there are four key scenarios with material upside for FWP: 1) Forward appears to have key patent positions that may be important for Biogen and may require meaningful royalties or even profit-sharing to FWP; 2) Forward's own oral drug FP187, a proprietary matrix tablet of dimethyl fumarate (DMF), which is the active drug in Tecfidera and entering Phase III in multiple sclerosis, should have similar efficacy as Tecfidera but fewer side effects and could be FDA approved in 2018–19 as a $1B + drug; 3) Forward can run a pivotal Phase III in psoriasis and have a high-efficacy oral drug that might be better than CELG's Otezla, which is a $1B+ drug; and 4) Forward could potentially become a take-out target by various MS/ immunology players.

Potential catalysts for the stock

- **Clinical:** Phase III trial initiations of FP187 in RRMS and psoriasis in 2016. We think FWP has an attractive, low-risk drug that is a proprietary matrix tablet of DMF with potentially similar efficacy to Tecfidera but fewer side effects.
- **Regulatory:** Settlement with BIIB before expected Court decision in H1:17. Consensus stands at a settlement for around a high mid-single digit royalty.

The following are risks to our investment thesis

- **Failure to maintain "senior status" on IP interference versus BIIB:** Within our price target, we consider a potential scenario wherein FWP wins the interference versus BIIB and earns a meaningful 10% royalty from Tecfidera's top line. However, patent litigation is a highly unpredictable process during which senior-party designation can change (e.g., Gilead Sciences versus Idenix). If FWP loses, then it would run the risk of infringing BIIB's IP and trying to develop a drug to compete with Tecfidera.
- **Failure to develop FP187 into safe and efficacious drugs for MS and psoriasis:** FWP's only clinical-stage drug is FP187, which is anticipated to enter pivotal trials for MS and psoriasis in 2016. The primary focus is on the MS market, but the drug does not have any clinical data from MS patients yet. Safety is another key variable that may not emerge until larger Phase III trials. Data to date look clean, but there is no guarantee that this will be replicated in larger and longer Phase III trials.
- **Regulatory risk:** There is inherent risk associated with any future regulatory approval process. Regulations may change over time, and filing of New Drug Applications (NDA) is both time-consuming and expensive.

2016 thoughts on FWP

We see large potential upside vs. downside risk, in our view, and thus we see at least three ways for the stock to go up over time: (1) a royalty settlement with BIIB, (2) an acquisition settlement by BIIB, (3) a legal patent win in the courts that confirm the patents, (4) development of their own fumarate tablet starting Phase III, or (5) a deal with a biopharma company whereby a partner develops/acquires the drug and runs Phase III. The US interference decision probably won't be until 2017 but a settlement is theoretically possible at any time. A patent interference "win" against BIIB could lead to the right to damages including a royalty above consensus e.g. 10-15% or higher vs. consensus mid-high single digits, which we believe has a potential upside valuation delta of 50-100% or higher from the current share price. We think a settlement would also be a winning scenario for FWP.

What are the next steps?

In the ongoing US FWP/BIIB interference case, where FWP holds senior status and won the first motion against BIIB (on filing dates), BIIB recently filed another motion (#6) in order to negate their first loss.

The court cross-examined BIIB's expert witnesses and preliminarily reviewed BIIB's priority filing, and further opposition filings/arguments are expected into 2016. Despite a combined motions and priority phase, continued delays, requests for extensions, and flood of filings (esp by BIIB) have continuously pushed out timelines. For example, recent lengthy diligence document by BIIB filed in December showing diligence and work on 480mg DMF since 2004 excluded sufficient references and FWP has requested additional time to respond. In mid-December, the Court also noted that the diligence report did not include sufficient citations for the diligence chart and the parties will need additional time to respond. Currently, final oral argument is scheduled for January 9, 2017 (delayed from original 1/22/16 date), thus a decision could come H1:17 (unless a settlement is reached beforehand).

The consensus is a settlement with some form of mid-high single-digit royalty (Fumapharma's 8% rate and other historical examples support 8-10% as low-end floor), because it's not consensus sentiment that they will win. We have it probability adjusted, but if they win, then probability goes to 100% on whatever royalty one assumes, which is 50-100% higher than current valuation.

In the German legal dispute on FWP's German utility model, an oral proceeding is still scheduled for March 24th, 2016. While the patent under contention is not the same as those under US interference, a win by FWP in Germany could help bolster confidence in FWP's IP portfolio. FWP also plans to initiate Phase III clinical studies next year (we think for psoriasis and RRMS), and studies supporting future regulatory filing for FP187 are continuing

Bear case

- No major catalysts anytime soon – interference is ongoing but no decision is really expected until at least 2017.
- Company talks about developing their own drug but it's unlikely they ever really materially move that forward or commit much money to it (more of a leverage tool).
- BIIB has high powered legal teams and could continue to push out or delay things and make compelling argument around their diligence chart that shows they were working on DMF 480mg for years before it was filed to USPTO.
- DMF market has gotten less interesting over the last year after BIIB lowered guidance and scripts have gone flattish and pricing in EU was 25-30% of what the US price is.

Royalty is unlikely to be over 10-15% like company wants and BIIB will unlikely settle until they get further down the process, if at all. BIIB probably also wants to see out their pipeline in 2016 before they decide on doing anything.

Exhibit 92: FWP SOTP Valuation (weighted probabilities for Case 1, Case 2, FP187 for MS, and FP187 for Psoriasis)

		Assumed Weight				
Tecfidera royalty	Case 1	0%	0%	55%	45%	0%
	Case 2	0%	0%	35%	55%	100%
FP187 developed for MS		0%	100%	10%	0%	0%

$/Share	Ultra Bear	Bear	Base Case	Bull	Ultra Bull
Tecfidera Royalty (Case 1)	$0	$0	$15	$19	$0
Tecfidera Royalty + Profit sharing (Case 2)	$0	$0	$20	$31	$56
FP187 - MS	$0	$11	$2	$0	$0
FP187 - Psoriasis	$4	$4	$8	$12	$12
	$4	**$15**	**$45**	**$62**	**$68**
Implied Market Cap ($M)	$201	$749	$2,238	$3,097	$3,401
Upside/downside	**-81%**	**-28%**	**116%**	**199%**	**228%**

Stock Price	FWP	**$20.6**
Share Count (in M)		50.2

Source: Company reports, RBC Capital Markets estimates

Exhibit 93: FP187 DCF for MS

Est. FP187 Revs as % of Tecfidera Launch ($M)	20%

Probability of pivotal trial start	75%
Probability of regulatory approval	60%
Probability to market	45%

Total $/share (probability adjusted) $20

BIIB Tecfidera Launch Ramp Year	2013 1	2014 2	2015 3	2016 4	2017 5	2018 6	2019 7	2020 8	2021 9	2022 10	2023 11	2024 12	2025 13	2026 14
Reported/Estimated WW Revenues ($MM)	$876	$2,800	$3,700	$4,200	$4,600	$4,830	$4,975	$5,074	$5,125	$5,125	$5,125	$5,125	$5,125	$5,125
Growth Y/Y		*220%*	*32%*	*14%*	*10%*	*5%*	*3%*	*2%*	*1%*	*0%*	*0%*	*0%*	*0%*	*0%*
				20%										
	2015E	**2016E**	**2017E**	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**
FP187 Est. WW revenues ($MM)		**Phase III**		**Filing**	**$175**	**$560**	**$740**	**$840**	**$920**	**$966**	**$995**	**$1,015**	**$1,025**	**$1,025**

DCF VALUATION	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	Terminal
WW revenue (in $M)		Phase III		Filing	$175	$560	$740	$840	$920	$966	$995	$1,015	$1,025	$1,025	
COGS (% of revs)					8%	8%	8%	8%	8%	8%	8%	8%	8%	8%	
					$14	$45	$59	$67	$74	$77	$80	$81	$82	$82	
R&D (% of revs)					20%	5%	4%	4%	3%	2%	2%	2%	2%	2%	
	$32	$50	$65	$40	$35	$28	$30	$34	$28	$19	$20	$20	$21	$21	
SG&A (% of revs)					80%	30%	23%	20%	15%	15%	15%	15%	15%	15%	
	$10	$15	$20	$100	$140	$168	$170	$168	$138	$145	$149	$152	$154	$154	
Total EBIT	-$42	-$65	-$85	-$140	-$14	$319	$481	$571	$681	$725	$746	$761	$769	$769	
Tax rate	0%	0%	0%	0%	0%	10%	18%	24%	24%	24%	24%	24%	24%	24%	
Profit	-$42	-$65	-$85	-$140	-$14	$287	$394	$434	$517	$551	$567	$578	$584	$584	
FCF (in $M)	-$43	-$62	-$78	-$132	-$7	$295	$403	$442	$526	$560	$576	$589	$597	$600	$1,050
Discount period		0	1	2	3	4	5	6	7	8	9	10	11	12	12
NPV		-$62	-$71	-$109	-$5	$202	$250	$250	$270	$261	$244	$227	$209	$191	$334

Terminal Growth (%)	-30%
Discount Rate	10%
NPV Sum ($M)	$2,192
Shares Outstanding (MM)	50.2
Probability of Success	45%

Prob. adjusted NPV ($M)	**$20**

Source: Company reports, RBC Capital Markets estimates

Exhibit 94: Case 1 - FWP wins interference against BIIB (10% royalty)

FP187 Royalty APP ---> Valuation scenario if FWP wins interference vs. BIIB Tecfidera on IP

Royalty rate to FWP	10%
Probability	75%

	NPV	$/share
Prob. adjusted NPV on WW royalties	$1,589	$32
Prob. adjusted NPV on US royalties only	$1,229	$24
Average prob. adjusted NPV (US + WV	$1,409	$28

Tecfidera Est. Sales	2014	2015	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
Worldwide	$2,909	$3,595	$3,875	$4,079	$4,269	$4,417	$4,549	$4,630	$4,666	$4,702	$4,738	$4,775
y/y growth		*24%*	*8%*	*5%*	*5%*	*3%*	*3%*	*2%*	*1%*	*1%*	*1%*	*1%*
U.S.	$2,426	$2,882	$3,055	$3,177	$3,304	$3,403	$3,506	$3,576	$3,611	$3,647	$3,684	$3,721
y/y growth		*19%*	*6%*	*4%*	*4%*	*3%*	*3%*	*2%*	*1%*	*1%*	*1%*	*1%*

Royalty to FWP											
Worldwide	$342	$368	$388	$406	$420	$432	$440	$443	$447	$450	$454
U.S. only	**$274**	**$290**	**$302**	**$314**	**$323**	**$333**	**$340**	**$343**	**$347**	**$350**	**$353**
SG&A	$22	$15	$5	$3	$3	$3	$3	$3	$3	$3	$3
Total EBIT (if US only)	$252	$275	$297	$311	$320	$330	$337	$340	$344	$347	$350
Tax Rate	24%	24%	24%	24%	24%	24%	24%	24%	24%	24%	24%
Profit	$191	$209	$226	$236	$243	$251	$256	$258	$261	$264	$266
Discount factor		0	1	2	3	4	5	6	7	8	9
NPV (US)		**$209**	**$205**	**$195**	**$183**	**$171**	**$159**	**$146**	**$134**	**$123**	**$113**
NPV (WW)		$268	$264	$253	$238	$223	$206	$189	$173	$159	$145

Discount rate	10%
Shares Outstanding	50.2

Source: Company reports, RBC Capital Markets estimates

Exhibit 95: Case 2 - FWP wins interference against BIIB (10% royalty and 50% BIIB profit share)

FP187 Royalty APP ---> Valuation scenario if FWP wins interference vs. BIIB Tecfidera on IP

Royalty rate to FWP	10%
Probability	75%

	NPV	$/share
Prob. adjusted NPV on WW royalties	$3,155	$63
Prob. adjusted NPV on US royalties only	$2,442	$49
Average prob. adjusted NPV (US + WV	$2,798	$56

Share of BIIB profit	50%
Profit Margin	55%

	Royalty Based						*Profit Share Based*					
Tecfidera Est. Sales	**2014**	**2015**	**2016E**	**2017E**	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**
Worldwide	$2,909	$3,595	$3,875	$4,079	$4,269	$4,417	$4,549	$4,630	$4,666	$4,702	$4,738	$4,775
y/y growth		*24%*	*8%*	*5%*	*5%*	*3%*	*3%*	*2%*	*1%*	*1%*	*1%*	*1%*
U.S.	$2,426	$2,882	$3,055	$3,177	$3,304	$3,403	$3,506	$3,576	$3,611	$3,647	$3,684	$3,721
y/y growth		*19%*	*6%*	*4%*	*4%*	*3%*	*3%*	*2%*	*1%*	*1%*	*1%*	*1%*
ROW	$483	$713	$820	$902	$965	$1,013	$1,044	$1,054	$1,054	$1,054	$1,054	$1,054
y/y growth		*48%*	*15%*	*10%*	*7%*	*5%*	*3%*	*1%*	*0%*	*0%*	*0%*	*0%*

Royalty to FWP						Profits owed to FWP					
Worldwide	$342	$368	$388	$406	$420	$1,251	$1,273	$1,283	$1,293	$1,303	$1,313
U.S. only	**$274**	**$290**	**$302**	**$314**	**$323**	**$964**	**$983**	**$993**	**$1,003**	**$1,013**	**$1,023**
SG&A	$22	$15	$5	$3	$3	$3	$3	$3	$3	$3	$3
Total EBIT (if US only)	$252	$275	$297	$311	$320	$961	$980	$990	$1,000	$1,010	$1,020
Tax Rate	24%	24%	24%	24%	24%	24%	24%	24%	24%	24%	24%
Profit	$191	$209	$226	$236	$243	$730	$745	$752	$760	$768	$775
Discount factor		0	1	2	3	4	5	6	7	8	9
NPV (US)		**$209**	**$205**	**$195**	**$183**	**$499**	**$463**	**$425**	**$390**	**$358**	**$329**
NPV (WW)		$268	$264	$253	$238	$648	$599	$549	$503	$461	$422

Discount rate	10%
Shares Outstanding	50.2

Source: Company reports, RBC Capital Markets estimates

Exhibit 96: FWP's registered utility model predates BIIB's EU patents

Drug (Company)	Patent Number	Region	Status	Expiration Date	Coverage
FP187 (Forward Pharma)	PCT/DK2005/000648	Int'l	pending	2025	controlled release pharmaceutical compositions; use of 480mg DMF/day dose to treat MS
	EP2316430	EU	granted	2025	DMF formulations with certain in vitro dissolution profiles
	EP05789026.1	EU	pending		parent application of EP2316430
	EP14172390.8	EU	pending		treatment of MS by a daily dose of 480mg with controlled release composition and in vitro dissolution profile
	EP14172396.5	EU	pending		treatment of MS by a daily dose of 480mg with controlled release composition
	EP14172398.1	EU	pending		treatment of MS by a daily dose of 480mg with enteric coating
	U.S. App. 14,213,399	US	pending		use of delayed release formulations of DMF to treat MS, with dose titration up to 480mg/day
	U.S. App. 14,212,503	US	pending		method of treating MS with 480mg/day, using delayed release formulations of 120-240mg
	U.S. App. 11/576,871	US	allowable		method of treating MS using ~480mg daily dose of DMF
	DE202005022112.0	Germany	registered	2015	registered utility model; similar to US11/576,871 and 14,213,399
	PCT/EP2010/050172	Int'l	pending	2030	delayed and slow release formulations of DMF
	EP2379063	EU	granted		matrix formulations with a thin enteric coating
	EP12193798.1	EU	pending		pharmaceutical formulation in form of an erosion matrix tablet with particular composition
	U.S. App. 13/143,498	US	allowed		US counterpart to EP2379063
Tecfidera (BIIB)	EP1131065	EU	granted	2019	formulations of DMF and uses for treating autoimmune diseases (incl MS)
	EP2137537	EU	granted	2028	counterpart to U.S. App. 8,399,514
	U.S. 6,509,376	US	granted	2019	formulations of DMF for treating autoimmune diseases (incl. MS)
	U.S. 7,320,999	US	granted	2020	method of treating MS using DMF
	U.S. 7,619,001	US	granted	2018	method of treating MS using DMF, MMF, or a combo thereof
	U.S. 7,803,840	US	granted	2018	method of treating an autoimmune disease (selected from autoimmune polyarthritis and MS) with DMF
	U.S. 8,399,514	US	granted	2028	dosing regimen of 240mg BID
	U.S. 8,524,773	US	granted	2018	method of treating MS using MMF

Highlighted blue indicate International applications that serve as basis for the patent family

Highlighted yellow indicate contended patents

Source: Company reports, RBC Capital Markets estimates

Exhibit 97: Upcoming events for the FWP/BIIB interference proceedings

Date	Event
03/24/16	File Forward Motion 19 (priority)
06/01/16	File oppositions to all motions (Time Period 3)
08/08/16	File all replies (Time Period 4)
08/31/16	File request for oral argument, motions to exclude, and observations (Time Period 5)
09/23/16	File oppositions to motions to exclude evidence, and file response to observations (Time Period 6)
10/12/16	File replies to oppositions to motions to exclude (Time Period 7)
10/21/16	File exhibits and sets of motions (Time Period 8)
01/09/17*	Default oral argument (Time Period 9)
* (9:30am)	

Source: Company reports, USPTO, RBC Capital Markets estimates

Exhibit 98: FWP's expected newsflow

Time	Expected News Flow	Program
Mar 24, 2016	Oral proceeding in Germany for infringement lawsuit filed against BIIB on FWP's German utility model	Patent Litigation
1H:16	Initiate Phase III trial of FP187 in RRMS	FP187-MS
2016	Initiate Phase III trial of FP187 in psoriasis	FP187-Psoriasis
2016	Initiate Phase II POC study of FP187 in psoriatic arthritis	FP187-PsA
Jan 9, 2017	Default oral argument for FWP/BIIB interference	Patent Litigation

Source: Company reports and RBC Capital Markets estimates

Exhibit 99: FWP's pipeline

Drug (Target)	Indication	Stage	Est. Year to Market
FP187	Relapse remitting multiple sclerosis	Phase II/III	2019
	Plaque psoriasis	Phase II/III	2018
	Psoriatic arthritis	Phase I/II	2019

Source: Company reports, RBC Capital Markets estimates

Exhibit 100: FWP's income statement

($ in millions, except per share) Fiscal Year Ends December	FYA 2014A	1QA Mar-15	2QA Jun-15	3QA Sep-15	4QE Dec-15	FYE 2015E	1QA Mar-16	2QA Jun-16	3QE Sep-16	4QE Dec-16	FYE 2016E	FYE 2017E	FYE 2018E	FYE 2019E
Revenues:														
Product Sales														17.5
Royalties											-	166.0	172.6	177.8
Other														
Total Revenues, net	-	-	-	-	-	-	-	-	-	-	-	**166.0**	**172.6**	**195.3**
Costs and expenses:														
Cost of product sales														1.4
Research and development	10.5	4.3	10.0	10.8	12.0	37.1	14.5	16.0	17.0	18.0	65.5	75.0	82.5	90.8
Selling, general and administrative	9.2	4.1	3.5	4.6	6.0	18.3	7.0	7.5	8.0	8.5	31.0	50.0	90.0	143.2
Total operating costs and expenses	19.7	8.4	13.5	15.4	18.0	55.4	21.5	23.5	25.0	26.5	96.5	125.0	172.5	235.3
Income (loss) from operations	**(19.7)**	**(8.4)**	**(13.5)**	**(15.4)**	**(18.0)**	**(55.4)**	**(21.5)**	**(23.5)**	**(25.0)**	**(26.5)**	**(96.5)**	**41.0**	**0.1**	**(40.0)**
Other:														
Fair value adjustment to net settlement obligations to shareholder warrants	(4.8)	-	-	-	(0.5)	(0.5)	-	-	-	-	-	-	-	-
Other finance costs	(5.5)	(14.4)	4.1	0.3	0.1	(9.9)	0.1	0.1	0.1	0.1	0.2	0.2	0.2	0.2
Total other income	0.7	14.4	(4.1)	(0.3)	(0.6)	9.4	(0.1)	(0.1)	(0.1)	(0.1)	(0.2)	(0.2)	(0.2)	(0.2)
Provision for Income Tax	-	0.8	-	-	-	0.8	-	-	-	-	-	-	-	-
Preferential distribution	42.7	-	-	-	-	-	-	-	-	-	-	-	-	-
Net income attributable to FWP	**(61.8)**	**5.3**	**(17.7)**	**(15.8)**	**(18.6)**	**(46.7)**	**(21.6)**	**(23.6)**	**(25.1)**	**(26.6)**	**(96.7)**	**40.8**	**(0.1)**	**(40.2)**
EPS (basic)	(1.79)	0.11	(0.38)	(0.34)	(0.39)	(1.00)	(0.46)	(0.49)	(0.52)	(0.55)	(2.03)	0.85	(0.00)	(0.82)
EPS (diluted)	(1.79)	0.11	(0.38)	(0.34)	(0.39)	(1.00)	(0.46)	(0.49)	(0.52)	(0.55)	(2.03)	0.81	(0.00)	(0.82)
Shares outstanding:														
Basic	34.5	46.5	46.7	46.9	47.1	46.8	47.3	47.6	47.8	48.1	47.7	48.2	48.7	49.1
Diluted	34.5	49.0	46.7	46.9	49.6	48.1	49.8	50.1	50.3	50.6	50.2	50.7	51.2	51.6

Source: Company reports and RBC Capital Markets estimates

Valuation

Our base case of $45/share is a sum of the parts (SOTP) analysis of the following assumptions of: 1) FWP wins the intellectual property (IP) interference vs. BIIB's Tecfidera and earns 10% royalty on Tecfidera net sales, with 55% weight; 2) FWP wins a 50% profit-share scenario with 35% weight, 3) FP187 developed as a wholly owned oral Multiple Sclerosis (MS) drug with peak sales ~$1B and 10% weight; and 4) FP187 developed as a wholly owned oral psoriasis drug with peak sales ~$500M. We use a 10% discount rate consistently across the three SOTP methods.

Price target impediments

Failure to maintain "senior status" on IP interference versus BIIB: Within our price target, we consider a potential scenario wherein FWP wins the interference versus BIIB and earns a meaningful 10% royalty from Tecfidera's top line. However, patent litigation is a highly unpredictable process during which senior-party designation can change (e.g., GILD versus IDIX). If FWP loses, it would then run the risk of infringing BIIB's IP and trying to develop a drug to compete with Tecfidera.

Failure to develop FP187 into safe and efficacious drugs for MS and psoriasis: FWP's only clinical-stage drug is FP187, which is anticipated to enter pivotal trials for MS and psoriasis in 2016. The primary focus is on the MS market, but the drug does not have any clinical data from MS patients yet. Safety is another key variable that may not emerge until larger Phase III trials. Data to date look clean, but there is no guarantee that this will be replicated in larger and longer Phase III trials.

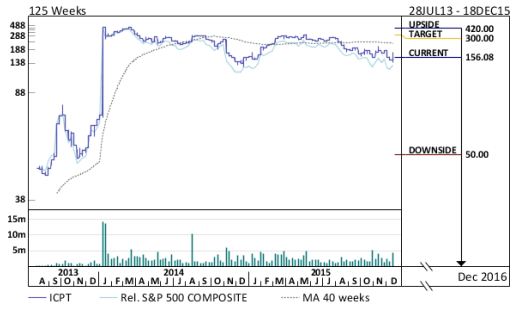
Intercept Pharmaceuticals (ICPT)

Outperform, Speculative Risk

Price Target USD $300.00

Target/Upside/Downside Scenarios

Exhibit 101: Intercept Pharmaceuticals.



Source: RBC Capital Markets estimates

Target price/base case

Our $300 price target (lowered from $490/share previously due to conservatism) is a sum-of-the-parts analysis of probability-adjusted value of OCA for PBC and NASH. We assign 80% and 60% probability for OCA to enter the PBC and NASH market successfully and become a peak $4B drug (probability adjusted). We assume: (1) PBC market entry in 2016 and NASH around 2018, (2) peak penetration of ~55% for PBC and ~30% for NASH, (3) terminal growth rates of -20% for both PBC and NASH, and (4) we discount risk-adjusted peak sales at 9%, which yields ~$30/ share (PBC) and ~$270/share (NASH).

Upside scenario

Our upside scenario of $420/share (lowered from $598/share for conservatism) assumes higher probability of success (NASH 70% versus 60% and PBC 85% versus 80%), yielding higher probability-adjusted peak sales of $4.5B. This could be justified if the data from the REGENERATE study (in 2018) were to replicate results from FLINT by showing reversal of fibrosis, benign tolerability, and convincing dose response. We assign a modest -15% terminal growth rate.

Downside scenario

Our downside scenario of $50/share (lowered from $107/share due to conservatism) assumes 15% probability that OCA works for NASH. If clinical data suggest potential serious safety concerns, particularly with regard to cardiovascular risk, then it would increase the risk for OCA approval while limiting the uptake if it does get to market. If this were the case, then we see lower peak sales of $1B worldwide. We also account for a more aggressive terminal discount rate of -30%.

Investment summary

We rate Intercept Pharmaceuticals Outperform, Speculative Risk, because we are long-term bullish on the company's lead drug, obeticholic acid (OCA), for two key liver diseases: the $500M orphan PBC opportunity and the $5B+ blockbuster NASH opportunity. We think investors significantly underestimate the very large NASH opportunity that we see, which could be the next big development in the hepatology field after Hep C over the last few years. We believe ICPT may be more range-bound in 2016 as investors focus on ICPT's execution on the upcoming PBC launch, which is expected in Q2:16 and should take an additional two quarters for investors to get a good handle on the launch trajectory. Longer-term, we believe the more important value driver – OCA in NASH -- will be a successful clinical program, with pivotal data reading out positively in 2018.

Potential catalysts for the stock

FDA AdCom panel for PBC April 7, 2016 and OCA approval in the US and EU: We see 80% probability of approval, which is expected May 29, 2016 for the US and Mid-2016 for the EU.

Better than expected WW sales for PBC: Launch expectations are relatively low at $45M for 2016, which is one of the lower launch estimates we've seen for orphan drugs. Upside surprise and strong execution and launch could shock the Street.

Risks to our investment thesis

Failure of OCA to show compelling efficacy in NASH: This is the significant market opportunity that could determine whether the drug could be a blockbuster or not. If the drug fails to show significantly better efficacy versus currently used, off-label options or emerging competitors, then it would greatly diminish the revenue potential of this drug.

Emergence of serious cardiovascular safety signals: One of the more common complications among NASH patients is heart disease. Thus, if OCA shows significant, adverse effects on lipid levels that cannot be well managed by the use of cholesterol-lowering drugs, then it would greatly limit its chance of FDA approval or market adoption potential.

May 29th PDUFA date for PBC in orphan indication PBC: Questions include whether something negative could come out on a label and whether the patient population could be narrowed were the FDA to issue warnings or identify issues that could impede initial sales uptake.

2016 thoughts on ICPT

We believe ICPT may be more range-bound in 2016 as this is a year primarily about execution on the PBC launch for obeticholic acid (OCA) which doesn't really get underway until at least Q2:16. Also, we think it will take at least two quarters to get a good handle on the launch trajectory. Based on survey work (November 11 note), expert conference calls (November 11 note), and an expert physician dinner event (November 11 note), we think 2016 consensus of $35-40M could be achievable but we think the launch will take some time to ramp up and we don't think that analysts are likely to need to significantly raise estimates or peak sales estimates. Bottom line is the first few quarters will take some time to determine launch and compliance/maintenance on therapy will also be a question for investors.

We acknowledge that investor expectations on the PBC launch aren't overly high, but Street is unlikely to be convinced either way (success or otherwise) until there are enough quarters on their hands and OUS launch will also be another question (doesn't start until H2:16 and takes even more time to get reimbursement – so quarterly sales there is more of a 2017 driver). Also important is that presuming NASH comes on in 2018-2019, the price of the drug will get dropped by 50-65% due to orphan pricing reverting to more normal pricing for NASH so the value of PBC goes down and it is really a NASH story long-term.

Longer-term, we are confident that the more important value driver – OCA in Phase III for NASH – will be a successful clinical program and pivotal data will be positive in 2018. In addition, ICPT is focused on completing other NASH studies (lipid study, a study in cirrhotics, etc) but all of these data are fairly far out in time for most investors (2017-2018) and thus the stock may be more range-bound in 2016.

Any issues with the recent PDUFA delay for PBC?

- Although there was a recent 90-day delay for the PBC PDUFA (now May 29, 2016), based on our conversations we do not believe there is any major concern with the PBC regulatory filing in the US
- The PBC application was under Priority Review so there was a short time to review the data and we believe the GI division has been extremely busy with other applications including tons of IND applications for other products in NASH over the last year that has kept the group extremely busy
- We believe there have been good ongoing conversations with the FDA and ICPT as this is a pretty high profile drug for the agency (it has Breakthrough Therapy in NASH) and we doubt they would do anything that would jeopardize/tarnish the overall profile of the drug.
- While disappointing there is a delay we don't believe this has any material change in probability for the likelihood of approval although we realize investors will be naturally nervous.

Bear case

- High expectations and already assumed positive AdCom vote (and delayed from January to April 2016) presents short-term risk into panel documents, panel discussion (such as bringing up any NASH safety data or lipid commentary) and safety commentary, and vote.
- Already assumed FDA approval for May 29, 2016 PDUFA and bears question if anything will come out on a label or the patient population could be narrowed of if there are any warnings or other issues that could impede uptake.
- Concerns on compliance of OCA in real-world settings given 20% increased absolute rate of pruritis (50% background rate goes to 70% incidence) and tolerability may require appropriate patient education and management.
- No major OCA NASH data readouts in 2016 yet there will be some competitor NASH data coming out in 2016 (TBRA data Q3:16, GILD YE:16 cirrhosis data and Phenex FXR H2:16 data, etc) which could increase competitor dynamics.
- Recent Phase II Japanese NASH data adds uncertainty to overall profile of OCA and fibrosis benefit and increases risk around ultimate Phase III study which is still far out.
- Uncertainty over risk/benefit profile for OCA given cholesterol effects and whether this will impact cardiovascular safety profile in large Phase III study.
- FDA is very conservative, especially with metabolic disease indications, any signs of CV risk they will ask for outcomes studies or be very cautious, particularly in a population of pts who already have increased CV risk.
- GILD also has data coming and they should show fibrosis reversal and work in cirrhotics too, and unlikely to have any safety issues. There are about 5 other NASH companies working on drugs too so ICPT has a lot of other oral companies to deal with.

Exhibit 102: OCA Model (for PBC and NASH)

Base Case

Prob. Of Success	PBC	80%	NASH	60%
PBC	Terminal Growth(%)			-20%
	Discount rate			9%
	NPV/share			**$29**
NASH	Terminal Growth(%)			-20%
	Discount rate			9%
	NPV/share			**$272**
Total $/share (probability adjusted)				**$300**

Tax Rate Assumption	
Tax Rate	35%

PBC Fundamental Assumptions

US	
Price of therapy	$75,000
Price growth	3%
Gross to net	10%

EU	
Price of therapy	$25,000
Price growth	3%
Gross to net	8%

Japan	
Price of therapy	$7,000
Price growth	2%
Gross to net	8%
Royalty rate	15%

NASH Fundamental Assumptions

US	
Price of therapy	$25,000
Price growth	2%
Gross to net	8%

EU	
Price of therapy	$10,000
Price growth	2%
Gross to net	8%

Japan	
Price of therapy	$7,000
Price growth	2%
Gross to net	8%
Royalty rate	15%

Bull Case

Prob. Of Success	PBC	85%	NASH	70%
Terminal Growth(%)				-15%
Discount rate				9%
Total $/share (probability adjusted)				**$420**

Bear Case

Prob. Of Success	PBC	70%	NASH	15%
Terminal Growth(%)				-30%
Discount rate				10%
Total $/share (probability adjusted)				**$50**

Ultra Bull Case

Prob. Of Success	PBC	90%	NASH	80%
Terminal Growth(%)				-10%
Discount rate				9%
Total $/share (probability adjusted)				**$506**

Ultra Bear Case

Prob. Of Success	PBC	50%	NASH	0%
Terminal Growth(%)				-30%
Discount rate				10%
Cash/share (YE:14E)				$12
Total $/share (probability adjusted)				**$49**

Penetration Summary	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
PBC													
US	0%	2%	7%	14%	21%	27%	33%	39%	44%	48%	52%	54%	56%
EU	0%	0%	2%	7%	14%	21%	27%	33%	39%	44%	48%	52%	54%
Japan	0%	0%	0%	2%	7%	14%	21%	27%	33%	39%	44%	48%	52%
NASH													
US	0%	0%	0%	2%	10%	15%	23%	25%	27%	28%	29%	29%	29%
EU	0%	0%	1%	2%	5%	8%	12%	15%	20%	25%	25%	25%	26%
Japan	0%	0%	0%	0%	2%	5%	8%	12%	18%	25%	25%	25%	25%

Unadjusted Sales (100% Probability of Succes)				PBC	100%	NASH	100%						
Total OCA Sales	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
PBC Sales, 100% Prob. ($MM)													
US	-	$23	$84	$60	$96	$128	$163	$200	$234	$264	$297	$320	$344
EU	-	-	$11	$15	$31	$48	$63	$80	$98	$114	$129	$145	$156
Japan	-	-	-	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Total	-	$23	$94	$75	$127	$176	$226	$280	$332	$379	$426	$466	$500
NASH Sales, 100% Prob. ($MM)													
US	-	-	-	$157	$876	$1,441	$2,416	$2,792	$3,204	$3,527	$3,874	$3,947	$4,017
EU	-	-	$39	$80	$214	$367	$587	$782	$1,109	$1,399	$1,483	$1,571	$1,636
Japan	-	-	-	-	$2	$5	$9	$14	$21	$29	$30	$31	$30
Total	-	-	$39	$237	$1,092	$1,813	$3,012	$3,588	$4,334	$4,955	$5,387	$5,548	$5,683
Total direct sales	-	$23	$134	$312	$1,217	$1,984	$3,229	$3,854	$4,646	$5,305	$5,782	$5,983	$6,153
Total royalties	-	-	-	$0	$2	$6	$9	$14	$21	$30	$30	$31	$30
Total Sales (100% Prob.	**-**	**$23**	**$134**	**$312**	**$1,219**	**$1,990**	**$3,238**	**$3,868**	**$4,667**	**$5,334**	**$5,813**	**$6,014**	**$6,183**

Source: Company reports and RBC Capital Markets estimates

Exhibit 103: PBC Model

Total PBC Revenue Opportunity: US, EU, Japan (Non-Probability Adjusted)

PBC Revenue Opportunity	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
US Gross revenue	-	-	$23	$84	$60	$96	$128	$163	$200	$234	$264	$297	$320	$344
EU Gross revenue	-	-	-	$11	$15	$31	$48	$63	$80	$98	$114	$129	$145	$156
Royalties from Japan	-	-	-	-	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Total WW gross revenue ($MM)	**-**	**-**	**$23**	**$94**	**$75**	**$127**	**$176**	**$226**	**$280**	**$332**	**$379**	**$426**	**$466**	**$500**

WW Patients Treated for PBC	**62,132**	**41,486**	**41,768**	**42,641**	**44,116**	**45,610**	**45,921**	**46,235**	**46,551**	**46,869**	**47,189**	**47,512**	**47,836**	**48,163**
WW Patients Eligible for OCA for PBC	**37,356**	**37,472**	**37,589**	**38,242**	**38,836**	**39,438**	**39,866**	**39,996**	**40,126**	**40,558**	**40,690**	**40,823**	**41,257**	**41,393**

US			2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
Price of therapy	$75,000	Population	320,000,000	322,240,000	324,495,680	326,767,150	329,054,520	331,357,901	333,677,407	336,013,149	338,365,241	340,733,797	343,118,934	345,520,766	347,939,412	350,374,988
Price (post NASH)	$25,000	Prevalence	96,000	96,672	97,349	98,030	98,716	99,407	100,103	100,804	101,510	102,220	102,936	103,656	104,382	105,112
Price growth	3%	% Diagnosed	**70%**	**70%**	**70%**	**71%**	**73%**	**75%**	**75%**	**75%**	**75%**	**75%**	**75%**	**75%**	**75%**	**75%**
Population	320,000,000	% who seek treatment	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%
Prevalence rate	0.030%	# Pts treated	40,320	40,602	40,886	41,761	43,238	44,733	45,046	45,362	45,679	45,999	46,321	46,645	46,972	47,301
Population growth	0.7%	% inadequate reponse to URSO	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%
Gross to net	10%	**# Pts eligible for OCA**	16,128	16,241	16,355	16,704	17,295	17,893	18,019	18,145	18,272	18,400	18,528	18,658	18,789	18,920
		Penetration	**0%**	**0%**	**2%**	**7%**	**14%**	**21%**	**27%**	**33%**	**39%**	**44%**	**48%**	**52%**	**54%**	**56%**
		# Pts treated by OCA	-	-	327	1,169	2,421	3,758	4,865	5,988	7,126	8,096	8,894	9,702	10,146	10,595
		Cost per month	$5,625	$5,794	$5,794	$5,968	$2,075	$2,137	$2,201	$2,267	$2,335	$2,405	$2,477	$2,552	$2,628	$2,707
		Gross revenue ($MM)	**-**	**-**	**$23**	**$84**	**$60**	**$96**	**$128**	**$163**	**$200**	**$234**	**$264**	**$297**	**$320**	**$344**

EU			2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
Price of therapy	$25,000	Population	742,000,000	742,146,545	742,293,119	742,439,722	742,586,354	742,733,014	742,879,704	743,026,423	743,173,171	743,319,947	743,466,753	743,613,588	743,760,451	743,907,344
Price growth	3%	Prevalence	146,545	146,574	146,603	146,632	146,661	146,690	146,719	146,748	146,777	146,806	146,835	146,864	146,893	146,922
Population	742,000,000	% Diagnosed	70%	70%	70%	71%	71%	71%	72%	72%	72%	73%	73%	73%	74%	74%
Prevalence	0.020%	% who seek treatment	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%
Population growth	0.1%	# Pts treated	61,549	61,561	61,573	62,465	62,478	62,490	63,382	63,395	63,408	64,301	64,314	64,326	65,220	65,233
Gross to net	8%	% inadequate reponse to URSO	34%	34%	34%	34%	34%	34%	34%	34%	34%	34%	34%	34%	34%	34%
		# Pts eligible for OCA	20,927	20,931	20,935	21,238	21,242	21,247	21,550	21,554	21,559	21,862	21,867	21,871	22,175	22,179
		Penetration	**0%**	**0%**	**0%**	**2%**	**7%**	**14%**	**21%**	**27%**	**33%**	**39%**	**44%**	**48%**	**52%**	**54%**
		# Pts treated by OCA	-	-	-	425	1,487	2,975	4,526	5,820	7,114	8,526	9,621	10,498	11,531	11,977
		Cost per month	$1,917	$1,974	$2,033	$2,094	$830	$855	$880	$907	$934	$962	$991	$1,021	$1,051	$1,083
		Gross revenue ($MM)	**-**	**-**	**-**	**$11**	**$15**	**$31**	**$48**	**$63**	**$80**	**$98**	**$114**	**$129**	**$145**	**$156**

Japan			2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
Price of therapy	$7,000	Population	127,600,000	127,344,800	127,090,110	126,835,930	126,582,258	126,329,094	126,076,436	125,824,283	125,572,634	125,321,489	125,070,846	124,820,704	124,571,063	124,321,921
Price growth	2%	Prevalence	2,459	2,454	2,449	2,444	2,439	2,435	2,430	2,425	2,420	2,415	2,410	2,405	2,401	2,396
Population	127,600,000	% Diagnosed	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%
Prevalence	0.002%	% who seek treatment	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%
Population growth	-0.2%	# Pts treated	885	883	882	880	878	876	875	873	871	869	868	866	864	862
Gross to net	8%	% inadequate reponse to URSO	34%	34%	34%	34%	34%	34%	34%	34%	34%	34%	34%	34%	34%	34%
Royalty rate	15%	**# Pts eligible for OCA**	301	300	300	299	299	298	297	297	296	296	295	294	294	293
		Penetration	**0%**	**0%**	**0%**	**0%**	**2%**	**7%**	**14%**	**21%**	**27%**	**33%**	**39%**	**44%**	**48%**	**52%**
		# Pts treated by OCA	-	-	-	-	6	21	42	62	80	98	115	130	141	152
		Cost per month	$537	$547	$558	$570	$581	$593	$604	$616	$629	$641	$654	$667	$681	$694
		Gross revenue ($MM)	**-**	**-**	**-**	**-**	**$0**	**$0**	**$0**	**$0**	**$1**	**$1**	**$1**	**$1**	**$1**	**$1**
		Royalties ($MM)	**-**	**-**	**-**	**-**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**

Ultra Bear Scenario Analysis, PBC Price does not change because NASH fails

PBC		2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027
U.S.															
	Cost per month	$5,625	$5,794	$5,794	$5,968	$6,147	$6,331	$6,521	$6,717	$6,918	$7,126	$7,339	$7,560	$7,786	$8,020
	Gross revenue ($MM)	-	-	$23	$84	$179	$285	$381	$483	$592	$692	$783	$880	$948	$1,020
EU															
	Cost per month	$1,917	$1,974	$2,033	$2,094	$2,157	$2,222	$2,289	$2,357	$2,428	$2,501	$2,576	$2,653	$2,733	$2,815
	Gross revenue ($MM)	-	-	-	$11	$38	$79	$124	$165	$207	$256	$297	$334	$378	$405
Japan															
	Cost per month	$537	$547	$558	$570	$581	$593	$604	$616	$629	$641	$654	$667	$681	$694
	Gross revenue ($MM)	-	-	-	-	$0	$0	$0	$0	$1	$1	$1	$1	$1	$1
	Royalties ($MM)	-	-	-	-	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Total WW gross revenue ($MM) if NASH fails		**-**	**-**	**$23**	**$94**	**$217**	**$365**	**$505**	**$647**	**$799**	**$948**	**$1,081**	**$1,215**	**$1,326**	**$1,424**

Source: Company reports and RBC Capital Markets estimates

Exhibit 104: NASH Model

NASH	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
US Gross revenue	$157	$876	$1,441	$2,416	$2,792	$3,204	$3,527	$3,874	$3,947	$4,017
EU Gross revenue	$80	$214	$367	$587	$782	$1,109	$1,399	$1,483	$1,571	$1,636
Royalties from Japan	-	$2	$5	$9	$14	$21	$29	$30	$31	$30
Total WW gross revenue($MM)	**$237**	**$1,092**	**$1,813**	**$3,012**	**$3,588**	**$4,334**	**$4,955**	**$5,387**	**$5,548**	**$5,683**
WW patients	14,333	57,615	96,088	155,075	188,255	235,517	275,548	290,083	294,832	296,135

US			2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
Price of therapy	$25,000	Population	324,729,648	331,224,241	337,848,726	344,605,700	351,497,814	358,527,771	365,698,326	373,012,293	380,472,538	388,081,989
Price growth	2.0%	Prevalence	6,494,593	6,624,485	6,756,975	6,892,114	7,029,956	7,170,555	7,313,967	7,460,246	7,609,451	7,761,640
		% Diagnosed	42%	43%	43%	44%	44%	45%	45%	46%	46%	47%
Population	300,000,000	% Under care	33%	35%	37%	39%	40%	41%	42%	43%	43%	43%
Prevalence	2.0%	% Advanced fibrosis	35%	35%	35%	34%	34%	33%	33%	32%	31%	30%
Population growth	2.0%	**# Pts eligible for OCA**	315,053	344,887	370,887	397,544	414,486	431,728	449,260	467,071	466,596	465,582
Gross to net	8%	**Penetration**	2%	10%	15%	23%	25%	27%	28%	29%	29%	29%
		# Pts treated by OCA	6,301	34,489	55,633	91,435	103,622	116,567	125,793	135,451	135,313	135,019
		Annual Price	$24,896	$25,394	$25,902	$26,420	$26,948	$27,487	$28,037	$28,598	$29,170	$29,753
		Gross revenue ($MM)	**$157**	**$876**	**$1,441**	**$2,416**	**$2,792**	**$3,204**	**$3,527**	**$3,874**	**$3,947**	**$4,017**

EU			2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
Price of therapy	10000	Population	502,003,002	502,505,005	503,007,510	503,510,518	504,014,028	504,518,042	505,022,560	505,527,583	506,033,110	506,539,143
Price growth	2%	Prevalence	10,040,060	10,050,100	10,060,150	10,070,210	10,080,281	10,090,361	10,100,451	10,110,552	10,120,662	10,130,783
Population	500,000,000	% Diagnosed	20%	21%	22%	23%	24%	25%	26%	27%	28%	29%
Prevalence	2.0%	% advanced fibrosis	20%	20%	20%	20%	20%	20%	19%	19%	19%	18%
Population growth	0.1%	**# Pts eligible for OCA**	401,602	422,104	442,647	463,230	483,853	504,518	498,962	518,671	538,419	528,827
Gross to net	8%	**Penetration**	2%	5%	8%	12%	15%	20%	25%	25%	25%	26%
		# Pts treated by OCA	8,032	21,105	35,412	55,588	72,578	100,904	124,741	129,668	134,605	137,495
		Annual Price	$ 9,958	$ 10,158	$ 10,361	$ 10,568	$ 10,779	$ 10,995	$ 11,215	$ 11,439	$ 11,668	$ 11,901
		Gross revenue ($MM)	**$ 80**	**$ 214**	**$ 367**	**$ 587**	**$ 782**	**$ 1,109**	**$ 1,399**	**$ 1,483**	**$ 1,571**	**$ 1,636**

Japan			2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
Price of therapy	7000	Population	126,582,258	126,329,094	126,076,436	125,824,283	125,572,634	125,321,489	125,070,846	124,820,704	124,571,063	124,321,921
Price growth	2%	Prevalence	2,531,645	2,526,582	2,521,529	2,516,486	2,511,453	2,506,430	2,501,417	2,496,414	2,491,421	2,486,438
Population	127,600,000	% Diagnosed	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
Prevalence	2.0%	% advanced fibrosis	20%	20%	20%	20%	20%	20%	20%	20%	20%	19%
Population growth	-0.2%	**# Pts eligible for OCA**	101,266	101,063	100,861	100,659	100,458	100,257	100,057	99,857	99,657	94,485
Gross to net	8%	**Penetration**	0%	2%	5%	8%	12%	18%	25%	25%	25%	25%
Royalty rate	15%	**# Pts treated by OCA**	-	2,021	5,043	8,053	12,055	18,046	25,014	24,964	24,914	23,621
		Annual Price	$ 6,971	$ 7,110	$ 7,252	$ 7,398	$ 7,545	$ 7,696	$ 7,850	$ 8,007	$ 8,167	$ 8,331
		Gross revenue ($MM)	$ -	$ 14	$ 37	$ 60	$ 91	$ 139	$ 196	$ 200	$ 203	$ 197
		Royalties	**$ -**	**$ 2**	**$ 5**	**$ 9**	**$ 14**	**$ 21**	**$ 29**	**$ 30**	**$ 31**	**$ 30**

Source: Company reports and RBC Capital Markets estimates

Exhibit 105: ICPT's expected news flow

Time	Expected News Flow	Product	Indication
March 2016	FDA to host a PSC endpoints workshop	OCA	PSC
April 7, 2016	FDA AdCom meeting	OCA	PBC
May 29, 2016	PDUFA decision for treatment of Primary Biliary Cholangitis	OCA	PBC
Mid 2016	Potential EMA approval for treatment of OCA in PBC	OCA	PBC
2017	Potential Phase II data on Primary Sclerosing Cholangitis (AESOP)	OCA	PSC
Mid 2018	Interim histology analysis for Phase III study (REGENERATE)	OCA	NASH
2022	Potential Phase IIIb confirmatory outcomes data (COBALT)	OCA	PBC

Source: Company reports and RBC Capital Markets estimates

Exhibit 106: ICPT's pipeline

Drug (Target)	Indication	Stage	To Market
Obeticholic Acid "OCA" (FXR Agonist)	Primary Biliary Cirrhosis (PBC)	NDA/MAA	2016
	Nonalcoholic Stetohepatitis (NASH)	Phase III	2018/2019
	Primary Sclerosing Cholangitis (PSC)	Phase II	2019+
	Biliary atresia	Phase II	2019+
INT-767 (Dual FXR/TGR5 Agonist)	Fibrosis	Phase I	2020+
INT-777 (TGR5 Agonist)	Type 2 Diabetes	Preclinical	

Source: Company reports and RBC Capital Markets estimates

Exhibit 107: ICPT's income statement

($ in millions, except per share) Fiscal Year Ends December	FY12	FY13	FY14	1Q15 Mar-15	2Q15 Jun-15	3Q15 Sep-15	4Q15E Dec-15	FY15E	1Q16E Mar-16	2Q16E Jun-16	3Q16E Sep-16	4Q16E Dec-16	FY16E	FY17E
Revenues:														
Licensing revenue	2.4	1.6	1.7	1.4	0.4	0.4	0.4	2.8	0.4	0.4	0.4	0.4	1.8	1.8
OCA	-	-	-	-	-	-	-	-	-	1.0	5.0	10.4	16.4	110.0
Total Revenue	**2.4**	**1.6**	**1.7**	**1.4**	**0.4**	**0.4**	**0.4**	**2.8**	**0.4**	**1.4**	**5.4**	**10.8**	**18.2**	**111.8**
Costs and expenses:	-	-	-	-	-	-	-	-	-	-	-	-	-	-
COGS	-	-	-	-	-	-	-	-	-	0.1	0.4	0.8	1.3	8.8
Research and development	16.2	27.9	80.3	28.0	28.3	27.5	32.0	115.7	47.0	62.0	77.0	95.0	281.0	410.0
Sales, General and administrative	5.2	13.1	34.6	13.1	21.0	24.7	30.0	88.9	37.0	45.0	52.0	59.0	193.0	250.0
Total operating costs and expenses	21.4	41.1	114.9	41.1	49.3	52.2	62.0	204.6	84.0	107.1	129.4	154.8	475.3	668.8
Income (loss) from operations	**(18.9)**	**(39.5)**	**(113.2)**	**(39.7)**	**(48.8)**	**(51.8)**	**(61.6)**	**(201.8)**	**(83.6)**	**(105.6)**	**(124.0)**	**(144.0)**	**(457.1)**	**(557.0)**
Total other income (expense)	(24.7)	(28.3)	(170.1)	0.3	0.9	0.9	0.9	3.0	0.9	0.9	0.9	0.9	3.6	3.6
Taxes	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Net Income	**(46.3)**	**(67.8)**	**(283.3)**	**(39.4)**	**(47.9)**	**(50.9)**	**(60.7)**	**(198.8)**	**(82.7)**	**(104.7)**	**(123.1)**	**(143.1)**	**(453.5)**	**(553.4)**
Net loss per share (basic)	($7.36)	($3.76)	($13.63)	($1.78)	($1.99)	($2.10)	($2.48)	($8.38)	($3.35)	($4.20)	($4.88)	($5.21)	($17.64)	($19.35)
Net loss per share (diluted)	($7.36)	($3.76)	($13.05)	($1.78)	($1.99)	($2.10)	($2.48)	($8.38)	($3.35)	($4.20)	($4.88)	($5.21)	($17.64)	($19.35)
Shares outstanding														
Basic	6.3	18.0	20.8	22.2	24.0	24.2	24.5	23.7	24.7	24.9	25.2	27.5	25.6	28.6
Diluted	16.2	20.7	21.7	22.2	24.0	24.2	24.5	23.7	24.7	24.9	25.2	27.5	25.6	28.6
Cash at end	110.2	144.8	229.6	402.0	732.3	695.7	627.4	559.5	536.4	422.8	290.3	564.2	496.2	468.2
Cash/share	$6.80	$7.00	$10.58	$18.13	$30.50	$28.73	$25.65	$23.59	$21.72	$16.95	$11.52	$20.55	$19.40	$16.37

Source: Company reports and RBC Capital Markets Estimates

Valuation

Our $300 price target (lowered from $490 previously due to conservatism) is a sum-of-the-parts analysis of probability-adjusted value of OCA for PBC and NASH. We assign 80% and 60% probability for OCA to enter the PBC and NASH market successfully and become a peak $4B drug (probability adjusted). We assume: (1) PBC market entry in 2016 and NASH around 2018, (2) peak penetration of ~55% for PBC and ~30% for NASH, (3) terminal growth rates of -20% for both PBC and NASH, and (4) we discount risk-adjusted peak sales at 9%, which yields ~$30/ share (PBC) and ~$270/share (NASH).

Price target impediments

Failure of OCA to show compelling efficacy in NASH: This is the significant market opportunity that could determine whether the drug could be a blockbuster or not. If the drug fails to show significantly better efficacy versus currently used, off-label options or emerging competitors, then it would greatly diminish the revenue potential of this drug.

Emergence of serious cardiovascular safety signals: One of the more common complications among NASH patients is heart disease. Thus, if OCA shows significant, adverse effects on lipid

levels that cannot be well managed by the use of cholesterol-lowering drugs, then it would greatly limit its chance of FDA approval or market adoption potential.

Continued delay in FDA approval: Timing is important to the success of OCA, but regulatory compliance may not accept ALP (alkaline phosphatase) as the end point and request running outcomes studies for PBC or CV outcomes for NASH. There are other pharmaceutical companies developing FXR agonist and treatment for NASH in earlier stages, and any delay in OCA getting to market could pose threats to the first-mover advantage.

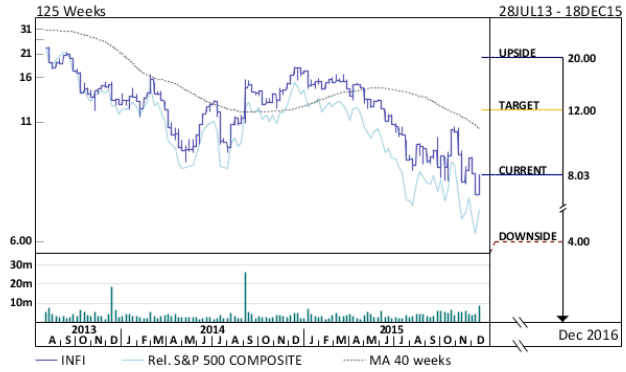
Infinity Pharmaceuticals (INFI)

Outperform, Speculative Risk

Price Target USD $12.00

Target/Upside/Downside Scenarios

Exhibit 108: Infinity Pharmaceuticals.



Source: RBC Capital Markets estimates

Target price/base case

We lowered our PT to $12 from $15 assuming a lower market share and probability of success given the competitive environment and no combination data yet with ABT-199 at this time. Our base case assumes that IPI-145 will become a differentiated treatment for CLL and iNHL, and gain 10% market share ($500M peak sales, assuming 50% probability of success). We use a discount rate of 10%, terminal growth of -45%, yielding $12/share. Our DCF incorporates the terms of INFI's partnership with AbbVie, assuming USA profit split and 25% ex-US royalty on net sales.

Upside scenario

We lowered our upside scenario from $24 to $20 assuming a lower market share and probability success given the competitive environment. Our upside scenario assigns a probability of success of 60%, that IPI-145 will become a best-in-class treatment for CLL and iNHL (we assume the two histology's peak sales are greater than $700M). We also assign a modest 10% probability for IPI-145 in DLBCL, which assumes peak sales of ~$50M. We use a discount rate of 10%, terminal growth of -50%, yielding $20/ share. Our upside scenario is also supported by a potential takeout scenario, where INFI could be acquired by ABBV for $1B+.

Downside scenario

We lowered our downside scenario from $6 to $4 assuming a lower market share and probability success given the competitive environment Our downside scenario assumes that IPI-145 advances in the iNHL indication (~7% probability) with peak sales of ~$70M. With 10% discount rate and -50% terminal value, these yield $4/share.

Investment summary

We believe Infinity is an attractive small-cap biotech investment candidate. Indeed, longer-term, our general positive thesis hinges on lead candidate IPI-145 as a potentially differentiated PI3K delta/gamma inhibitor (particularly in combo with ABT-199) and the stock currently prices in very bearish expectations at a $350M market cap and more than half the stock i.e. $230-250M in cash. We believe positive combo data in 2016-2017 could mark INFI as an attractive acquisition target by ABBV. Also, INFI is moving beyond a one-drug company, with new PI3k "gamma" drug IPI-549 starting mono and PD1 combo studies in 2016, which Street is not yet crediting. With more clinical data in cancer potentially coming from other trials expected next year, we believe multiple catalysts could increase investor confidence in the differentiated safety and/or efficacy profile of IPI-145 in advanced hematological cancers (e.g. CLL and iNHL).

Potential catalysts for the stock

Phase II DYNAMO pivotal duvelisib response rate data in iNHL in Q3:16, which could lead to accelerated approval if positive.

Phase Ib/II combo trial with INFI's duvelisib + ABT-199 starting YE:15: If future data (data readout timing undisclosed) is positive, the trial would show synergism between PI3K and BCL2 inhibitors, differentiating duvelisib and creating upside for INFI.

New PI3k "gamma" drug IPI-549 starting mono and PD1 combo studies next year. IPI549 is a "diamond in the rough" that grants INFI optionaility and enables it to eventually become beyond a one-drug company.

The following are risks to our investment thesis

Undifferentiated profile of IPI-145 compared to GILD's Zydelig: A second-to-market product is bound to face difficulty in uptake if it is not differentiated in any way from earlier entrants. If IPI-145 substantially fails to prove as the best-in-class PI3k and oral agent in development for CLL and NHL, then interest on the stock would continue to diminish.

ABBV could give the drug back to INFI: If DYNAMO (Phase III) data are uninteresting next year and undifferentiated from Zydelig, we think ABBV could hand back IPI-145 to INFI. We believe ABBV would want to see ABT-199 combo data first (which is in early 2017) before it considers terminating the partnership.

Unexpected safety results: IPI-145 is still relatively in early development (mostly Phase II) and lacks a long follow-up in large patient numbers. Unexpected safety events may occur in later stages of development, which could potentially increase its risk in coming to market.

2016 thoughts on INFI

INFI is likely to remain range-bound through at least the first half of 2016 as key Phase II pivotal data in iNHL does not come until H2:16. INFI management has been bullish on the potential combination of duvelisib and ABBV's ABT-199 as the "real reason" ABBV partnered the drug and how the preclinical data are very exciting. However, this study is just getting underway so there is unlikely any data soon (not sure if this could be at ASCO '16). In any case –data are not coming soon and ABBV is in charge of the data.

Indeed, longer-term, our general positive thesis hinges on lead candidate IPI-145 as a potentially differentiated PI3K delta/gamma inhibitor (particularly in combo with ABT-199), and the stock currently prices in very bearish expectations at a $350M market cap and more than half the stock i.e. $230-250M in cash.

With a partnership with ABBV (initiating Phase Ib/II venetoclax ABT-199 combo trial by YE:15), we believe Infinity is an attractive small-cap biotech and probably longer-term best suited to simply be acquired by ABBV for the economics if INFI data starts to look interesting in 2016-17 rather than pay out all the milestones and a royalty to INFI; but this will take time and we need data**.**

Furthermore, INFI has another oral PI3Kgamma candidate (IPI549 going into clinic for solid tumors Q1:16), which Street is not yet crediting.

Key catalysts although further out in 2016:

- **Phase II DYNAMO pivotal duvelisib response rate data in iNHL in Q3:16, which could lead to accelerated approval if positive**; we would view "positive differentiated" duvelisib iNHL data as an ORR well above 60%+ and CR rates in double-digits, with 1 year durability of response, and clean safety (little/no colitis or serious infections). Zydelig label in follicular lymphoma data shows a 54% ORR (median duration not reached) and 8% CR rate but 14% serious/fatal diarrhea and liver tox with black box.
- **Phase Ib/II combo trial with INFI's duvelisib + ABT-199 starting YE:15** - management shied away from a specific timeline for data readouts, emphasizing that the Phase Ib dose finding portion would be the key step; but if positive, future data would demonstrate synergy between PI3K and BCL2 inhibitors, and would be significant upside that differentiates duvelisib,
- **INFI is moving beyond a one-drug company, with new PI3k "gamma" drug IPI-549 starting mono and PD1 combo studies next year** - where INFI hopes to target the microenvironment of solid tumors more effectively through synergy with checkpoint inhibitors. We see the IPI549 opportunity as a "diamond in the rough" that's an optionality play for enabling INFI to eventually become more than a one-trick pony.

Bear case

- No catalysts until YE:16 for iNHL data and so far duvelisib not differentiated from lackluster GILD Zydelig and could show the same infections and colitis issues.
- ABBV could give the drug back if the DYNAMO data are uninteresting next year and un-differentiated (they'd probably want to see ABT-199 combo data first though and that's also by early '17).
- New drug IPI-549 is too early for any credit as it hasn't even started Phase I.
- There's no room for this drug in the whole CLL scheme of things since ABT-199 is also out there and that can be used after Ibrutinib – which is ironic because ABBV is their partner, so do they want pts to use ABT-199 or IPI-145?
- Now they have a partnership but they gave up half the drug on a small drug. Previously it wasn't even going to be that big of a drug and now they only get half of a small drug.

Key question and debate for INFI

1. How is IPI-145 differentiated from GILD's idelalisib (GS-1101) and other PI3Ks?

IPI-145 is a potent PI3k-delta/gamma inhibitor, while idelalisib only targets the delta-isoform of PI3k. By targeting both the delta/gamma isoform, which are both primarily expressed by leucocytes, IPI-145 could have greater efficacy as a single agent. So far in clinical trials, albeit still early, IPI-145 has shown signs as potentially the best-in-class PI3K inhibitor with higher ORRs and CRs in CLL, iNHL, and MCL versus idelalisib as well as responses in T-cell and Hodgkin's lymphoma.

We would view "positive differentiated" duvelisib iNHL data as an ORR well above 60%+ and CR rates in double-digits, with 1 year durability of response, and clean safety (little/no colitis or serious infections). Zydelig label in follicular lymphoma data shows a 54% ORR (median duration not reached) and 8% CR rate but 14% serious/fatal diarrhea and liver toxicity with black box.

Exhibit 109: Table of ongoing clinical trials for IPI-145

Indication	Study Name	Stage	Clinical Trial Details	Drug Arm	Comparator Arm	Enrollment	Trial Initiated	Data	Key endpoint
Advanced Hematologic Malignancies		Phase Ib/II	Evaluating dose combinations, safety and efficacy (expansion cohorts planned across multiple indications)	IPI-145 + venetoclax (ABT-199)		TBD	Q4:15E	TBD	Dose combinations, safety and efficacy
		Phase Ib	Patients with relapsed/refectoary hematologic malignancies	IPI-145 + Rituxan, or IPI-145 + Bendamustine + Rituxan		55	Q2:13	Q2:16E	Tolerability and Safety
iNHL/FL	DYNAMO+R	Phase III	Randomized, placebo-controlled combo study in relapsed FL	IPI-145 + Rituxan	Placebo + Rituxan	400	Q4:14	Q1:19E	Progression-Free Survival (PFS)
	BRAVURA	Phase III	Patients with relapsed iNHL	IPI-145 + Bendamustine/ Rituxan	Placebo + Bendamustine/ Rituxan	600	Q4:15E	TBD	Progression-Free Survival (PFS)
	DYNAMO	Phase II	Single-agent, open-label study in refractory iNHL patients	IPI-145		120	Q2:13	Q3:16E	Overall response rate (ORR)
	FRESCO	Phase II	Patients with relapsed FL (1st or 2nd relapse); progression < 24 months after start of alkylator-based therapy	IPI-145 + Rituxan	Rituxan-CHOP	200	Q4:15E	TBD	Progression-Free Survival (PFS)
	CONTEMPO	Phase II	Patients with first-line FL	IPI-145 + Gazyva	IPI-145 + Rituxan	120	Q4:14	Q2:17E	Safety measures, Complete Reponse Rate
		Phase Ib	Patients with first-line FL	IPI-145 + Gazyva and Rituxan					
CLL	DUO	Phase III	Randomized, monotherapy study of IPI-145 in R/R CLL patients	IPI-145	Ofatumumab (Arzerra)	300	Q4:13	2016E	Progression-free survival (PFS)
		Phase III	Extension study of IPI-145 vs. Ofatumumab in previously enrolled patients in study IPI-145-07	IPI-145	Ofatumumab (Arzerra)	150	Q4:13	Q4:18E	Overall response rate (ORR)
	SYNCHRONY	Phase Ib	Open-label, dose-escalation study in patients with prior BTK use (expansion phase will include IPI-145 + Gazyva)	IPI-145 + Gazyva		64	Q1:15	Q1:18E	Dose-limiting toxicities, AEs
		Phase Ib/II	IPI-145 plus FCR in previously untreated, younger patients with CLL	IPI-145 + FCR (fludarabine, cyclophosphamide, and rituxan)		26	Q3:14	Q4:21E	Rate of MRD-negative CR in the bone marrow

Source: Company reports, www.clinicaltrials.gov

Exhibit 110: Table of ongoing clinical trials for IPI-549

Table of oingoing clinical trials for IPI-549

Indication	Study Name	Stage	Clinical Trial Details	Drug arm	Comparator Arm	Enrollment	Trial Initiated	Data	Key endpoint
Solid Tumors		Phase I	IPI-549 dose escalation monotherapy for NSCLC, Melanoma and other solid tumors	Monotherapy		TBD	Q1:16E	YE:16E	Safety, early efficacy
			Combination therapy with IPI-549+anti-PD1 antibody	Combo with PD1		TBD	2016E	2017E	Safety, early efficacy

Source: Company reports, www.clinicaltrials.gov

Exhibit 111: INFI's expected news flow

Time	Expected News Flow	Program
Q4:15	Initiate Phase 1b/2 study evaluating IPI-145 in combination with ABBV's venetoclax	IPI-145
Q4:15	Initiate Phase II study in patients with relapsed follicular lymphoma (FRESCO)	IPI-145
Q4:15	Initiate Phase III study in patients with relapsed iNHL (BRAVURA)	IPI-145
Q4:15	Complete enrollment in DUO trial of 25mg IPI-145 vs. Ofa in R/R CLL	IPI-145
Q1:16	Initiate Phase 1 clinical development of IPI-549 (oral) for treatment in solid tumors	IPI-549
Q3:16	Potentially report results from Phase II "DYNAMO" trial of IPI-145 in double-refractory iNHL	IPI-145
2016	Potentially report results from Phase III "DUO" trial of IPI-145 vs. Ofa in R/R CLL	IPI-145
YE:16	Submit global regulatory filings for double-refractory iNHL	IPI-145

Source: Company reports and RBC Capital Markets estimates

Exhibit 112: INFI's income statement

($ in millions, except per share) Fiscal Year Ends December	FYA 2012E	FYA 2013A	FYA 2014A	1QA Mar-15	2QA Jun-15	3QA Sep-15	4QE Dec-15	FYE 2015E	1QE Mar-16	2QE Jun-16	3QE Sep-16	4QE Dec-16	FYE 2016E	FYE 2017E
Revenues:														
IPI-145	-	-	-	-	-	-	-	-	-	-	-	-	-	20.0
Retaspimycin (IPI-504)	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Collaborative revs	47.1	-	165.0	4.6	4.9	90.7	8.8	109.0	9.6	10.5	11.4	128.4	159.7	258.0
Total revenue	**47.1**	**-**	**165.0**	**4.6**	**4.9**	**90.7**	**8.8**	**109.0**	**9.6**	**10.5**	**11.4**	**128.4**	**159.7**	**278.0**
Operating expenses:	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Cost of sales	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Research and development	118.6	99.8	143.6	88.4	34.1	37.7	40.0	200.2	43.0	46.0	50.0	54.0	193.0	231.6
General and Administrative	27.9	27.9	29.3	8.6	9.4	9.8	10.5	38.2	11.3	12.0	12.8	14.0	50.0	65.0
Total Operating Expenses	146.5	127.7	172.9	97.0	43.5	47.5	50.5	238.4	54.3	58.0	62.8	68.0	243.0	296.6
Gain/payment on partnership	46.6	-	-	-	-	-	-	-	-	-	-	-	-	-
Income (loss) from operations	(52.8)	(127.7)	(7.9)	(92.3)	(38.6)	43.3	(41.8)	(129.4)	(44.7)	(47.6)	(51.4)	60.4	(83.3)	(38.6)
Other income (expense):	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Interest Expense	(1.9)	-	(9.6)	(0.6)	(0.1)	(0.3)	(0.3)	(1.4)	(0.3)	(0.3)	(0.3)	(0.3)	(1.2)	(1.2)
Other non-recurring income:	0.2	-	-	-	-	-	-	-	-	-	-	-	-	-
Interest and investment income	0.6	0.9	0.3	(0.0)	0.3	0.1	0.1	0.3	0.1	0.1	0.1	0.1	0.2	0.2
Total other expenses	(1.2)	0.9	(9.3)	(0.7)	0.2	(0.2)	(0.3)	(1.0)	(0.3)	(0.3)	(0.3)	(0.3)	(1.0)	(1.0)
Income Tax Expense (Benefit)	-	-	-	-	-	(0.5)	-	(0.5)	-	-	-	-	-	-
Net income	**(54.0)**	**(126.8)**	**(17.2)**	**(93.0)**	**(38.4)**	**42.5**	**(42.0)**	**(130.9)**	**(45.0)**	**(47.8)**	**(51.7)**	**60.1**	**(84.3)**	**(39.6)**
EPS (basic)	**(1.70)**	**(2.64)**	**(0.35)**	**(1.90)**	**(0.78)**	**0.85**	**(0.85)**	**(2.66)**	**(0.90)**	**(0.96)**	**(1.03)**	**1.19**	**(1.69)**	**(0.77)**
EPS (diluted)	(1.70)	(2.64)	(0.35)	(1.90)	(0.78)	0.84	(0.85)	(2.66)	(0.90)	(0.96)	(1.03)	1.17	(1.69)	(0.77)
Shares outstanding:														
Basic	31.7	47.9	48.6	48.9	49.1	49.2	49.4	49.2	49.7	49.9	50.2	50.4	50.1	51.6
Diluted	34.8	51.9	52.6	52.9	53.1	49.8	50.4	51.6	50.7	50.9	51.2	51.4	51.1	52.6
Financing	248.7	0.0	114.4	0.0	0.0	130.0	0.0	130.0	0.0	0.0	0.0	0.0	0.0	0.0
Cast at end	327.0	214.9	333.2	233.6	199.5	163.0	246.0	246.0	203.0	158.2	109.6	172.6	172.6	144.0

Source: Company reports and RBC Capital Markets Estimates

Valuation

We lowered our PT to $12 from $15 assuming a lower market share and probability of success given the competitive environment and no combination data yet with ABT-199 at this time. Our base case assumes that IPI-145 will become a differentiated treatment for CLL and iNHL, and gain 10% market share ($500M peak sales, assuming 50% probability of success). We use a discount rate of 10%, terminal growth of -45%, yielding $12/share. Our DCF incorporates the terms of INFI's partnership with AbbVie, assuming USA profit split and 25% ex-US royalty on net sales.

Price target impediments

Our price target is primarily dependent on clinical, regulatory, and commercial success of IPI-145 in multiple haematological indications (e.g. CLL and iNHL). Risks include clinical setbacks (fewer than expected response rates in each patient population, shorter than expected duration of response or unexpected safety, or tolerability issues), lack of differentiation of IPI-145 from more clinically advanced PI3K in development, regulatory delays, failure to reach probability-adjusted peak sales.

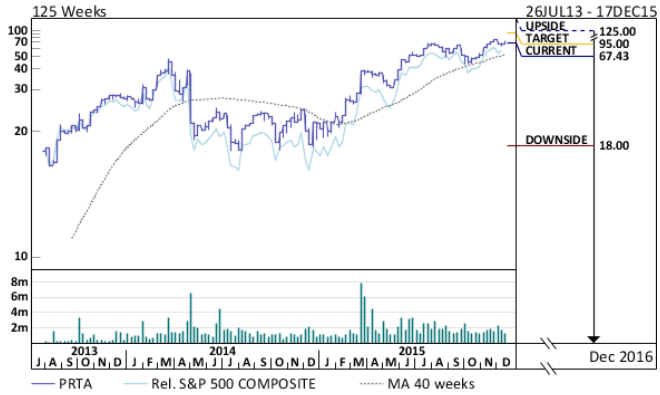
Prothena Corporation (PRTA)

Outperform, Speculative Risk

Price Target USD $95.00

Target/Upside/Downside Scenarios

Exhibit 113: Prothena Corporation



Source: RBC Capital Markets estimates

Target price/base case

Our $95 price target uses a one-year forward discount period of 2016-2017 and is a sum-of-the-parts analysis of probability-adjusted value of two pipeline indications. 1) We assign a 75% probability for lead program in AL amyloidosis to become a $1B indication and discount it back to present value. 2) We assume 30% probability of success for PRX-002's potential in Parkinson's post-Roche partnership.

Upside scenario

Our $125 upside scenario discounted now to 2016-17 from prior 2015 represents a higher 85% probability discounted back to present value. We also assume a higher 50% probability of success for PRX-002 in Parkinson's. However, there is upside to this if it is moved to 100% probability for each and Phase III works and we have conservatively assumed lower end orphan pricing and this is not a takeout value scenario.

Downside scenario

Our $18 downside scenario represents extremely conservative assumptions on probability of success (15% for AL) for the lead AL amyloidosis indications and can be justified if either program fails and one program is left (either Parkinson's or Amyloidosis). Biologics have consistently demonstrated higher (~20%) probability of eventuality to market. We also assign a reduced value ($20M EV) to the remaining two programs and only include $3/share of cash in valuation, assuming higher than expected cash burn.

Investment summary

Prothena Outperform, Speculative Risk, is one our best SMID cap long ideas because this is an off-the-radar therapeutics company with biologic assets in three indications of high unmet need: amyloidosis, neurogenerative diseases (Parkinson's), and inflammation (psoriasis). For amyloidosis, we expect full Phase I/II data coming in 2016, and we think the subsequent Phase III data has a very legitimate chance of working in 2017. Positive data should de-risk the asset. Our positive view on the asset is predicated on good scientific rationale, defendable mechanism of action, and the overall high success rates of antibodies in the targeting and clearing of proteins, which are believed to be the direct culprit in amyloidosis. Separately, Prothena is conducting trials for a second pipeline drug, PRX-002, a novel antibody for Parkinson's disease, which is partnered with Roche. PRTA is also investigating treatment for inflammatory diseases. Lastly, we believe the stock's valuation is attractive, especially compared to other orphan drug biotech comparables that trade at 3-5x higher enterprise value.

Potential catalysts for the stock

NEOD-001 Phase III data in 2017: Positive data could send the stock 100% higher were we to impute a 100% probability in the model and assuming a 4-5x multiple on peak sales.

NEOD001 (amyloidosis) has Phase I/II data on 42-pt cohort 'expansion' in Q2:16: Also, enrollment completion of frontline Phase III study (VITAL) possibly YE:16.

Parkinson's data from Phase I MAD portion of '002 in H1:16, and PRTA's partner Roche to bring PRX-002 into Phase II. In addition, BIIB started a Phase I alpha-synuclein antibody BIIB-054 which helps to validate PRTA's work.

Phase I psoriasis data for PRX003 in H1:16: Data could show acute proof of concept that their novel approach is working and could go after rare diseases or lead to a partnership.

The following are risks to our investment thesis

Inability of NEOD001 to demonstrate organ function benefit: Differentiation versus currently available treatments is crucial in validating that its "faucet shutting/plug draining" dual mechanism confers an overall survival benefit for patients compared to chemotherapy or proteasome inhibitors. A lack of differentiation would reduce our commercial peak sales estimate of $500M-1B (risk-adjusted to $300MM currently).

Emergence of serious safety signal that precludes continued development of NEOD001: Serious cardiac or renal toxicities, or very high immunogenicity rates that result in generation of neutralizing autoantibodies could stop development. Even though amyloidosis is a dire disease, treatments will need to demonstrate good enough safety, tolerability, and sustained efficacy.

2016 thoughts on PRTA

PRTA remains one of our best SMID cap long ideas because we think the Phase III program for NEOD-001 in amyloidosis has a very legitimate chance of working in 2017. If data are positive, then the stock could be up 100% (if we impute a 100% probability into the model and assuming a 4-5x multiple on peak sales like other comps DYAX, GEVA, NPSP, etc). We think there is a near-term catalyst in that Phase II NEOD-001 "response rate" data from a 45-patient expansion cohort in Q2:16 should be positive and re-affirm the confidence in the potential positive pivotal data and increase investor confidence in this program.

We also think the 2nd drug ('002) is getting increased interest after recent positive Phase I data, along with securing a Roche partnership. Also, BIIB has begun to talk about this target and is starting their own Phase I antibody in 2016. '002 is the 2nd program that is a Phase I antibody for the treatment of Parkinson's disease. This has shown positive safety and a 96% knockdown of the target alpha-synuclein in healthy patients' blood. New '002 data in H1:16 could be positive and re-affirm safety in Parkinson's patients and demonstrate penetration of the blood brain barrier and imply the drug is now getting into the brain and should be engaging the target (alpha-synuclein).

Bear case

- For cardiac amyloidosis, no clinical event rate or other cardiac function measurement data (e.g. ECHO). Just a biomarker NTproBNP from an open-label Phase I safety study.
- Is the actual drug working better in renal amyloidosis than cardiac? The renal data seems interesting (reversing proteinurea and eGFR) – is the Phase III going to fail and then post-hoc they find out it was a renal amyloidosis drug?
- Very long time-lines to get the Phase III data – they are just enrolling – no data on Phase III until perhaps 2017+.
- Parkinson's is extremely high risk, high reward. No evidence that blocking alpha synuclein will result in any meaningful clinical improvements in the UPDRS scale. How do we know what binding alpha-synuclein will do?
- Upcoming Phase I data in H1:16 is just safety data. They say they'll look at biomarkers but which ones? Whichever ones are positive?
- The timelines are very long until we get any Phase II data on UPDRS or clinical efficacy. Starting Phase II would be 2016-17 and could be a year or more to get the Phase II data with 6-mo efficacy readout (2018?).
- Velcade and other background therapy is highly active already in hematologic and eventually, organ responses – so it's hard to say that adding NEOD-001 will add any more efficacy and it's very difficult to power a study like this if you don't know what the control arm should do on OS or hospitalizations.
- Dose response not clear at all and was a bit worse at the higher doses yet they're going forward with the high dose.
- The Phase I patients just came off VGPR/CR, so can't tell if it's drug or prior therapy driving NTproBNP lower.
- The NTproBNP jumps around a lot from month to month, so hard to interpret if clearly sustainable or real drug effect.
- Cannot definitively say it's the drug causing drops because no control arm.
- NTproBNP can bounce around month to month plus or minus 20–30% with diet and care, so can't tell what's really going on and needs more durable data.

Key questions and debates for PRTA

1. Why would anyone use NEOD-001 when chemo or MM drugs such as Velcade already work in AL amyloidosis?

It is true that select regimens such as melphalan+dex or Velcade currently work in AL amyloidosis but they are not great and have lots of room for improvement. These current regimens have shown robust hematologic responses but mortality rates remain high as the organ response rates are not as deep and come too slow.

NEOD-001 directly targets the amyloid deposits accumulated in organs, which could potentially lead to earlier and deeper organ response rates. This could lead to improved survival outcomes for AL amyloidosis patients, whom still face dismal outcomes with median survival of nearly three years.

2. What data do we have on '001?

Recent data and our analysis on new 12-month follow up shows: 1) Cardiac amyloidosis pts are showing 50% responses and they are durable in a sick population after a year; 2) renal amyloidosis patients now have a 50%+ response rate, too, showing a reversing of kidney damage; and 3) analysis of multiple baseline measurements of NTproBNP shows patients were stable or getting worse and after drug they are going the other way (improving) and it's not due to prior therapies (email us for the data). Lastly, regulatory discussions are productive as EMA now allowing approvability on a biomarker (Phase II PRONTO) and the FDA just hosted a workshop stating awareness of unmet need, potential biomarkers, and a need for new therapies.

3. Where are the AL amyloidosis patients treated and by whom?

AL amyloidosis is a rare disease, and due to its complexity of disease and lack of familiarity by many physicians, management of these patients is carried out at a select few "centers of excellence" in the country (in the US, BU, Mayo, Stanford, etc.). They are usually taken care of by a coordinated team of physicians consisting of cardiologists, oncologists, and hematologists.

4. What other pipeline drugs make PRTA attractive?

Investors are figuring out Phase I '002 for Parkinson's. Phase Ia data was positive in Spring 2015 and Phase IB has been ongoing for months now with no issues at high doses. We think H1:16 data will be positive, safe/tolerable, with good PK/PD. It's possible PRTA/Roche go to even higher doses (good for safety and more drug into brain) in H1:16, thus data would come later in H2:16. Meanwhile, BIIB has started to talk up their enthusiasm for this alpha-synuclein target, the genetic evidence for culpability, and pre-clinical data.

Exhibit 114: PRTA's expected news flow

Time	Expected News Flow	Program
Q4:15	Initiate Phase IIb trial (PRONTO) in previously-treated patients with AL amyloidosis and persistent cardiac dysfunction	NEOD001
Q4:15/Q1:16	Initiate open label extension (OLE) study for patients having completed Phase I/II or PRONTO trial	NEOD001
Feb 16	Update on enrollment timeline of VITAL Amyloidosis study	NEOD001
H1:16	Data from Phase I MAD portion of PRX002 in PD patients	PRX002
H1:16	Data from Phase I single ascending dose study in healthy volunteers	PRX003 (MCAM)
Q2:16	Full data from Phase 1/2 clinical trial of NEOD001 (including expansion cohort) to be presented at a medical conference	NEOD001
YE:16	Estimated enrollment completion for Phase III VITAL trial in AL amyloidosis (cardiac involvement)	NEOD001
2016	Initiate Phase I MAD proof-of-biology study	PRX003 (MCAM)
2017	File IND/Phase I for treatment of TTR amyloidosis	NEOD004
YE:17 - early '18	Data from Phase IIb PRONTO trial in previously-treated patients with AL amyloidosis and persistent cardiac dystfunction	NEOD001
mid '18	Full data from pivotal Phase 3 VITAL trial in patients with AL amyloidosis (cardiac involvement)	NEOD001

*Note: Highlighted in blue indicates events of high significance

Source: Company reports and RBC Capital Markets estimates

Exhibit 115: PRTA's pipeline

Drug (Target)	Indication	Stage	Est. Completion
Clinical Stage Assets			
NEOD001	AL Amyloidosis	Phase III	~2018
PRX002	Parkinsons's disease	Phase I	MAD data in H1:16
PRX003	Inflammatory disease	Phase I	SAD data in H1:16
Pre-clinical Programs			
NEOD004	TTR amyloidosis	Preclinical	File IND/Phase I in 2017

Source: Company reports and RBC Capital Markets estimates

Exhibit 116: PRTA's income statement

Fiscal Year (Ending in December) ($ figures in MM, except per share)	FY14	1Q15 Mar-15	2Q15 Jun-15	3Q15 Sep-15	Q4:15E Dec-15	FY15E	Q1:16E Mar-16	Q2:16E Jun-16	Q3:16E Sep-16	Q4:16E Dec-16	2016E	2017E
Revenues:												
Revenues from related party	0.5	-	-	-	-	-	-	-	-	-	-	-
NEOD001	-	-	-	-	-	-	-	-	-	-	-	-
Milestone and reimbursement from Roche	50.3	0.6	0.3	0.4	0.4	1.7	0.4	0.4	25.0	0.4	26.3	72.0
Total revenue	**50.9**	**0.6**	**0.3**	**0.4**	**0.4**	**1.7**	**0.4**	**0.4**	**25.0**	**0.4**	**26.3**	**72.0**
Cost of sales	-	-	-	-	-	-	-	-	-	-	-	-
Total Operating Expenses	**57.5**	**15.6**	**18.3**	**23.1**	**24.5**	**81.5**	**25.0**	**25.8**	**26.5**	**27.7**	**104.9**	**136.4**
Research and development	38.5	10.6	12.8	17.2	18.0	58.5	18.0	18.3	18.5	18.5	73.3	95.3
General and Administrative	19.1	5.0	5.5	5.9	6.5	23.0	7.0	7.5	8.0	9.1	31.6	41.1
Income (loss) from operations	**(6.6)**	**(15.0)**	**(18.0)**	**(22.7)**	**(24.1)**	**(79.8)**	**(24.6)**	**(25.3)**	**(1.5)**	**(27.2)**	**(78.6)**	**(64.4)**
Total other income/expenses	0.3	0.1	(0.0)	(0.1)	0.2	0.1	0.1	0.1	0.1	0.1	0.4	0.4
Income Tax	0.8	0.3	0.2	0.2	0.2	0.8	0.2	0.2	0.2	0.2	0.8	0.8
Net income	**(7.2)**	**(15.2)**	**(18.3)**	**(23.0)**	**(24.1)**	**(80.5)**	**(24.7)**	**(25.4)**	**(1.6)**	**(27.3)**	**(79.0)**	**(64.7)**
EPS (basic)	(0.29)	(0.55)	(0.59)	(0.73)	(0.76)	(2.66)	(0.78)	(0.80)	(0.05)	(0.85)	(2.47)	(1.93)
EPS (diluted)	**(0.29)**	**(0.55)**	**(0.59)**	**(0.73)**	**(0.76)**	**(2.66)**	**(0.78)**	**(0.80)**	**(0.05)**	**(0.85)**	**(2.47)**	**(1.93)**
Basic	24.7	27.4	30.8	31.4	31.6	30.3	31.8	31.9	32.1	32.2	32.0	33.5
Diluted	**26.1**	**27.4**	**30.8**	**31.4**	**31.6**	**30.3**	**31.8**	**31.9**	**32.1**	**32.2**	**32.0**	**33.5**
Cash at end	**293.6**	**279.9**	**402.4**	**387.8**	**364.6**	**357.1**	**335.5**	**313.1**	**314.5**	**290.2**	**290.2**	**237.4**

Source: Company reports and RBC Capital Markets estimates

Valuation

Our $95 price target is a sum-of-the-parts analysis of probability-adjusted value of two pipeline indications. 1) We assign a 75% probability for lead program in AL amyloidosis to become a $1B indication. 2) We assume 30% probability of success for PRX-002's potential in Parkinson's post-Roche partnership. We use probability-adjusted sales for both indications and discount back to present value. Our PT revision adjusts our discount period to 2016-17 from 2015 on a 12-month horizon and hasn't changed any probability of success.

Price target impediments

- **Inability of NEOD-001 to demonstrate organ function benefit:** Differentiation versus currently available treatments is crucial in validating that its "faucet shutting/plug draining" dual mechanism confers an overall survival benefit for patients compared to chemotherapy or proteasome inhibitors. A lack of differentiation would reduce our commercial peak sales estimate of $500M-1B (risk-adjusted to $300MM currently).
- **Emergence of serious safety signal that precludes continued development of NEOD-001:** Serious cardiac or renal toxicities, or very high immunogenicity rates that result in generation of neutralizing autoantibodies could stop development. Even though amyloidosis is a dire disease, treatments will need to demonstrate good enough safety, tolerability, and sustained efficacy.
- **Failure of PRX-002 to advance to Phase II**, as $31/share of our price target is based on nominal 30% probability of ultimate success that the program will gain clinical, regulatory, and commercial success in becoming a $5B drug.

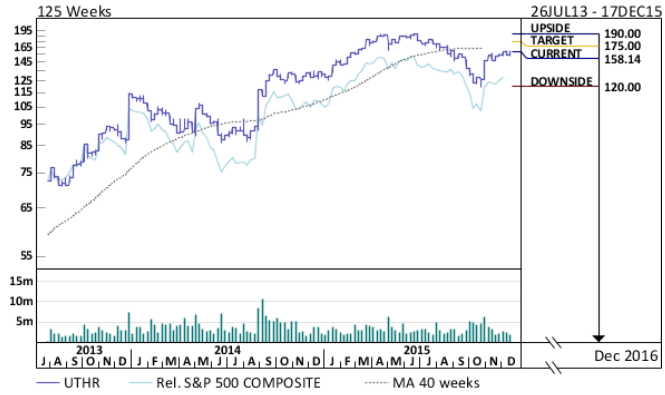
United Therapeutics (UTHR)

Sector Perform

Price Target USD $175.00

Target/Upside/Downside Scenarios

Exhibit 117: United Therapeutics.



Source: RBC Capital Markets estimates

Target price/base case

Our base case $175 price target is derived by applying a ~12.5x forward P/E multiple on fully taxed non-GAAP 2017E EPS. We believe 12.5x is a fair and reasonable multiple given it is on par with other peer profitable mid- to large-cap biotechs with low single-digit growth projections. Our valuation is supported by a DCF assuming healthy 7-9% top-line growth post-2017, while adjusting to 30% probability that generic Remodulin enters post-2017, albeit at a modest -5% terminal rate. We apply a 10% discount rate.

Upside scenario

Our upside scenario of $190/share implies a 13.5x forward P/E of fully taxed Non-GAAP 2017E EPS. We believe this higher multiple can be attained if UTHR's core Remodulin products continue to maintain healthy growth while its patent protection post-2017 becomes more concrete.

Downside scenario

Our downside scenario of $120/share assumes an 8-9x forward P/E of fully taxed Non-GAAP 2017E EPS. This downside scenario can be realized if UTHR's core Remodulin products fail to meet near-term sales projections while its patent protection post-2017 weakens from generic challengers such as Teva.

Investment summary

We rate UTHR Sector Perform due to competitive risks in pulmonary arterial hypertension (PAH) from potentially Actelion (selexipag). UTHR's entire business is based on providing PAH therapies to patients in various stages of the disease, and new oral therapies could compete for market share, potentially delaying patient initiation on later-stage therapies (e.g. Tyvaso and Remodulin). UTHR's oral Remodulin (Orenitram) could cannibalize sales from its own higher-priced inhaled and IV therapies, as Orenitram could be used as substitution for subQ or IV Remodulin. We believe UTHR will have to demonstrate growth in an increasingly competitive market, where Tracleer generics are available and where competitors Bayer and Actelion could take market share with Adempas and Macitentan (Opsumit), respectively, the latter of which is the first to demonstrate a mortality benefit. However, UTHR is interesting as it boasts 50% operating margins, routinely engages in stock buybacks, and trades at a $175-$200M acquisition value.

Potential catalysts for the stock

Near-term catalysts: (1) potential approval for Remodulin label with Medtronic System in mid-2016, and (2) a potential FDA approval of the Remodulin implantable pump. Long-term, the next important data is the Phase III Orenitram readout (FREEDOM-EV) in 2017.

Strong Orenitram sales: UTHR is transitioning patients from subQ/IV to oral Orenitram over time, which may mute any generic risk. Orenitram averages a higher in price so the drug could be accretive for every switch from subQ/IV.

The following are risks to our investment thesis

Earlier than expected generic Remodulin entry: Our core thesis depends on the sustained growth of its Remodulin franchise beyond 2017. However, the PAH market is seeing generic entries of drugs like blockbuster Tracleer. We assign a 70% probability that Remodulin IP extends to 2023 against another generic company, Teva (Sandoz settled for June 2018). However, if the IP does not extend to 2023 (as many investors assume) due to a negative outcome from litigation against Teva, the achievement of our price target would also be impeded.

Competition from ATLN with oral selexpiag: ATLN has December 22nd PDUFA for oral selexipag prostacyclin, and this could directly compete with Orenitram.

Generic Tyvaso entry: UTHR received a paragraph IV from Watson in June 2015. Thirty months from receipt of Watson's notice letter translates to December 2017.

IPR risk from SteadyMed: Filed October 2015 by SteadyMed, the inter partes review is against key '393 patent (affects Tyvaso, Orenitram and Remodulin). A decision whether to institute the IPR is expected April 2016.

2016 thoughts on UTHR

Overall, UTHR remains an interesting contrarian long mid-cap value stock with potential takeout upside longer-term, but we think there could be some near-medium term headwinds and uncertainty for the stock from a new drug that will launch in oral selexipag (Actelion) in Q1:16, which has very compelling efficacy, easy oral administration, and a strong label with mortality and morbidity benefit. This could pressure near-term sales execution for UTHR Remodulin, Tyvaso, and oral Orenitram and makes quarterly visibility more challenging for investors.

In addition, there is uncertainty about a possible generic Remodulin that could launch in 2018 and UTHR has experienced a delay in their implantable pump program as Medtronic had an FDA warning letter regarding manufacturing. We won't know about whether this will delay everything until later in 2016.

In the short-term, investors may be concerned about that upcoming ATLN PDUFA on December 22nd for a new oral competitor, but UTHR does have an active buyback that starts up in January, which could offset that stock issue.

Longer-term, there are some positive considerations that make the stock interesting, although it seems more attractive in the lower $100-120 levels versus current levels and would price in more of the uncertainties. Considering this, we think UTHR could be a potential takeout candidate given the following positive aspects:

- $1.5B+ revenue business which has new Orenitram and life-cycle extension products like implantable pump Remodulin, DEKA semi-disposable pump, and other variations of Remodulin.
- 50%+ operating margins that could be much higher under a larger global specialty biopharma.
- High 35%+ tax rates that could be lowered over time.
- A 14-15x multiple on $13-15+ in earnings power without any cost cuts and flattish revenues (ie oral and implantable pump offset erosion of old Remodulin) and/or a DCF can get to $175-200 in acquisition value.
- The company has also previously said they buy stock in the open market under $200 and they announced a new $500M buyback plan through 2016.

Bear case

- They have literally no pipeline and they never do any decent business development deals.
- General patent risk including Sandoz generic Remodulin. In September 2015, Sandoz agreed to a settlement with UTHR for June 26, 2018.
- Potential large erosion from generics (or SteadyMed competitor) given high priced orphan drug and managed care sensitivity, and small molecule-based drug (not biologic).
- Competition from ATLN with oral selexipag for PDUFA December 22, 2015, which could take new starts from Orenitram and market share from other UTHR drugs given high efficacy and morbidity/mortality endpoint data (UTHR doesn't have that data yet).
- UTHR all leveraged to one franchise, i.e. PAH and Remodulin with weak pipeline and insufficient business development activity; they haven't done any major pipeline deals in years.

- DCF valuation doesn't work well unless all expenses removed and tucked under another larger company. Expense structure high and given patent risk, the DCF doesn't yield big upside unless expenses are wiped out and erosion is slower.
- The fact is selexipag has strong morbidity/mortality data and UTHR doesn't have that. UTHR also doesn't have any good data in "combo" which is the standard of care.

Key questions and debates for UTHR

1. Is generic Remodulin in late 2017-2018 a major risk?

In September 2015, Sandoz agreed to a settlement with UTHR to market a generic Remodulin starting June 26, 2018, which removed the worst-case scenario that a generic could arrive as early as 2015. Separately, UTHR has received another paragraph IV for Remodulin from TEVA, with the 30-month stay expiring December 2017. The bottom line is that we expect a generic to be available in 2018 that will take some modest market share around 10-20% over time but not immediately. This is due to: 1) most patients are on therapy, and doctors are unlikely to want to switch patients off branded Remodulin immediately, so Sandoz may get a share of "new" patients not existing patients, 2) price of the generic may not be significantly lower to make the vast majority of payors force a switch (e.g., if Remodulin is doing $500M and the generic cuts the price in half and then gets 100% share, then the maximum sales would only be $250M, which is small, but also they would not get 100% share, so it may be better to keep the price fairly healthy), 3) GSK's Flolan also saw a generic for PAH, but Teva and others have launch generics, and they still only get single-digit market share due in part to the factors above (although Flolan is a niche PAH drug only).

In addition, UTHR is transitioning patients from subQ/IV to oral Orenitram over time, which may mute any generic risk. Since oral Orenitram is higher in price on average, the switches over time are not cannibalizing or net-neutral but could actually be accretive for every switch.

2. Is Actelion's selixipag oral PAH drug a threat to UTHR's prostacyclin franchise?

We agree that the pending approval and launch of selexipag provides a serious competitor to UTHR's offerings starting in 2016. Selexipag is an oral prostacyclin and has positive Phase III data with a morbitidy and mortality benefit and in combination therapy with existing PAH drugs. This is in stark contrast to UTHR's oral, which only has positive data in monotherapy, which is not widely used in practice and only a 6MWD benefit, which is modest and no other data on mortality or morbidity. Thus, we expect a superior ATLN label and product profile could eat into share for Orenitram, which has none of those benefits aforementioned. UTHR has a Phase III study FREEDOM-C3 reading out in 2016+ that tests for morbitity and mortality, but we have only modest confidence that it will be successful given the weak efficacy seen to date across three Phase III clinical trials.

3. What will UTHR do with all its cash?

UTHR has $1B in cash ($20/share) and has continued to buy back stock modestly in an ongoing repurchased plan. The company has said before a dividend is unlikely. However, and more importantly, it is unclear if the company will consider doing more business development or acquisitions with its cash, and it has not done many deals at all or any meaningful acquisitions ever. Given the sizable cash position, we would like to see UTHR do more partnerships or acquisitions to bring in more pipeline products as we view the pipeline quite sparse. This would re-invigorate investors and build confidence that there are more things behind just Remodulin.

Exhibit 118: UTHR's expected news flow

Timing	Expected News Flow	Program
Dec 22, 2015	PDUFA date for selexipag (Uptravi) in PAH	Selexipag (ATLN)
Dec 2015	Refile NDA for implantable pump	Remodulin
Dec 2015	File amendment PMA for Remodulin label with Medtronic System	Medtronic
mid 2016	Potential approval for Remodulin label with Medtronic System	Medtronic
YE:16	Potential FDA approval of implantable pump	Remodulin
2016	Complete enrollment of patients in FREEDOM-EV	Orenitram
2017	Phase III results of FREEDOM-EV	Orenitram
2018	Potential approval for subQ Remodulin pump system	DEKA

Source: Company reports and RBC Capital Markets estimates

Exhibit 119: UTHR's pipeline

Product Pipeline	Indication	Stage	Partner
Remodulin	Pulmonary arterial hypertension	Commercial	
Tyvaso	Pulmonary arterial hypertension	Commercial	NEBU-TEC
Adcirca (tadalafil) Tablets	Pulmonary arterial hypertension	Commercial	Lilly
Orenitram	Pulmonary arterial hypertension	Commercial	
Unituxin (ch14.18)	Neuroblastoma	Commercial	NCI
Remodulin Implantable Pump	Pulmonary arterial hypertension	Phase III	Medtronic
Esuberaprost 314d	Pulmonary arterial hypertension	Phase III	Toray
-	Ex-vivo lung perfusion technology	Phase III	
UV-4B	Dengue	Phase I	
PLX cells	Pulmonary arterial hypertension	Phase I	Pluristem
Glycobiology antiviral drugs	Viruses	Pre-clinical	Oxford University
UV-4B	Influenza	Pre-clinical	

Source: Company reports and RBC Capital Markets estimates

Exhibit 120: Orenitram Revenue Model

US Market	Q2:14	Q3:14	Q4:14	Q1:15	Q2:15	Q3:15	Q4:15E	Q1:16E	Q2:16E	Q3:16E	Q4:16E
Patients on Therapy	250	564	762	790	980	1,195	1,425	1,682	1,951	2,224	2,490
Q/Q Growth		125.7%	35.0%	3.7%	24.0%	22.0%	19.2%	18.0%	16.0%	14.0%	12.0%
Y/Y Growth					291.8%	111.8%	87.1%	112.8%	99.1%	86.1%	74.8%
Average Daily Dose	8.0	9.0	9.3	9.3	10.2	10.1	10.1	10.2	10.3	10.5	10.7
Quaterly Cost per Patient	$22,782	$25,630	$26,484	$26,484	$29,047	$28,762	$28,762	$29,047	$29,332	$29,901	$30,471
Q/Q Growth		12.5%	3.3%	0.0%	9.7%	(1.0%)	0.0%	1.0%	1.0%	1.9%	1.9%
Estimated Revenue Before Inventory Adjustm	$5.7	$14.5	$20.2	$20.9	$28.5	$34.4	$41.0	$48.8	$57.2	$66.5	$75.9
Reported Revenue ($M)	**$6.6**	**$14.5**	**$20.2**	**$20.9**	**$25.9**	**$34.4**					
Inventory ($M)	$0.9	-	-	($0.0)	($2.6)	$0.0	-	-	-	-	-
Projected Quartery Revenue (Adjusted)	**$6.6**	**$14.5**	**$20.2**	**$20.9**	**$25.9**	**$34.4**	**$41.0**	**$48.8**	**$57.2**	**$66.5**	**$75.9**
Projected Annual Revenue (Adjusted)			**$41.3**				**$122.1**				**$248.4**

Source: Company reports and RBC Capital Markets estimates

Exhibit 121: Income statement for UTHR

Fiscal Year (Ending in December) ($ figures in MM, except per share)	FY12	FY13	FY14	1Q15 Mar-15	2Q15 Jun-15	3Q15 Sep-15	4Q15E Dec-15	FY15E	1Q16E Mar-16	2Q16E Jun-16	3Q16E Sep-16	4Q16E Dec-16	FY16E	FY17E
Remodulin	458.0	491.2	553.7	146.3	136.0	150.1	145.6	577.9	150.0	142.0	145.0	138.0	575.0	557.8
Tyvaso	325.6	438.8	463.1	113.4	115.8	121.7	118.1	469.0	115.0	118.0	122.0	118.0	473.0	477.7
AdCirca	122.5	177.0	221.5	45.4	68.1	73.8	77.5	264.7	65.0	80.0	85.0	95.0	325.0	331.5
Orenitram (Oral Remodulin)	-	-	41.3	20.9	25.9	34.4	43.0	124.1	46.0	55.0	60.0	70.0	231.0	325.0
Unituxin	-	-	-	-	-	4.7	7.0	11.7	9.0	12.0	15.0	16.0	52.0	102.0
Other	10.0	10.0	9.0	1.6	1.4	1.5	1.5	6.0	1.5	1.5	1.5	1.5	6.0	6.0
Total Revenue	**916.1**	**1,117.0**	**1,288.5**	**327.5**	**347.2**	**386.2**	**392.6**	**1,453.5**	**386.5**	**408.5**	**428.5**	**438.5**	**1,662.0**	**1,800.0**
Research and development	173.4	299.3	242.5	110.2	49.4	9.5	86.4	255.5	77.3	77.6	79.3	78.9	313.1	333.0
Selling, general and administrative	201.7	394.0	381.3	211.3	110.0	(17.3)	117.8	421.8	108.2	114.4	120.0	122.8	465.4	504.0
Cost of product sales	119.3	131.1	125.9	20.8	16.1	6.9	19.6	63.4	34.8	32.7	34.3	21.9	123.7	135.0
Total operating expenses	**494.4**	**824.5**	**749.7**	**342.3**	**175.5**	**(0.9)**	**223.8**	**740.7**	**220.3**	**224.7**	**233.5**	**223.6**	**902.1**	**972.0**
Income from operations	**421.6**	**292.5**	**538.8**	**(14.8)**	**171.7**	**387.1**	**168.8**	**712.8**	**166.2**	**183.8**	**195.0**	**214.9**	**759.9**	**828.0**
Total other (expense) income, net	19.0	(13.6)	(13.7)	(2.0)	(3.4)	349.8	(1.0)	343.4	(1.0)	(1.0)	(1.0)	(1.0)	(4.0)	(4.0)
Interest income	3.9	3.8	3.5	-	-	-	-	-	-	-	-	-	-	-
Interest expense	(16.6)	(18.1)	(17.6)	(2.1)	(1.3)	(0.8)	(1.0)	(5.2)	(1.0)	(1.0)	(1.0)	(1.0)	(4.0)	(4.0)
Equity (loss) income in affiliate	(0.1)	(0.1)	(0.1)	-	-	-	-	-	-	-	-	-	-	-
Other, net	31.9	0.8	0.5	0.1	(2.1)	0.6	-	(1.4)	-	-	-	-	-	-
Income before income tax	**440.7**	**278.9**	**525.1**	**(16.8)**	**168.3**	**736.9**	**167.8**	**1,056.2**	**165.2**	**182.8**	**194.0**	**213.9**	**755.9**	**824.0**
Income tax benefit (expense)	(136.2)	(104.3)	(185.1)	0.2	(69.1)	(272.4)	(58.7)	(400.2)	(57.8)	(64.0)	(67.9)	(74.9)	(264.5)	(288.4)
Net income	**304.4**	**174.6**	**340.0**	**(16.6)**	**99.2**	**464.4**	**109.1**	**656.1**	**107.4**	**118.8**	**126.1**	**139.0**	**491.3**	**535.6**
GAAP Basic EPS	$5.84	$3.49	$7.06	($0.36)	$2.15	$10.20	$2.38	$14.25	$2.37	$2.67	$2.87	$3.22	$11.12	$13.50
GAAP Diluted EPS	$5.67	$3.28	$6.28	($0.36)	$1.91	$9.24	$2.14	$12.74	$2.14	$2.40	$2.58	$2.89	$9.99	$11.99
Non-GAAP Basic EPS	$8.98	$11.95	$12.26	$2.89	$2.88	$3.92	$3.14	$12.81	$3.15	$3.45	$3.67	$4.03	$14.28	$17.15
Non-GAAP Diluted EPS	**$8.72**	**$11.24**	**$10.91**	**$2.55**	**$2.55**	**$3.55**	**$2.83**	**$11.45**	**$2.84**	**$3.11**	**$3.30**	**$3.61**	**$12.83**	**$15.23**
Basic	52.1	50.1	48.2	46.7	46.1	45.5	45.9	46.1	45.2	44.5	43.9	43.2	44.2	39.7
Diluted	53.7	53.2	54.2	53.0	51.9	50.2	50.9	51.5	50.2	49.5	48.9	48.2	49.2	44.7

Y/Y Growth	FY12	FY13	FY14	1Q15	2Q15	3Q15	4Q15E	FY15E	1Q16E	2Q16E	3Q16E	4Q16E	FY16E	FY17E
Remodulin	6%	7%	13%	7%	(2%)	5%	7%	4%	3%	4%	(3%)	(5%)	(0%)	(3%)
Tyvaso	35%	35%	6%	6%	(4%)	2%	3%	1%	1%	2%	0%	(0%)	1%	1%
AdCirca	74%	44%	25%	10%	23%	44%	5%	20%	43%	18%	15%	23%	23%	2%
Orenitram (Oral Remodulin)					290%	138%	113%	201%	120%	113%	75%	63%	86%	41%
Total Revenue	23%	22%	15%	13%	8%	17%	13%	13%	18%	18%	11%	12%	14%	8%
Non-GAAP Diluted EPS	44%	29%	(3%)	62%	11%	(9%)	(12%)	5%	11%	22%	(7%)	28%	12%	19%

Source: Company reports and RBC Capital Markets estimates

Valuation

Our base case $175 price target is derived by applying a ~12.5x forward P/E multiple on fully taxed non-GAAP 2017E EPS. We believe 12.5x is a fair and reasonable multiple given it is on par with other peer profitable mid- to large-cap biotechs with low single-digit growth projections. Our valuation is supported by a DCF assuming healthy 7-9% top-line growth post-2017, while adjusting to 30% probability that generic Remodulin enters post-2017, albeit at a modest -5% terminal rate. We apply a 10% discount rate.

Price target impediments

Our price target is primarily dependent on the prospects that UTHR's key franchises — Remodulin, Tyvaso, AdCirca, and oral Remodulin (Orenitram) — demonstrate revenue stability and growth, amid new competitive products from Bayer and potentially Actelion. The PAH market is also seeing generic entries of blockbuster Tracleer. Lastly, we assign a 70% probability that Remodulin IP extends to 2023 against another generic company, Teva (Sandoz settled for June 2018). However, if the IP does not extend to 2023 (as many investors assume) due to a negative outcome from litigation against Teva, the achievement of our price target would also be impeded.

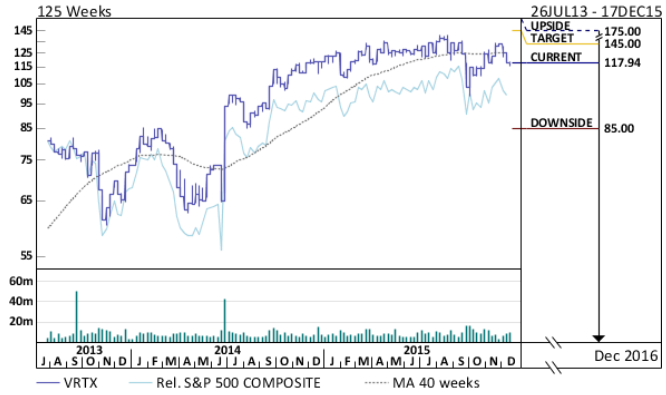
Vertex Pharmaceuticals (VRTX)

Outperform

Price Target USD $145.00

Target/Upside/Downside Scenarios

Exhibit 122: Vertex Pharmaceuticals



Source: RBC Capital Markets estimates

Target price/base case

Our base case of $145/share is based on two approaches: (1) our DCF valuation and (2) a 20x to our 2019E non-GAAP EPS and then discounting back at 10%. We believe this is appropriate because VRTX is on the verge of a major earnings inflection due to the recent launch of Orkambi. In our view, a 20x EPS multiple is reasonable, as it is not far from the 18x mean multiple for high-growth, profitable large-cap biotech companies.

Upside scenario

Our upside scenario of $175 is based on: (1) a more aggressive 25x multiple on our 2019 non-GAAP EPS and then discounting back at 10%, and (2) a DCF approach that assumes 100% POS in heterozygous patients. We believe this higher multiple is achievable if VRTX is successful in building a robust pipeline beyond cystic fibrosis (CF) that can help in the company's continued growth in its top and bottom line.

Downside scenario

Our downside scenario of $85 is based on a more conservative 12-13x PE multiple on potential $9+ EPS power (FY19) and based on a conservative DCF approach using only the base business and no heterozygous upside potential. This may result if VRTX fails to bolster its pipeline with promising drugs or to offset any competitive risk to its core CF franchise.

Investment summary

Our positive view of VRTX is based on confidence in its leadership in the discovery and development of cystic fibrosis therapies for F508del homozygous and heterozygous patients, which would expand its addressable market from 4% to 80% of affected patients. We believe the stock is likely to have continued upward momentum as we believe clinical and regulatory success will enable VRTX's leadership position in a significant market opportunity ($7–8B WW peak sales, 60,000 patients WW, pricing of $150K–$250K per patient), which could propel strong revenue growth for the next decade. Bottom line, we see the stock trending higher based on a very profitable, high-margin, biotech earnings growth story starting to become clearer. We see other positives for VRTX in addition to potential drug catalysts, including the company being: (1) relatively under owned by mutual funds and (2) an attractive takeout candidate in the long-term.

Potential catalysts for the stock

Phase II data of 'triple pill' combo (v3.0) in H2:16: VRTX is building beyond Orkambi (v1.0) by developing VX-661/Kaly combo (v2.0) and triple pill combo (VX-661 + Kaly + 3rd gens VX-440 and VX-152), the latter of which is entering Phase I and is expected to enter Phase II in H2:16. A quick 28-day study should read out soon and provide the biggest upside catalyst for VRTX. If v3.0 combos work in heteros, they could bring $2B of additional revenue to VRTX. These drugs have shown 2-3x the early efficacy than VX-661 (v2.0) in assays.

Continued strong sales of '809 (Orkambi): Q3:15 Orkambi was $131M ($114M ex-inventory) vs consensus $90M. 3,000 US patients (ages 12+), or 35% of the market, have started and we think this will be 75% by YE:16. We think VRTX has the necessary bandwidth and experience in securing EU reimbursements in a timely fashion.

Strong 2016 Kalydeco guidance exceeding consensus: VRTX has been getting additional label expansions.

The following are risks to our investment thesis

Our price target is dependent primarily on the regulatory and commercial success of Kalydeco and VX-809 for CF. At Vertex's current valuation, a base level of sales in the broader CF patient population is already assumed. The magnitude of the combo commercial launch and additional pipeline readouts will likely be essential in determining the upside (or downside) from current levels. Any delayed launch in EU countries, increased competition, regulatory setbacks, or other limitations to the market potential of CF therapies could negatively affect our valuation. Upside should come from pricing, better than anticipated market penetration, setbacks for competition, new partnerships, and clinical success of earlier-stage programs.

2016 thoughts on VRTX

We continue to see the stock going higher based on a very profitable, high-margin, biotech earnings growth story starting to become clear. We think the stock is undervalued based on $9+ earnings power (so a 15-17x multiple on our FY19E EPS is $135-155) and more importantly for longer term investors, we're going to continue to track the new "triple" CF pill (in Phase I with data Spring 2016) and key proof-of-concept (Phase II) coming around YE:16. If "triple" shows positive Phase II data, VRTX could be at $175+ as this would add another ~$2B or ~$5+ in EPS power, getting us to $14+ earnings power.

We think the Street has not yet appreciated the fact that there are two shots on goal for the heteros. The two "triple" pills are now entering Phase I and this program is not in consensus estimates. This data should be a catalyst in Spring 2016 as the Street starts to shift towards the high value propositions as the "triples" go into Phase II.

We think Phase II data for the "triple" in heterozygous is the most important catalyst for this stock and could have positive data by YE:16 or more likely early 2017. If positive data, this could make the $2B heterozygous opportunity in play and drive the stock to $175-200 (assuming taking current 45% probability up towards 80%+ in 2017).

We believe the stock is relatively under-owned in the mutual fund community as Orkambi has just launched, the company is still unprofitable, and there is no current P/E valuation, making it currently an untraditional large cap company for most generalist portfolios.

While competition has been somewhat of an overhang and GLPG has been issuing many press releases about their programs, we think enrollment, combination safety, and ultimate efficacy are not low bars. In fact, we don't think there will be any real efficacy data from GLPG in 2016 but if there are any safety issues with these drugs in 2016-17 then the program could be in serious jeopardy and would be a big catalyst for VRTX.

Competitor clinical timelines: GLPG/ABBV have multiple programs underway. Phase I potentiator data could be YE:16 in CF pts, Phase I "corrector" data in healthies could be 2016, and "2nd corrector" is going into clinic in 2016. Separately, PRQR gene therapy data is expected in mid 2016.

Finally, we think VRTX continues to be an attractive long-term potential takeout candidate (e.g. JNJ or ABBV per our prior notes and comments) given its long duration revenue franchise, high barrier to entry (they keep improving on the drugs and now doing platform technology partnerships to add on), high 50-55% potential margins that could go towards 70%+ if acquirer wiped expenses, and pipeline upside.

For Q4:15, we think the company will pre-announce in early January with solid Orkambi sales and importantly – in-line expense guidance (consensus 2016 OpEx of $1,132M vs 2015 $1071M). It is possible they guide upside Kalydeco for 2016 and may provide US Orkambi guidance but we do not expect any comments/guidance on OUS sales given they just got approved.

Bear case

- Already high expectations on the US launch (Street generally assumes strong launch) and OUS launch will have reimbursement delays and headline risk. Kalydeco had significant pricing delays and Orkambi addresses a 3-5x bigger market and budget request.
- OUS consensus estimates appear too high at ~$500M for 2016 and we are much lower around $300M. This is because Germany will be the primary country in 2016 and for Kalydeco, it took three quarters to get the next country on board (UK) – hence base-case Orkambi OUS sales should be relatively modest until Q3.
- Competition is the Achilles heel – consensus has no competition in the models and GLPG/ABBV have multiple programs underway. Phase I potentiator data could be YE:16 in CF pts, Phase I "corrector" data in healthies could be 2016, and "2nd corrector" is going into clinic in 2016. Separately, PRQR gene therapy data in mid '16 (although delayed from YE:15).
- What if the company buys something? If the company does any meaningful M&A acquisitions, then this could turn investor sentiment negative given most bulls do not want higher expenses and dilutive acquisitions (and primarily want VRTX to be sold).
- EU launch is going to have a lot of negative headline risk and pricing issues. This is inevitable. OUS launch will be a big disappointment given all the issues we saw when they launched Kalydeco years ago. The '809 homozygous market is 5x the size of that so imagine what governments are going to say.
- The company spends too much and now they're bringing cancer and pain drugs to the clinic in 2016, which they have no expertise in.

Key questions and debates for VRTX

1. Why could Phase I data on the v3.0 drugs (VX-440 and VX-152) be important and a key catalyst?

Phase I data for new VX-152 or VX-440 in H1:16 would be de-risking because the company believes that as long as they get the "exposure" in Phase I/II (i.e., good PK linearity, bioavailability, half-life, etc.) and safety/ tolerability, then these efficacy levels seen in-vitro (2–3x the chloride transport levels vs. Orkambi) should lead to at least 2–3% or even more of FEV-1, meaningful benefits on exacerbations, etc. The doses planned across Phase I will cover therapeutic ranges predicted in-vitro. Thus, if Phase I looks good, management have said they would feel a lot better, as you don't know what things can occur until you put it in humans. Refining 152/440 drug properties has been going on for a year and competitors, e.g., GLPG, may not have spent the same rigorous time doing tox, DDI work, metabolite work, etc. as they are mainly looking to get programs in the clinic. Ultimately, we estimate key Phase II "triple" data around YE:16 (key catalyst).

2. What is the strategy to have a therapy to treat the 30% extra "heterozygous" patients?

There are two primary approaches to target the heterozygous "minimally residual" (het-min) large population where '809 has not shown any efficacy. The first is that VX-661 entered Phase III in multiple heterozygous studies starting H1:15, and we estimate data H2:16-2017. Secondly, VRTX is advancing a number of potent candidates as a "dual corrector" to add on top of the Kalydeco and '809 combo and make a "three-drug" combo (v3.0). These drugs enter the clinic YE:15/early 2016, and may have Phase I data by H1:16 end. VRTX could initiate Phase II studies with data readouts by H2:16. So by YE:16 we should have a clearer answer on whether one of these "works" in heterozygous CF patients.

3. Are there buyers out there for VRTX?

Our conversations with investors suggests that many believe JNJ (covered by Glenn Novarro) could be one possible acquirer as it actively pursues assets that could accelerate growth; it didn't buy PCYC at $21B earlier this year and ABBV did; public comments suggests that JNJ is not wedded to its AAA debt rating and is willing to do a larger deal than historical (see RBC JNJ note 10/22). ABBV remains another possibility later given consensus need to fill erosion from Humira biosimilar risk and recent addition of senior M&A expert to management team.

Exhibit 123: VRTX's CF franchise yields a probability-adjusted $145/share

Probability of Success (PoS) Assumptions	Ph3 Start	Approval	PoS
Gating mutations (G551D, R117H, etc.)	100%	100%	100%
F508del homozygous	100%	100%	100%
F508del heterozyous	100%	20%	45%

Peak Sales Estimate ($M)	US Sales	Ex-US Sales	PoS	$/Share
Gating mutations (G551D, R117H, etc.)	$532	$549	100%	$28
F508del homozygous	$2,298	$1,785	100%	$98
F508del heterozyous	$1,224	$808	45%	$20
Total $/Share (Prob. Adjusted Value)				$145

Mutation in CFTR Gene: Approximate Percentage of CF Patients in the U.S.	
G551D mutation on at least one allele	4%
non-G551D gating mutation on at least one allele	1%
R117H mutation on at least one allele	3%
F508del mutation on both alleles (homozygous)	47%
F508del mutation on one allele but not both alleles (heterozygous)	40%

CF population	
U.S.	30,000
EU	33,000

Revenue Summary ($M)	2013	2014	2015	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
By Geography															
US Revenue	**$213**	**$260**	**$706**	**$1,501**	**$1,868**	**$2,844**	**$3,546**	**$3,918**	**$4,054**	**$4,054**	**$4,054**	**$4,054**	**$4,054**	**$4,054**	**$4,054**
Kalydeco	213	260	354	384	431	490	520	532	532	532	532	532	532	532	532
Orkambi	-	-	351	1,117	1,436	1,756	2,075	2,298	2,298	2,298	2,298	2,298	2,298	2,298	2,298
Triple	-	-	-	-	-	598	952	1,088	1,224	1,224	1,224	1,224	1,224	1,224	1,224
Ex-US Revenue	**$158**	**$206**	**$261**	**$543**	**$1,081**	**$1,732**	**$2,520**	**$3,093**	**$3,190**	**$3,197**	**$3,204**	**$3,210**	**$3,210**	**$3,176**	**$3,142**
Kalydeco	158	206	261	295	412	563	584	591	598	604	611	618	618	584	549
Orkambi	-	-	-	248	669	1,115	1,487	1,785	1,785	1,785	1,785	1,785	1,785	1,785	1,785
Triple	-	-	-	-	-	54	449	718	808	808	808	808	808	808	808
Total	**$371**	**$466**	**$967**	**$2,044**	**$2,949**	**$4,577**	**$6,066**	**$7,011**	**$7,244**	**$7,250**	**$7,257**	**$7,264**	**$7,264**	**$7,230**	**$7,195**
By Mutation															
Gating mutations (G551D, R117H, etc.)	$371	$466	$615	$679	$843	$1,053	$1,104	$1,122	$1,129	$1,136	$1,143	$1,150	$1,150	$1,115	$1,081
F508del homozygous	-	-	351	1,365	2,106	2,871	3,562	4,083	4,083	4,083	4,083	4,083	4,083	4,083	4,083
F508del heterozyous	-	-	-	-	-	652	1,401	1,806	2,031	2,031	2,031	2,031	2,031	2,031	2,031
Total	**$371**	**$466**	**$967**	**$2,044**	**$2,949**	**$4,577**	**$6,066**	**$7,011**	**$7,244**	**$7,250**	**$7,257**	**$7,264**	**$7,264**	**$7,230**	**$7,195**

Pricing Assumptions			
U.S.			
Annual Kalydeco price ($)	$300,000	Annual Orkambi price ($)	$259,000
Gross to Net	13%	Gross to Net	15%
Annual Net Kalydeco Price ($)	**$262,500**	**Annual Net Orkambi Price ($)**	**$220,150**
EU			
Annual Kalydeco price ($)	$277,500	Annual Orkambi price ($)	$155,400
Gross to Net	0%	Gross to Net	0%
Annual Net Kalydeco Price ($)	**$277,500**	**Annual Net Kalydeco Price ($)**	**$155,400**

Revenue Model		2013	2014	2015	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
US																
Gating mutations (G551D, R117H, etc.), Kalydeco																
Prevalence	2,250	2,250	2,250	2,250	2,250	2,250	2,250	2,250	2,250	2,250	2,250	2,250	2,250	2,250	2,250	2,250
Market Penetration (%)		36%	44%	60%	65%	73%	83%	88%	90%	90%	90%	90%	90%	90%	90%	90%
Patients Treated		810	990	1,350	1,463	1,643	1,868	1,980	2,025	2,025	2,025	2,025	2,025	2,025	2,025	2,025
Annual Cost		$262,500	$262,500	$262,500	$262,500	$262,500	$262,500	$262,500	$262,500	$262,500	$262,500	$262,500	$262,500	$262,500	$262,500	$262,500
Growth Rate			0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Revenue		**$213**	**$260**	**$354**	**$384**	**$431**	**$490**	**$520**	**$532**	**$532**	**$532**	**$532**	**$532**	**$532**	**$532**	**$532**
F508del Homozygous (Orkambi)																
Prevalence	14,500	14,500	14,500	14,500	14,500	14,500	14,500	14,500	14,500	14,500	14,500	14,500	14,500	14,500	14,500	14,500
Market Penetration (%)		0%	0%	11%	35%	45%	55%	65%	72%	72%	72%	72%	72%	72%	72%	72%
Patients Treated		-	-	1,595	5,075	6,525	7,975	9,425	10,440	10,440	10,440	10,440	10,440	10,440	10,440	10,440
Annual Cost		$220,150	$220,150	$220,150	$220,150	$220,150	$220,150	$220,150	$220,150	$220,150	$220,150	$220,150	$220,150	$220,150	$220,150	$220,150
Growth Rate			0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Revenue		-	-	**$351**	**$1,117**	**$1,436**	**$1,756**	**$2,075**	**$2,298**	**$2,298**	**$2,298**	**$2,298**	**$2,298**	**$2,298**	**$2,298**	**$2,298**
F508del - Heterozygous (VX-770 + VX-661 + VX152 or VX-440)																
Prevalence	10,500	10,500	10,500	10,500	10,500	10,500	10,500	10,500	10,500	10,500	10,500	10,500	10,500	10,500	10,500	10,500
Market Penetration (%)		0%	0%	0%	0%	0%	22%	35%	40%	45%	45%	45%	45%	45%	45%	45%
Patients Treated		-	-	-	-	-	2,310	3,675	4,200	4,725	4,725	4,725	4,725	4,725	4,725	4,725
Annual Cost		$259,000	$259,000	$259,000	$259,000	$259,000	$259,000	$259,000	$259,000	$259,000	$259,000	$259,000	$259,000	$259,000	$259,000	$259,000
Growth Rate			0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Revenue		-	-	-	-	-	**$598**	**$952**	**$1,088**	**$1,224**	**$1,224**	**$1,224**	**$1,224**	**$1,224**	**$1,224**	**$1,224**
EU																
Gating mutations (G551D, R117H, etc.), Kalydeco																
Prevalence	2,475	2,475	2,475	2,475	2,475	2,475	2,475	2,475	2,475	2,475	2,475	2,475	2,475	2,475	2,475	2,475
Market Penetration (%)		23%	30%	38%	43%	60%	82%	85%	86%	87%	88%	89%	90%	90%	85%	80%
Patients Treated		569	743	941	1,064	1,485	2,030	2,104	2,129	2,153	2,178	2,203	2,228	2,228	2,104	1,980
Annual Cost		$277,500	$277,500	$277,500	$277,500	$277,500	$277,500	$277,500	$277,500	$277,500	$277,500	$277,500	$277,500	$277,500	$277,500	$277,500
Growth Rate			0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Revenue		**$158**	**$206**	**$261**	**$295**	**$412**	**$563**	**$584**	**$591**	**$598**	**$604**	**$611**	**$618**	**$618**	**$584**	**$549**
F508del Homozygous (Orkambi)																
Prevalence	15,950	15,950	15,950	15,950	15,950	15,950	15,950	15,950	15,950	15,950	15,950	15,950	15,950	15,950	15,950	15,950
Market Penetration (%)		0%	0%	0%	10%	27%	45%	60%	72%	72%	72%	72%	72%	72%	72%	72%
Patients Treated		-	-	-	1,595	4,307	7,178	9,570	11,484	11,484	11,484	11,484	11,484	11,484	11,484	11,484
Annual Cost		$155,400	$155,400	$155,400	$155,400	$155,400	$155,400	$155,400	$155,400	$155,400	$155,400	$155,400	$155,400	$155,400	$155,400	$155,400
Growth Rate			0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Revenue		-	-	-	**$248**	**$669**	**$1,115**	**$1,487**	**$1,785**	**$1,785**	**$1,785**	**$1,785**	**$1,785**	**$1,785**	**$1,785**	**$1,785**
F508del - Heterozygous (VX-770 + VX-661 + VX152 or VX-440)																
Prevalence	11,550	11,550	11,550	11,550	11,550	11,550	11,550	11,550	11,550	11,550	11,550	11,550	11,550	11,550	11,550	11,550
Market Penetration (%)		0%	0%	0%	0%	0%	3%	25%	40%	45%	45%	45%	45%	45%	45%	45%
Patients Treated		-	-	-	-	-	347	2,888	4,620	5,198	5,198	5,198	5,198	5,198	5,198	5,198
Annual Cost		$155,400	$155,400	$155,400	$155,400	$155,400	$155,400	$155,400	$155,400	$155,400	$155,400	$155,400	$155,400	$155,400	$155,400	$155,400
Growth Rate			0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Revenue		-	-	-	-	-	**$54**	**$449**	**$718**	**$808**	**$808**	**$808**	**$808**	**$808**	**$808**	**$808**

Source: Company reports, RBC Capital Markets estimates

Exhibit 124: VRTX consensus comparison

($ Figures in MM)	Q4:15			2015			2016		
	Guidance[1]	Consensus[2]	RBC Est.	Guidance	Consensus[2]	RBC Est.	Guidance	Consensus[2]	RBC Est.
Kayldeco WW	$154 - $169	$167	$164	$605 - $620	$618	$615	-	$747	$679
Orkambi	-	$238	$220	-	$365	$351	-	$1,681	$1,375
US	-	*232*	*220*	-	*362*	*351*	-	*1320*	*1165*
ex-US	-	*0*	*0*	-	*0*	*0*	-	*345*	*210*
Non-GAAP OpEx	$272 - $322	$287	$293	$1,050 - $1,100	$1,063	$1,071	-	$1,167	$1,196

[1] Derived by subtracting the sum of Q1:15, Q2:15 and Q3:15 actuals from 2015 guidance

[2] Mean

Source: Company reports and RBC Capital Markets estimates

Exhibit 125: VRTX's expected news flow

Timing	Expected News Flow	Program
Cystic Fibrosis (Kalydeco) - Indication Expansion		
Feb 6, 2016	PDUFA for people ages 2+ with one of 23 residual function mutations (sNDA)	Kalydeco
Q1:16	Initiate study to evaluate safety of treating infants and toddlers <24 months	Kalydeco
Cystic Fibrosis (Kalydeco + VX-809 aka Lumacaftor) - Combo "Orkambi"		
H1:16	Submit sNDA for kids ages 6-11 based on Phase III safety study	Orkambi
2016	Poentially Initiate a study to evaluate safety of treating ages 2-5	Orkambi
Cystic Fibrosis (Kalydeco,VX-661) - Combo		
mid-2016	Complete enrollment for all four Phase III pivotal programs	VX-661 + Kalydeco
H2:16	Potential data from first three Phase III pivotal programs (excluding "heterozygous")	VX-661 + Kalydeco
H2:16-2017	Phase III "heterozygous" futility analysis data on 150 patients	VX-661 + Kalydeco
Cystic Fibrosis (VX-371 and VX-371/Orkambi combo; Collaboration with Parion Sciences)		
early '16	Initiate Phase IIa study on VX-371 + Orkambi for homozygous F508del patients	Orkambi +/ VX-371
mid-2016	Phase IIa data of inhaled VX-371 in 120 people with any CFTR mutation (CLEAN-CF)	VX-371 (P-1037)
Cystic Fibrosis VX-152 and VX-440 - Next gen correctors (triple combo)		
H1:16	Phase I data of VX-152 alone and in combination with VX-661/ivacaftor in healthies	VX-152 +/- VX-661/ivacaftor
H1:16	Phase I data of VX-440 alone and in combination with VX-661/ivacaftor in healthies	VX-440 +/- VX-661/ivacaftor
H2:16	Initiate Phase II study evaluating VX-152 in combination with VX-661/ivacaftor	VX-152 +/- VX-661/ivacaftor
H2:16	Initiate Phase II study evaluating VX-440 in combination with VX-661/ivacaftor	VX-440 +/- VX-661/ivacaftor
H2:16	Initiate Phase II triple combination study in patients with F508del mutation	VX-152/VX-661/ivacaftor
H2:16	Initiate Phase II triple combination study in patients with F508del mutation	VX-440/VX-661/ivacaftor
YE:16	VX-152, VX-440 potential Phase II efficacy data in hetero CF	VX-440, VX-152
Pain		
YE:15	Initiate Phase II PoC in 100 patients with symptomatic osteoarthritis of the knee	VX-150
H1:16	Start clinical development of second sodium channel inhibitor	VX-241
Influenza		
2019	NME filing of JNJ-872 for treatment of Influenza A	JNJ-872 (VX-787)
Oncology		
early 2016	Initiate clinical study to evaluate escalating doses of VX-984 alone and in combo with chemotherapy drug pegylated liposomal doxorubicin	VX-984
2016	Complete two Phase I open-label in combination with DNA-damaging chemotherapies across various solid tumors; includes triple-negative breast cancer patients and NSCLC patients	VX-970
2016	Complete Phase I open-label trial evaluating escalating doses of VX-803 alone and in combination with chemotherapy	VX-803

Source: Company reports and RBC Capital Markets estimates

Exhibit 126: VRTX's pipeline table

Drug	Phase	Indication
Cystic Fibrosis		
VX-661	Phase III	F508del mutation
VX-371	Phase II	F508del mutation
VX-152	Phase I	F508del mutation
VX-440	Phase I	F508del mutation
Oncology		
VX-970	Phase I	Solid tumors
VX-803	Phase I	Undisclosed
VX-984	Pre-clinical	Undisclosed
Pain		
VX-150	Phase II	Symptomatic osteoarthritis (knee)
VX-241	Pre-clinical	Sodium channel inhibitor
Influenza		
VX-787	NME filing	Influenza A

Source: Company reports and RBC Capital Markets estimates

Exhibit 127: Income statement for VRTX

Fiscal Year (Ending in December) ($ figures in MM, except per share)	FY14	1Q15 Mar-15	2Q15 Jun-15	3Q15 Sep-15	4Q15E Dec-15	FY15E	1Q16E Mar-16	2Q16E Jun-16	3Q16E Sep-16	4Q16E Dec-16	FY16E	FY17E	FY18E	FY19E
Non-GAAP Income Statement														
Telaprevir Revenue	$24.0	$0.7	$5.5	$5.8	$1.9	$13.9	-	-	-	-	-	-	-	-
Kalydeco	**$463.9**	**$130.2**	**$154.9**	**$165.9**	**$164.0**	**$615.0**	**$166.0**	**$168.0**	**$171.0**	**$174.0**	**$679.0**	**$833.4**	**$1,052.9**	**$1,085.0**
Kalydeco - US	*262.6*	*72.0*	*93.0*	*95.0*	*93.0*	*353.0*	*94.0*	*95.0*	*97.0*	*99.0*	*385.0*	*433.4*	*491.0*	*520.0*
Kalydeco - ROW	*201.3*	*58.2*	*61.9*	*70.9*	*71.0*	*262.0*	*72.0*	*73.0*	*74.0*	*75.0*	*294.0*	*400.0*	*561.9*	*565.0*
Orkambi	-	-	-	**$130.8**	**$220.0**	**$350.8**	**$247.0**	**$315.0**	**$376.0**	**$437.0**	**$1,375.0**	**$2,100.0**	**$2,590.0**	**$3,030.0**
Orkambi - US	-	-	-	*130.8*	*220.0*	*350.8*	235.0	270.0	*310.0*	*350.0*	*1,165.0*	*1,425.0*	*1,490.0*	*1,530.0*
Orkambi - ROW	-	-	-	-	-	-	12.0	45.0	*66.0*	*87.0*	*210.0*	*675.0*	*1,100.0*	*1,500.0*
GSK Royalty Revenues (non-cash)	*40.9*	*6.8*	*5.1*	*5.8*	*6.0*	*23.6*	*5.0*	*5.0*	*5.0*	*5.0*	*20.0*	*20.0*	*20.0*	*20.0*
Collaborative R&D and milestones	*51.7*	*0.8*	*0.6*	*1.5*	*0.6*	*3.6*	*2.0*	*2.0*	*2.0*	*2.0*	*8.0*	*12.0*	*15.0*	*15.0*
Total GAAP Revenue	$580.4	$138.5	$166.1	$309.8	$392.5	$1,006.9	$420.0	$490.0	$554.0	$618.0	$2,082.0	$2,965.4	$3,677.9	$4,150.0
Revenue Adjustments	(44.6)	(3.1)	(6.2)	(7.5)	(6.0)	(22.8)	(4.0)	(4.0)	(4.0)	(4.0)	(16.0)	(10.0)	(10.0)	(10.0)
Total non-GAAP Revenue	**$535.8**	**$135.4**	**$159.9**	**$302.3**	**$386.5**	**$984.2**	**$416.0**	**$486.0**	**$550.0**	**$614.0**	**$2,066.0**	**$2,955.4**	**$3,667.9**	**$4,140.0**
Cost of product revenues and royalty expenses	45.0	10.7	16.5	33.5	69.4	130.1	69.3	64.3	67.1	68.7	269.5	301.3	372.3	419.5
Research and Development	694.2	177.2	181.9	201.6	215.0	775.7	210.0	215.0	220.0	225.0	870.0	891.0	912.4	934.3
Sales, General and Administrative	225.6	69.1	72.0	76.1	78.0	295.3	79.0	80.0	82.0	85.0	326.0	314.5	303.2	292.1
Total Costs and Expenses	**$964.8**	**$257.0**	**$270.4**	**$311.2**	**$362.4**	**$1,201.1**	**$358.3**	**$359.3**	**$369.1**	**$378.7**	**$1,465.5**	**$1,506.9**	**$1,587.9**	**$1,645.8**
Operating Income (Loss)	**($429.0)**	**($121.6)**	**($110.5)**	**($8.9)**	**$24.1**	**($216.9)**	**$57.7**	**$126.7**	**$180.9**	**$235.3**	**$600.5**	**$1,448.5**	**$2,080.0**	**$2,494.2**
Other Income/(Expense), Net	(79.2)	(26.4)	(19.7)	(22.5)	(21.0)	(89.6)	(21.0)	(21.0)	(21.0)	(21.0)	(84.0)	(84.0)	(84.0)	(84.0)
Income (Loss) before Tax	(508.1)	(148.0)	(130.2)	(31.4)	3.1	(306.5)	36.7	105.7	159.9	214.3	516.5	1,364.5	1,996.0	2,410.2
Provision for Income Tax	3.1	0.4	0.5	0.6	0.1	1.5	(0.1)	0.2	0.5	0.7	1.3	26.9	31.7	52.0
Net Income (Loss), non-GAAP	**($511.2)**	**($148.4)**	**($130.7)**	**($31.9)**	**$3.0**	**($308.0)**	**$36.8**	**$105.5**	**$159.4**	**$213.5**	**$515.3**	**$1,337.7**	**$1,964.3**	**$2,358.2**
EPS, Basic (non-GAAP)	($2.17)	($0.62)	($0.54)	($0.13)	$0.01	($1.28)	$0.15	$0.43	$0.65	$0.86	$2.09	$5.38	$7.82	$9.30
EPS, Diluted (non-GAAP)*	**($2.17)**	**($0.62)**	**($0.54)**	**($0.13)**	**$0.01**	**($1.28)**	**$0.15**	**$0.43**	**$0.65**	**$0.86**	**$2.09**	**$5.38**	**$7.82**	**$9.30**
Basic Shares Outstanding	235.3	239.5	240.8	242.0	243.2	241.3	244.4	245.6	246.8	248.1	246.2	248.7	251.2	253.7
Diluted Shares Outstanding*	235.3	239.5	240.8	242.0	243.2	241.3	244.4	245.6	246.8	248.1	246.2	248.7	251.2	253.7
EPS, Diluted (Non-GAAP, as reported)*	**($2.17)**	**($0.62)**	**($0.54)**	**($0.13)**	**$0.01**	**($1.28)**	**$0.15**	**$0.43**	**$0.65**	**$0.86**	**$2.09**	**$5.38**	**$7.82**	**$9.30**

Source: Company reports and RBC Capital Markets estimates

Valuation

Our base case of $145/share is based on two approaches: (1) our DCF valuation and (2) a 20x to our 2019E non-GAAP EPS and then discounting back at 10%. We believe this is appropriate because VRTX is on the verge of a major earnings inflection due to the recent launch of Orkambi. In our view, a 20x EPS multiple is reasonable, as it is not far from the 18x mean multiple for high-growth, profitable large-cap biotech companies.

Price target impediments

Our price target is dependent primarily on the regulatory and commercial success of Kalydeco and VX-809 for cystic fibrosis. At Vertex's current valuation, a base level of sales in the broader cystic fibrosis patient population is already assumed. The magnitude of the combo commercial launch and additional pipeline readouts will likely be essential in determining the upside (or downside) from current levels. Any delayed launch in EU countries, increased competition, regulatory setbacks, or other limitations to the market potential of CF therapies could negatively affect our valuation. Upside could come from pricing, better than anticipated market penetration, setbacks for competition, new partnerships, and clinical success of earlier-stage programs that are not included in our valuation.

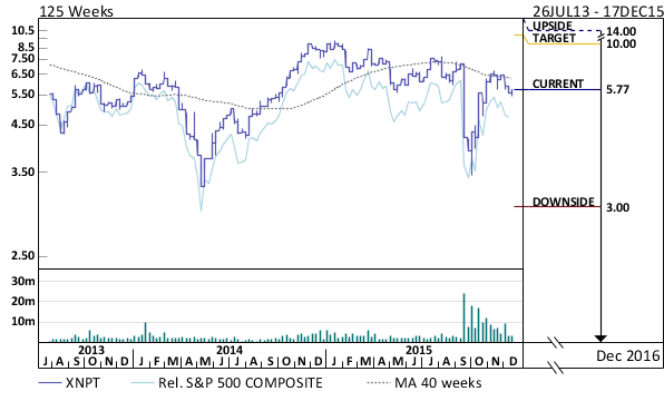
Xenoport, Inc. (XNPT)

Outperform

Price Target USD 10.00

Target/Upside/Downside Scenarios

Exhibit 128: Xenoport Inc.



Source: RBC Capital Markets estimates

Target price/base case

Our base case of $10/share assumes that: 1) Horizant can grow to $100M+ franchise over time and should be valued at 4-5x sales, and 2) '829 will garner partnership interest in either neurology or dermatology. We include ~$1 net cash in valuation.

Upside scenario

Our upside scenario of $14/share assumes 4-5x sales on a bigger $200M+ drug and some modest probability of success for '829 (30% probability of $800M drug) should it attract partnership interest in both psoriasis and MS indications.

Downside scenario

Our downside scenario of $3/share assumes zero value for '829 and 3-4x sales on a $60M drug and assumes they burn the $1 net cash through 2016+.

Investment summary

We believe XNPT, rated Outperform, is an attractive small-cap play with an FDA-approved drug Horizant for RLS and pain. This makes for an interesting specialty pharma acquisition given the potential leverage and growth Horizant could drive for another company. We believe XNPT could be sold and there should be interested parties for the Horizant asset now doing a $45M+ run rate of sales and/or any interest or value included for the DMF fumarate drug, which showed positive Phase II psoriasis data. However, we believe a potential acquisition could take time (e.g. into mid-2016) as partnering discussions for '829 have just started and XNPT may need to prove that they can achieve a $70M+ annual run rate in 2016.

Potential catalysts for the stock

Better than expected Horizant sales growth: Consistent quarterly sales growth since the relaunch of Horizant in RLS and PHN should increase investor confidence that it is a viable market ($100-150M peak sales at 4-5x multiple yields $400-$600M or $6-$10/share, plus $1 share net cash).

Potential partnership to develop '829: We think changes in management, including the October 2015 resignation of CEO, is a step closer to the right direction for XNPT, given investor frustration with multiple clinical programs over the past 5 years. XNPT has indicated they are engaging in partnership discussions for '829.

Potential sale of the company: Monetization or sale of the whole company to a spec pharma acquirer could be the best and fastest way to maximize shareholder value at this point.

The following are risks to our investment thesis

Our price target is significantly dependent on Horizant sales and secondarily the clinical and regulatory success of Xenoport's product candidate '829. Impediments to our price target include: (1) deceleration in Horizant sales, 2) delays in securing a partnership for '829, 3) unexpected safety or adverse events (if '829 goes into Phase III), and 4) competition. Any negative or unexpected developments related to these issues would significantly affect the company's outlook and the ability of the stock to reach our price target.

DMF would require a large and costly Phase III program for psoriasis: Were XNPT to advance '829 into Phase III by themselves, the ROI may not be justified depending on the assumed niche market share, IP protection, and other alternatives in dermatology. DMF may also require a PML class warning, which would hamper its use in psoriasis. MS would also require hundreds of millions to run a Phase III program and there is significant uncertainty here as Tecfidera sales have slowed and a once-daily is not a significant enough differentiator to matter down the road.

2016 thoughts on XNPT

The bull case here for us is simply that XNPT could be sold and there should be interested parties for the Horizant asset now doing a $45M+ run-rate of sales and/or any interest or value included for the DMF fumarate drug, which had positive Phase II psoriasis data. Horizant is on a $40-50M run-rate by YE:15 and reach $60-70M+ in 2016, thanks to an expanded salesforce only hitting 25% of the target market of prescribers. A bigger salesforce drives more sales and better margins. We think Horizant could probably grow to $100-150M+. With an average 4-5x peer sales multiple. This implies ~$400-600M or $6-10/share, plus $1/ share net cash, yielding up to ~50% average upside from current prices.

The key is this might take time into mid-16 as partnering discussions for '829 have only just started, and it will take time to prove the $70M+ run-rate and pharma may not initially want to pay 4-5x $100-150M and instead something less given that's the upside to them they take home and given the opportunity cost of doing this deal over anything else. If they paid $10, a buyer might get '829 for free in that. Thus, $10 seems reasonable (and is our PT) and a ballpark value for either '829 and Horizant or just a higher multiple paid for Horizant alone.

The fumurate program could also have some value, given there are no approved DMF drugs for psoriasis in the US and even as an oral (although with GI effects in first month) could be a $100-500M drug.

Bear case

- DMF drug should be minimal value at this point and offered as upside to any buyer given the profile is concerning with the very high rate of GI and diarrhea for a psoriasis drug (different risk/benefit for MS where Tecfidera is approved) and compliance and maintenance may be an issue as oral Otezla is also in the market with a cleaner profile.
- DMF would require a large and costly Phase III program to run for psoriasis, which may not be worth the ROI depending on the assumed niche market share, IP protection, and other alternatives in dermatology. DMF may also require a PML class warning which would hamper its use in psoriasis. MS would also require hundreds of millions to run a Phase III program and there is significant uncertainty here as Tecfidera sales have slowed and a once-daily is not a significant enough differentiator to matter down the road.
- Horizant sales are still fairly small in the big picture and spec pharma companies may not be that interested given other opportunities and considerations for more accretive and synergistic assets. Spec pharma companies are also re-evaluating their M&A strategies and an obvious buyer like VRX may be re-considering all these deals and unlikely to do anything soon.
- Lyrica is also going off patent soon and is another commonly used drug in RLS, and it could add pressure to the visibility in this market (although a different class of drug).

Key question and debate for XNPT

1. Will XNPT partner or will they sell?

With the discontinued development of '829 and plan to partner it out, the focus is on growing Horizant sales and maximizing its potential to drive shareholder value. However, XNPT indicated they've just started engaging in partnership discussions for '829 so it might take time to weigh options and who would be interested in '829 + Horizant or just Horizant? One issue management said they are cognizant of is their 120-person salesforce selling only one drug so they'd be open to considering bringing in other drugs. We do not favor that idea because we do not think they have a big enough balance sheet to bring anything on that would move the needle. Horizant is small, and there is high execution risk for a small team.

Exhibit 129: Comparing PASI responder ratios amongst approved psoriasis drugs and DMF drug candidates

Company	Drug	Stage	N	Study Design	Indication	Trial	Weeks	Dose	PASI 100	vs Pbo	PASI 75	vs. Pbo	PASI 50	vs. Pbo	Discontinuation	Safety/Side Effects
BIIB	BG-12 (Tecfidera)	Phase III	175	Randomized, double-blind, parallel-group trials across 10 EU centers	Moderate-to-severe	N/A	16	240mg TID	N/A	**N/A**	39%	**1%**	65%	**14%**	N/A	(>10%) Flushing, Diarrhea, Nasopharyngitis, upper abdominal pain, headache, nausea
		Phase II	144	Double-blind, dose-finding, parallel-group study across 4 Poland centers	Severe	N/A	12	240mg TID	N/A	**N/A**	42%	**11%**	64%	**14%**	35%	Flushing, Nasopharyngitis were most common
								120mg TID	N/A	**N/A**	25%	**11%**	50%	**14%**		
								120mg QD	N/A	**N/A**	8%	**11%**	39%	**14%**		
						N/A	8	240mg TID	N/A	**N/A**	17%	**0%**	47%	**11%**	N/A	
								120mg TID	N/A	**N/A**	8%	**0%**	28%	**11%**		
								120mg QD	N/A	**N/A**	3%	**0%**	25%	**11%**		
	Fumaderm	N/A	100	Double-blind, randomized, study; first-line, refractory to topicals	Moderate-to-severe	N/A	16	105mg-1290mg	N/A	**N/A**	57%*	**10%***	N/A	**N/A**	30-40%	Diarrhea, abdominal pain, facial flushing
Forward Pharma	FP187	Phase II	252	Randomized, double-blind study with three FP187 dose groups with two dosage levels and an open, flexible up-titration group carried out in 17	Moderate-to-severe	N/A	20	250mg BID	N/A	**N/A**	31% (46%)**	**10% (14%)****	N/A	**N/A**	40% - 48% for 199-patient blinded arm; 56% for pbo	Flushing; mild-moderate GI events
								375mg BID or 250mg TID	N/A	**N/A**	21% (35%)**	**10% (14%)****	N/A	**N/A**		
XNPT	XP23829	Phase II	200	Randomized, Double-Blind, Multicenter, Parallel-Group Study	Moderate-to-severe	N/A	12	400mg QD	N/A	**N/A**	13%	**9%**	36%	**14%**	~33%	Diarrhea (22% to 40%), >10% nausea, abdominal pain, vomiting and headache
								800mg QD			14%	**9%**	38%	**14%**		
								400mg BID			22%	**9%**	39%	**14%**		
Almirall	LAS41008 (Verum)	Phase III	690	Randomized, double-blind, multi-center study in comparison to active	Moderate-to-severe	N/A	16	(LAS41008) TBD (Fumaderm) TBD	N/A	**N/A**	TBD	**TBD**	N/A	**N/A**	TBD	TBD
AZN/VRX	Brodalumab	Phase III	4373	Double-blind, active comparator- and placebo-controlled induction phase **(AMAGINE)**	Moderate-to-severe	AMAGINE-3	12	140mg Q2W	37%	**0%**	69%	**6%**	N/A	**N/A**	4%	(>5%) Cold, joint pain, upper respiratory tract infection and headache
								240mg Q2W	27%	**0%**	85%	**6%**	N/A	**N/A**	3%	
						AMAGINE-2		140mg Q2W	44%	**1%**	67%	**8%**	N/A	**N/A**	N/A	
								210mg Q2W	26%	**1%**	86%	**8%**	N/A	**N/A**		
						AMAGINE-1		140mg Q2W	23%	**1%**	60%	**3%**	N/A	**N/A**	5%	
								210mg Q2W	42%	**1%**	83%	**3%**	N/A	**N/A**	5%	
		Phase II	198	Randomized, double-blind, placebo-controlled, dose-ranging trial	50% had taken TNF inhibitors	N/A	12	140mg day 1, wk 2, & Q2W	38%	**N/A**	77%	**N/A**	N/A	**N/A**	N/A	(>5%) Cold, respiratory tract infection, injection site redness
								210mg day 1, wk 2, & Q2W	62%	**N/A**	82%	**N/A**	N/A	**N/A**		
NVS	Secukinumab	Phase III	2403	Randomized, double-blind, placebo-controlled trials	Moderate-to-Severe	Trial 4	12	150mg at wks 0-4, then Q4W	Results similar to Trials 1 and 2*		71%	**4%**	N/A	**N/A**	N/A	Nasopharyngitis, diarrhea, upper respiratory tract infaction, rhinitis, oral herpes, pharyngitis, urticaria, rhinorrhea
								300mg at wks 0-4, then Q4W			82%	**4%**	N/A	**N/A**	N/A	
						Trial 3		150mg at wks 0-4, then Q4W	Results similar to Trials 1 and 2*		67%	**5%**	N/A	**N/A**	N/A	
								300mg at wks 0-4, then Q4W			76%	**5%**	N/A	**N/A**	N/A	
						Trial 2		150mg at wks 0-4, then Q4W	39%*	**1%***	69%	**0%**	N/A	**N/A**	N/A	
								300mg at wks 0-4, then Q4W	59%*	**1%***	75%	**0%**	N/A	**N/A**	N/A	
						Trial 1		150mg at wks 0-4, then Q4W	42%*	**2%***	70%	**3%**	N/A	**N/A**	N/A	
								300mg at wks 0-4, then Q4W	54%*	**2%***	87%	**3%**	N/A	**N/A**	N/A	
LLY	Ixekizumab	Phase III	3866	Randomized, double-blind, multicenter **(UNCOVER)**	Moderate-to-severe	UNCOVER-3	12	80mg Q2W or Q4W	36%	**0%**	84-87%	**7%**	N/A	**N/A**	~2%	Infections in ~30%, injection-site reactions
						UNCOVER-2		80mg Q2W or Q4W	36%	**1%**	78-90%	**2%**	N/A	**N/A**	~1%-2%	
						UNCOVER-1		80mg Q2W or Q4W	34%	**0%**	83-89%	**4%**	N/A	**N/A**	~2%	
		Phase II	142	Randomized, double-blind, placebo-controlled, parallel-group, dose-ranging	Moderate-to-severe	NA	12	10mg Q2W	NM	**NM**	NM	**NM**	N/A	**N/A**	7%	Nasopharyngitis, upper respiratory infection, injection site reaction, headache, allergy/ hypersensitivity
								25mg Q2W	NM	**NM**	77%	**8%**	N/A	**N/A**	3%	
								75mg Q2W	38%	**0%**	83%	**8%**	N/A	**N/A**	0%	
								150mg Q2W	39%	**0%**	82%	**8%**	N/A	**N/A**	0%	
JNJ	Guselkumab	Phase IIb	293	Randomized, placebo- and active comparator-controlled, parallel-group, multicenter dose-ranging seven-arm study **(X-PLORE)**	Moderate-to-severe	X-PLORE	16	5mg Wks 0, 4; Q12W	34%*	**2%***	44%	**5%**	34%	**7%**	N/A	AEs in 50% of patients receiving guselkumab vs 52% of patients receiving placebo; Lung abscess, appendicitis
								15mg Q8W	34%*	**2%***	76%	**5%**	61%	**7%**	N/A	
								50mg Wks 0,4; Q12W	45%*	**2%***	81%	**5%**	79%	**7%**	N/A	
								100mg Q8W	62%*	**2%***	79%	**5%**	86%	**7%**	N/A	
								200mg Wks 0, 4; Q12W	81%*	**2%***	81%	**5%**	83%	**7%**	N/A	
PFE	Tofacitinib	Phase III	1861	Randomized, double-blind, placebo-controlled, parallel-group studies in patients on systemic therapy or phototherapy **(OPT Pivotal)**	Moderate-to-severe	OPT 2, OPT 1	16	5mg BID	22%*	**3%***	43%	**9%**	N/A	**N/A**	Low	(>5%) Nasopharyngitis, upper respiratory infection, headache
								10mg BID	39%*	**3%***	59%	**9%**	N/A	**N/A**		
CELG	Apremilast (Otezla)	Phase III	1257	Randomized, double-blind , multicenter, placebo-controlled study **(PSOR)**	Moderate-to-severe	PSOR-2	16	30mg BID	N/A	**N/A**	29%	**6%**	56%	**20%**	6%	Depression (1.3%), (>4%) Diarrhea, nausea, upper respiratory tract infection, and headache
						PSOR-1		30mg BID	N/A	**N/A**	33%	**5%**	59%	**17%**		
AMGN	Enbrel	Phase III	1245	Randomized, double-blind, placebo-controlled studies in patients who are candidates for systemic therapy or phototherapy **(Study I and II)**	Moderate-to-severe	Study I	12	25mg QW	N/A	**N/A**	14%	**4%**	37%	**14%**	N/A	(>5%) Infections, injection site reactions, diarrhea
								25mg BIW	N/A	**N/A**	32%	**4%**	54%	**14%**		
								50mg BIW	N/A	**N/A**	47%	**4%**	71%	**14%**		
						Study II		25mg BIW	N/A	**N/A**	32%	**3%**	61%	**9%**	N/A	
								50mg BIW	N/A	**N/A**	46%	**3%**	72%	**9%**		
ABBV	Humira	Phase III	1696	Randomized, double-blind, placebo-controlled studies in patients who are candidates for systemic therapy or phototherapy **(Ps Sudy)**	Moderate-to-severe	Ps-I	16	40mg Q2W	N/A	**N/A**	71%	**7%**	N/A	**N/A**	N/A	(>10%) Infections, injection site reactions, headache and rash
						Ps-II		40mg Q2W	N/A	**N/A**	78%	**19%**	N/A	**N/A**	N/A	
Janssen	Remicade	Phase III	1462	Randomized, double-blind, placebo-controlled studies in patients who are candidates for systemic therapy or phototherapy **(EXPRESS; SPIRIT)**	Severe	Express I	10	3mg/kg Wks 0, 2, and 6	N/A	**N/A**	N/A	**N/A**	N/A	**N/A**	N/A	(>10%) Infections, infusion-related reactions, headache and abdominal pain
								5mg/kg Wks 0, 2, and 6	N/A	**N/A**	80%	**3%**	N/A	**N/A**		
						Express II		3mg/kg Wks 0, 2, and 6	N/A	**N/A**	70%	**2%**	N/A	**N/A**	N/A	
								5mg/kg Wks 0, 2, and 6	N/A	**N/A**	75%	**2%**	N/A	**N/A**		
						Spirit		3mg/kg Wks 0, 2, and 6	N/A	**N/A**	72%	**6%**	N/A	**N/A**	N/A	
								5mg/kg Wks 0, 2, and 6	N/A	**N/A**	88%	**6%**	N/A	**N/A**		
Janssen	Stelara	Phase III	1996	Randomized, double-blind, placebo-controlled studies in patients who are candidates for systemic therapy or phototherapy **(Ps STUDY)**	Moderate-to-severe	Ps STUDY 1	12	45mg Wks 0, 4, and 16	N/A	**N/A**	67%	**3%**	N/A	**N/A**	N/A	(>~5%) Nasopharyngitis, Upper Respiratory tract infection, Headache
								90mg Wks 0, 4, and 16	N/A	**N/A**	66%	**3%**	N/A	**N/A**		
						Ps STUDY 2		45mg Wks 0, 4, and 16	N/A	**N/A**	67%	**4%**	N/A	**N/A**	N/A	
								90mg Wks 0, 4, and 16	N/A	**N/A**	76%	**4%**	N/A	**N/A**		

**Fumaderm results are PASI 70; Secukinumab results are PASI 90*

***Values in ( ) indicate results based on per-protocol analysis*

Source: Company reports and RBC Capital Markets estimates

Exhibit 130: Expected news flow for XNPT

Timing	Expected News Flow	Program
H1:17	Potential results from Phase II AUD trial to support sNDA for AUD	Horizant

Source: Company reports and RBC Capital Markets estimates

Exhibit 131: XNPT's pipeline table

Product	Stage of Development	Indication	Partner
XP-13512 (Horizant)	Commercial	Restless legs syndrome (RLS)	GlaxoSmithKline, Astellas
	Commercial	Post herpetic neuralgia (PHN)	GlaxoSmithKline
XP21279	Phase II	Parkinson's disease	Proprietary
XP23829 (discontinued)	Phase II	Psoriasis	Proprietary
	Phase I	RRMS	Proprietary

Source: Company reports and RBC Capital Markets estimates

Exhibit 132: XNPT's income statement

($ in millions, except per share) Fiscal Year Ends December	FY13	FY14	1Q15 Mar-15	2Q15 Jun-15	3Q15 Sep-15	4Q15E Dec-15	FY15	1Q16E Mar-16	2Q16E Jun-16	3Q16E Sep-16	4Q16E Dec-16	FY16	FY17
Revenue:													
Horizant (US)	6.4	20.2	6.6	8.2	11.0	14.0	39.8	15.0	16.0	17.0	18.0	66.0	88.0
Royalty - Ex-US	0.4	0.6	0.1	0.1	0.1	0.1	0.6	0.1	0.1	0.1	0.1	0.6	0.6
Collaboration Revenue/Milestones	1.1	26.1	0.3	0.3	0.3	0.3	1.1	0.3	0.3	0.3	0.3	1.1	1.1
Total Revenue	**8.0**	**46.9**	**7.1**	**8.6**	**11.4**	**14.4**	**41.5**	**15.4**	**16.4**	**17.4**	**18.4**	**67.7**	**89.7**
EXPENSES:													
Cost of Product Sales	1.3	2.1	0.5	0.5	0.7	0.9	2.5	0.9	1.0	1.0	1.1	4.0	5.3
Research and Development	33.3	23.7	6.4	6.2	6.8	6.0	25.4	5.0	5.0	5.0	5.0	20.0	20.0
Sell, generative and administrative	59.1	70.2	20.1	25.6	27.1	24.0	96.8	23.0	23.0	23.0	23.0	92.0	92.0
Total Expenses	93.7	96.0	26.9	32.3	34.6	30.9	124.7	28.9	29.0	29.0	29.1	116.0	117.3
Income from operations (EBIT)	**(85.7)**	**(49.1)**	**(19.9)**	**(23.7)**	**(23.2)**	**(16.4)**	**(83.2)**	**(13.5)**	**(12.5)**	**(11.6)**	**(10.7)**	**(48.3)**	**(27.6)**
Total Other Income	(0.3)	(0.2)	(0.5)	(0.8)	(0.9)	(0.9)	(3.1)	(0.9)	(0.9)	(0.9)	(0.9)	(3.6)	(3.6)
Pre-tax income	(85.9)	(49.3)	(20.4)	(24.5)	(24.1)	(17.3)	(86.3)	(14.4)	(13.4)	(12.5)	(11.6)	(51.9)	(31.2)
Taxes	-	-	-	-	-	-	-	-	-	-	-	-	-
Net Income	**(85.9)**	**(49.3)**	**(20.4)**	**(24.5)**	**(24.1)**	**(17.3)**	**(86.3)**	**(14.4)**	**(13.4)**	**(12.5)**	**(11.6)**	**(51.9)**	**(31.2)**
EPS Diluted*	**(1.81)**	**(0.81)**	**(0.33)**	**(0.39)**	**(0.38)**	**(0.23)**	**(1.31)**	**(0.19)**	**(0.18)**	**(0.16)**	**(0.15)**	**(0.68)**	**(0.35)**
Shares Outstanding - Basic	47.5	60.9	62.7	62.9	63.1	75.4	66.0	75.8	76.2	76.5	76.9	76.3	89.9
Shares Outstanding - Diluted	48.6	63.2	63.9	64.1	63.1	76.6	66.9	77.0	77.4	77.7	78.1	77.5	91.1

Source: Company reports and RBC Capital Markets estimates

Valuation

Our base case of $10/share assumes that: 1) Horizant can grow to a $100M+ franchise over time and should be valued at 4-5x sales, and 2) '829 will garner partnership interest in either neurology or dermatology. We include ~$1 net cash in valuation.

Price target impediments

Our price target is significantly dependent on the commercial success of Horizant sales. Impediments to our price target include: 1) inability of leveraging an expanded salesforce to generate $100M+ in Horizant revenue, 2) inability for XNPT to find a partner willing to advance '829 further in clinical trials, and 3) competition. Any negative or unexpected developments related to these issues would significantly affect the company's outlook and the ability of the stock to reach our price target.

Company profiles – (Simeonidis)

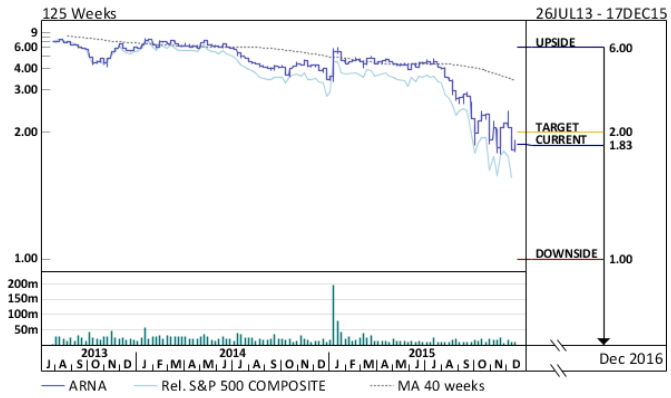
Arena Pharmaceuticals, Inc. (ARNA)

Sector Perform, Speculative Risk

Price Target USD $2.00

Target/Upside/Downside Scenarios

Exhibit 133: Arena Pharmaceuticals, Inc.



Source: RBC Capital Markets estimates

Target price/base case

We derive our $2/share price target based on a sum-of-the-parts methodology. We estimate the probability-adjusted NPV of the following: 1) Belviq royalties (~$0.60/share); 2) Arena's early-stage pipeline portfolio (~$1/share); and 3) the company's projected net cash position (~$0.40/share).

Upside scenario

Our upside scenario of $6/share assumes positive readouts of data from Arena's pipeline molecules, including the APD371 Phase I trial in pain and the ralinepag Phase II trial in PAH, which we expect could add a total of ~$950MM in value. This would add $4/share to our base case.

Downside scenario

Our downside scenario of $1/share assumes a combination of potential safety signals in the APD334 program and negative data from the ongoing trials of the rest of the pipeline molecules. Removing the early-stage pipeline leads to $1/share.

Investment summary

We view ARNA shares as fairly valued as the sum of two very different stories. The first one is that of an approved product, Belviq, for which Arena is receiving royalties on sales, but it is not living up to expectations. The second one is the company's early-stage pipeline, and more specifically, its novel, oral, S1P1 receptor modulator, APD334, which recently entered a 240-patient, Phase II trial in ulcerative colitis. There is investor interest in this compound, especially given the recent Celgene acquisition of Receptos, whose lead asset, ozanimod (RPC1063), is a novel, oral S1P1 receptor agonist being developed for autoimmune diseases, including UC. However, given that we have only seen very early and limited data from this agent, and the fact that Phase II data will not be available until YE:16, we are staying on the sidelines on ARNA and maintain our Sector Perform rating.

Potential catalysts for the stock: APD334, ralinepag and APD371 may be the way to upside. With the discontinuation of the Belviq + phentermine and smoking cessation programs, pipeline focus for Arena now centers on earlier stage compounds. Arena recently announced Phase I data in healthy volunteers with S1P1 agonist APD334. The data look promising, in terms of the compound's lymphocyte lowering efficacy, and a Phase II study in ulcerative colitis recently began enrolling, with topline data expected by YE:16. In addition, ralinepag, an oral non-prostanoid prostacyclin (IP) receptor agonist, entered a Phase II trial in January 2015 for the treatment of pulmonary arterial hypertension (PAH). Data from this 22-week, 60-patient, placebo-controlled trial are expected in 2016. Finally, APD371, an oral agonist of the cannabinoid 2 (CB2) receptor deing development for the treatment of pain, began a 36-patient, placebo-controlled Phase Ib multiple-ascending dose trial in healthy patients in October 2015. Positive data from these compounds, particularly APD334, could represent additional upside not fully captured in our base case model.

Risks: 1) Belviq sales further slowdown; 2) lack of progress on EU regulatory process; 3) slowdown in obesity drug reimbursement progress; and 4) negative data from pipeline compounds. These risks, if they materialize, may result in significant volatility, and the fact that the majority of the value comes from a single product accounts for the Speculative Risk qualifier on our rating.

Key questions

Our view

1. Can Belviq scripts grow to a meaningful level?

The answer here is "it depends"… 1) on one's definition of "meaningful", **2)** on the time horizon one is looking at, and **3)** on the number of indications that would be included. We believe that it would be difficult for Belviq sales to meet most investors' definition of a "meaningful" drug as a single agent in obesity in the near to medium term, and this in large part, contributes to our Sector Perform rating.

2. What about the new kid-on-the-block, $S1P_1$ agonist APD334?

Data look very promising, but it is still early days. Arena recently announced Phase I data in healthy volunteers with $S1P_1$ agonist APD334. The data look promising, in terms of the compound's lymphocyte-lowering activity, which was both strong (up to 69%) and dose-dependent. In addition, lymphocyte counts recovered to baseline, on average, within one week of the conclusion of dosing. We still view the data as early, especially given that subjects were only treated for 21 days and it is thus too soon to make longer-term claims about its safety. This is obviously a promising compound, given its oral administration and its theoretical potential for broad applicability in autoimmune diseases. APD334 could possibly be the most exciting molecule that Arena co-founder Dr. Dom Behan has discovered at Arena and one that we will monitor closely.

3. How does the recent restructuring affect Arena's pipeline?

With the discontinuation of Belviq lifecycle management programs, the pipeline focus for Arena is now centered on its earlier stage compounds: (i) APD334, the oral modulator of the S1P1 receptor, which entered a Phase II trial in July 2015 for the treatment of ulcerative colitis. Enrollment for this 12-week, 240- patient, placebo-controlled trial is expected to be complete by YE:16, with topline data also by YE;16; (ii) Ralinepag, an oral non-prostanoid prostacyclin (IP) receptor agonist, entered a Phase II trial in January 2015 for the treatment of pulmonary arterial hypertension (PAH). Data from this 22-week, 60-patient, placebo-controlled trial are expected in 2016; (iii) APD371, an oral agonist of the cannabinoid 2 (CB2) receptor under development for the treatment of pain, began a 36-patient, placebo-controlled Phase Ib multiple-ascending dose trial in healthy patients in October 2015. On their 3Q:15 earnings call, management noted that Arena cannot afford to take all of these programs through Phase II and that one or more, but not all of them, will be partnered.

Exhibit 134: Arena's pipeline

Drug (Target)	Indication	Stage
BELVIQ (5-HT_{2C})	Chronic weight management	Marketed
APD334 (S1P1 receptor)	Ulcerative colitis (UC)	Phase II
Ralinepag (prostacyclin receptor)	Pulmonary arterial hypertension (PAH)	Phase II
APD371 (CB2 receptor)	Pain	Phase I

Source: RBC Capital Markets estimates

Exhibit 135: Arena expected newsflow

Event	Drug	Timing
Complete enrollment for Phase II APD334 trial in UC	APD334	YE16
Top-line data from APD 334 Phase II trial in UC	APD334	YE16
Phase II data from ralinepag in PAH	ralinepag	2016

Source: RBC Capital Markets

Exhibit 136: ARNA quarterly P&L ($MM)

($MM)	FY 2010A	FY 2011A	FY 2012A	FY 2013A	FY 2014A	Q1: 15A	Q2: 15A	Q3: 15A	Q4: 15E	FY 2015E	Q1: 16E	Q2: 16E	Q3: 16E	Q4: 16E	FY 2016E	FY 2017E
Total WW BELVIQ sales	**0.0**	**0.0**	**0.0**	**16.2**	**45.2**	**17.6**	**12.9**	**12.6**	**10.8**	**53.9**	**12.9**	**14.0**	**15.9**	**18.7**	**61.5**	**87.9**
% increase (y/y)					*179%*	*110%*	*30%*	*-25%*	*7%*	*19%*	*-27%*	*9%*	*26%*	*74%*	*14%*	*43%*
Total revenue on WW BELVIQ sales to ARNA	**0.0**	**0.0**	**0.0**	**5.7**	**16.0**	**6.6**	**4.3**	**4.9**	**3.9**	**19.7**	**4.7**	**5.1**	**5.8**	**6.8**	**22.3**	**28.7**
Manufacturing services	7.1	5.3	3.8	2.7	1.5	0.3	1.4	1.5	0.3	3.4	0.2	0.2	0.2	0.2	0.8	1.0
Milestones/License Fees - Eisai	9.6	7.4	23.6	72.4	18.6	2.1	3.2	2.1	2.1	9.6	0.0	0.0	0.0	10.0	10.0	0.0
Milestones/License Fees - EU partnership (Eisai)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	50.0
Milestones/License Fees - Ildong	0.0	0.0	0.2	0.6	0.4	3.2	0.3	0.7	0.7	4.9	0.0	0.0	0.0	0.0	0.0	0.0
Milestones/License Fees - CYB	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total Revenues	**16.6**	**12.7**	**27.6**	**81.4**	**37.0**	**12.3**	**9.2**	**9.1**	**7.0**	**37.6**	**4.9**	**5.3**	**6.0**	**17.0**	**33.1**	**79.7**
Cost of Goods Sold	**7.4**	**8.1**	**3.7**	**6.2**	**7.8**	**3.6**	**3.1**	**3.2**	**2.2**	**12.1**	**2.1**	**2.3**	**2.5**	**3.0**	**9.8**	**11.1**
R&D	**75.5**	**58.7**	**54.1**	**66.5**	**100.3**	**22.0**	**24.2**	**22.1**	**23.7**	**91.9**	**13.9**	**14.2**	**12.8**	**11.9**	**52.8**	**33.5**
SG&A	**27.9**	**24.2**	**26.2**	**31.7**	**34.1**	**8.4**	**8.8**	**9.0**	**7.0**	**33.3**	**6.5**	**6.1**	**5.5**	**5.1**	**23.2**	**23.3**
Total Operating Expenses	**113.0**	**95.5**	**84.7**	**104.3**	**142.2**	**34.0**	**36.2**	**34.3**	**36.2**	**140.6**	**22.5**	**22.6**	**20.8**	**20.0**	**85.8**	**67.9**
Operating Income	**(96.4)**	**(82.8)**	**(57.1)**	**(22.9)**	**(105.3)**	**(21.7)**	**(27.0)**	**(25.2)**	**(29.1)**	**(103.0)**	**(17.6)**	**(17.3)**	**(14.9)**	**(3.0)**	**(52.8)**	**11.8**
Total Non-Operating Income	(28.2)	(28.7)	(31.2)	3.5	44.8	(2.6)	0.2	(1.2)	(1.7)	(5.3)	(1.7)	(1.7)	(1.7)	(1.7)	(6.8)	(6.8)
Pretax Income	(124.5)	(111.5)	(88.3)	(19.4)	(60.5)	(24.3)	(26.8)	(26.4)	(30.8)	(108.3)	(19.3)	(19.0)	(16.6)	(4.7)	(59.6)	5.0
Income tax expense	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net Income - Operations	**(124.5)**	**(111.5)**	**(88.3)**	**(19.4)**	**(60.5)**	**(24.3)**	**(26.8)**	**(26.4)**	**(30.8)**	**(108.3)**	**(19.3)**	**(19.0)**	**(16.6)**	**(4.7)**	**(59.6)**	**5.0**
Non-Recurring Gains (Losses)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net Income - Reported	**(124.5)**	**(111.5)**	**(88.3)**	**(19.4)**	**(60.5)**	**(24.3)**	**(26.8)**	**(26.4)**	**(30.8)**	**(108.3)**	**(19.3)**	**(19.0)**	**(16.6)**	**(4.7)**	**(59.6)**	**5.0**
Basic EPS	**($1.14)**	**($0.80)**	**($0.45)**	**($0.09)**	**($0.28)**	**($0.10)**	**($0.11)**	**($0.11)**	**($0.13)**	**($0.45)**	**($0.08)**	**($0.08)**	**($0.07)**	**($0.02)**	**($0.24)**	**$0.02**
Diluted EPS	**($1.14)**	**($0.80)**	**($0.45)**	**($0.09)**	**($0.28)**	**($0.10)**	**($0.11)**	**($0.11)**	**($0.13)**	**($0.45)**	**($0.08)**	**($0.08)**	**($0.07)**	**($0.02)**	**($0.24)**	**$0.02**

Source: Company reports and RBC Capital Markets estimates

Valuation

We derive our $2/share price target based on a sum-of-the-parts methodology. We estimate the probability-adjusted NPV of the following: 1) Belviq royalties (~$0.60/share); 2) Arena's early-stage pipeline portfolio (~$1/share); and 3) the company's projected net cash position (~$0.40/share).

Price target impediments

Factors that can negatively influence our valuation include increased competition (considering that a fourth obesity drug Saxenda has now entered the market), lower than projected penetrations for Belviq, and discontinuation of its earlier-stage pipeline candidates. Factors that can positively affect our valuation include increased investment in commercial infrastructure from Eisai that can lead to more Belviq sales, continued release of positive data from its early-stage programs that would lead to more valuation, and passing of any legislation that enforces Medicare reimbursement for obesity therapeutics.

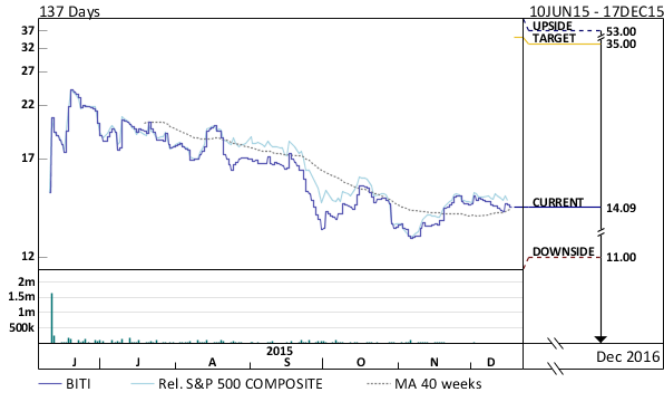
Biotie Therapies Corp. (BITI)

Outperform, Speculative Risk

Price Target USD $35.00

Target/Upside/Downside Scenarios

Exhibit 137: Biotie Therapies Corp.



Source: RBC Capital Markets estimates

Target price/base case

We use a sum-of-the-parts methodology to value BITI ($35/ADS), and estimate the probability-adjusted NPV of the following: (1) tozadenant sales and royalties (55% probability of success) in Parkinson's disease ($21/ADS), (2) Selincro royalties (90% probability of success) ($5/ADS), and (3) the company's projected net cash position ($9/ADS). We have not assigned value to the SYN120 and BTT1023 programs in our price target due to both programs being early stage. We may revisit valuation for these early pipeline assets as they progress in the clinic.

Upside scenario

Our upside scenario ($53/ADS) assumes a faster-than-anticipated uptake of Selincro in the EU, authorization of more patents that would increase Selincro's IP protection out to 2029 in the EU, and successful readouts of the Phase II trials for SYN120 and BTT1023. We do not increase the probability of success for tozadenant in our upside scenario since topline data for the Phase III trial is still 2.5 years away (YE:17). These in combo would increase our estimates to $11/ADS for Selincro royalties and $12/ADS for pipeline.

Downside scenario

An unexpected safety signal during the early stages of the tozadenant Phase III trial could raise concerns and/or delay launch by one year, cut penetration rates by one-half, lower the economics of the ex-US commercialization agreement, and reduce the probability of success to 20%.

Investment summary

Tozadenant could be the first Parkinson's disease drug approved in the US with a new mechanism of action in a generation. Currently available Parkinson's disease (PD) drugs for the treatment of motor fluctuations (levodopa, COMT and MAO-B inhibitors) rely on dopamine-centric approaches. By contrast, tozadenant, an A2A receptor antagonist, provides a new non-dopaminergic approach to treating PD OFF time. While other A2A receptor antagonists failed to translate promising Phase II results into Phase III success, we believe Biotie can avoid the same fate by learning from competitors' mistakes and focusing on careful clinical trial design and execution. Initial Phase III data read out in YE:17, and if positive could result in US/EU approval in 2019, and potentially help tozadenant reach forecasted peak 2030 WW sales of ~$1B.

Biotie pipeline includes two more promising, albeit early, shots on goal. The company has two drugs in Phase II trials, with data readouts expected YE:16: (1) SYN120 is a dual antagonist of the 5HT2A/5HT6 receptors being evaluated in Parkinson's disease Dementia (PDD). This disease is usually treated with drugs approved for Alzheimer's, with Novartis' Exelon being the only drug currently approved for PDD. All current treatments have different mechanisms of action from SYN120, opening the door for this drug to emerge as both a novel and a unique treatment option for PDD patients (2) BTT1023 is a monoclonal antibody targeting VAP-1 being developed for Primary Sclerosing Cholangitis (PSC), an orphan liver disease with no approved therapies. With a novel mechanism of action, BTT1023, which has orphan drug designation in the EU, aims to enter the liver fibrosis arena, an area of both unmet medical need and investor interest.

Lundbeck's royalty payments for Selincro, approved for alcohol dependence in the EU, flow straight to Biotie's bottom line. Biotie's pipeline assets are coupled by Selincro, an opioid receptor antagonist recently launched by Lundbeck in the EU for alcohol dependence. Following approval in 2013, Selincro generated ~$10.3MM in FY14 sales and ~$6.2MM in 1Q:15 sales and is now on the market in 29 EU countries.

Risks: (1) Tozadenant delays and/or clinical setbacks; (2) competition in the Parkinson's disease space from other drugs in development, such as istradefylline (A2A inhibitor) or Xadago (MAO-B inhibitor); (3) unexpected safety signals in the tozadenant clinical trials. These risks, if they materialize, may result in significant volatility, and given that the majority of the value in the stock comes from a single product, lead to the Speculative Risk qualifier on our rating.

Key questions

		Our view
1.	**What are tozadenant's chances for success in Phase III?**	**While there's obviously significant risk with extrapolating from any Phase II trial to Phase III, especially in neurology, we see a better than 50/50 chance for success:** First, we believe that tozadenant's positive impact is real, since it is demonstrated not only by a reduction in OFF time, but in a number of secondary endpoints, including increase in ON time etc. Second, this Phase III trial has a very similar trial design and setup as the successful Phase IIb, with a focus on the doses that worked best. Finally, the Phase III sites have been carefully selected based on the Phase IIb experience, such that centers with physicians who could reliably select appropriate patients and train them to correctly complete the patient diaries, will be the ones selected to conduct the Phase III trial. This may help alleviate issues of noise and variability that frequently cause failure of Phase III trials in Parkinson's disease.
2.	**Why don't previous A2A receptor antagonists' failures suggest a similar fate for tozadenant?**	**Although other A2A receptor antagonists (i.e. Merck's preladenant and Kyowa Hakko Kirin's istradefylline) have not been successful in Phase III, we do not see a direct readthrough to tozadenant.** An array of different issues contributed to these two molecules' development setbacks. These included chemical and pK properties that may not have supported the dosing regimen used, along with suboptimal trial recruitment and conduct. We believe that coming after these two drugs could actually help tozadenant and Biotie by learning from and avoiding some of the same mistakes, especially pitfalls of trial conduct and patient selection, and thus maximizing the drug's chances for Phase III success.
3.	**What is the market opportunity for tozadenant in the treatment of Parkinson's disease?**	**As a potential first in a new class of drugs in 20 years for the treatment of PD OFF episodes, tozadenant could be widely used.** Our (key opinion leaders) KOLs indicate that an increase of ~1 hr in OFF time is clinically meaningful and comparable to other categories of levodopa adjunctive treatments. One key advantage may be the *non-dopaminergic* mechanism of action for tozadenant that differentiates it from other existing therapies that modulate the levels of available dopamine from levodopa precursor. Moreover, once patients run out of adjunct treatments to treat OFF episodes, the only remaining option is surgical (i.e. deep brain stimulation or perhaps duodopa). By assuming penetration in the 15% range, tozadenant could reach our forecasted peak 2030 worldwide sales of ~$1B.
4.	**Is there a hidden gem in the Biotie pipeline?**	**We believe that SYN120, a potent, dual antagonist of the 5HT6 and 5HT2a receptors, is worth paying attention to.** This is especially true in the context of the unmet medical need and investor interest in the space, including Axovant's lead program RVT-101, another 5HT6 receptor antagonist, a company that raised $362MM in its recent IPO at a ~$2B valuation to support its studies in Alzheimer's disease. While obviously further behind in development, SYN120, via its dual targeting mechanism, may have both pro-cognitive and anti-psychotic effects for PDD patients. In addition, Roche was successful in their studies to help alleviate QT concerns that had been previously an issue for drugs in this class. The first glimpse of what this drug may be able to do would come when Phase II data for SYN120 in Parkinson's disease Dementia (PDD) read out YE:16.

Exhibit 138: Biotie's pipeline and commercial product

Drug	Target	Partner	Indication	Stage
Selincro	Opioid receptor	Lundbeck	Alcohol dependence	Marketed
Tozadenant	**A2A receptor**	**None**	**Parkinson's Disease end-of-dose wearing off**	**Phase III**
SYN120	5HT6/5HT2A receptors	None	Parkinson's Disease Dementia	Phase II
			Alzheimer's Disease	Phase II
BTT1023	VAP-1	None	Primary Sclerosing Cholangitis	Phase II

Source: RBC Capital Markets and Company reports

Exhibit 139: Biotie expected newsflow

Event	Drug	Timing
Top-line data for SYN120 Phase II study in Parkinson's Disease Dementia	SYN120	YE16
Interim analysis for Phase II study in primary sclerosing cholangitis (PSC)	BTT-1023	YE16
Topline data for pivotal tozadenant Phase III study in Parkinson's Disease end-of-dose wearing off	tozadenant	YE17
NDA submission for tozadenant in Parkinson's Disease end-of-dose wearing off	tozadenant	mid 2019
FDA approval for tozadenant in Parkinson's Disease end-of-dose wearing off	tozadenant	early 2020

Source: RBC Capital Markets and Company reports

Exhibit 140: BITI quarterly P&L (€MM)

(€MM)	2014A	Q1:15A	Q2:15A	Q3:15A	Q4:15E	2015E	Q1:16E	Q2:16E	Q3:16E	Q4:16E	2016E	2017E
Total WW tozadenant sales ($MM)	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Total revenue on WW tozadenant sales (€MM)	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
WW Selincro Sales (€MM)	**10.2**	**5.5**	**6.7**	**6.3**	**7.1**	**25.6**	**8.0**	**9.0**	**10.0**	**11.2**	**38.1**	**48.1**
Total Revenue on EU/JPN Selincro Sales (€MM)	**1.0**	**0.7**	**0.8**	**0.8**	**0.8**	**3.1**	**1.0**	**1.1**	**1.2**	**1.3**	**4.6**	**5.8**
Selincro royalties from Lundbeck license agreement	0.9	0.7	0.8	0.8	0.8	3.1	1.0	1.1	1.2	1.3	4.6	5.8
Milestones from Lundbeck	0.0	0.0	0.5	0.0	0.0	0.5	0.0	0.0	5.0	0.0	5.0	5.0
Milestones from UCB	8.0	0.2	0.0	0.0	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0
Milestones from tozadenant ex-US partnership	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Revenue from WW tozadenant sales	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total Revenue (€MM)	**14.9**	**0.9**	**1.3**	**0.8**	**0.8**	**3.8**	**1.0**	**1.1**	**6.2**	**1.3**	**9.6**	**10.8**
Cost of product sales	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
R&D	**17.3**	**4.8**	**7.6**	**7.3**	**8.0**	**27.6**	**8.2**	**8.4**	**8.3**	**8.6**	**33.5**	**35.2**
SG&A	**7.4**	**1.7**	**1.8**	**2.2**	**2.2**	**7.9**	**2.3**	**2.5**	**2.4**	**2.5**	**9.7**	**10.9**
Other Operating Income (Expenses)	**(26.5)**	**0.0**	**0.1**	**0.2**	**0.0**	**0.2**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Total Operating Expenses	**(9.2)**	**6.5**	**9.3**	**9.3**	**10.2**	**35.3**	**10.5**	**10.9**	**10.7**	**11.1**	**43.2**	**46.1**
Operating Income (loss)	**24.1**	**(5.6)**	**(8.0)**	**(8.5)**	**(9.4)**	**(31.5)**	**(9.5)**	**(9.8)**	**(4.5)**	**(9.8)**	**(33.6)**	**(35.3)**
Other net financial income (expenses)	1.3	(0.1)	(0.9)	0.7	0.0	(0.3)	0.0	0.0	0.0	0.0	0.0	0.0
Pretax income	(35.3)	(5.9)	(9.0)	(7.9)	(9.4)	(32.2)	(9.5)	(9.8)	(4.5)	(10.0)	(33.8)	(35.3)
Income Taxes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net Income (Loss)	**(35.3)**	**(5.9)**	**(9.0)**	**(7.9)**	**(9.4)**	**(32.2)**	**(9.5)**	**(9.8)**	**(4.5)**	**(10.0)**	**(33.8)**	**(35.3)**
ADS												
Basic EPS	**(€ 6.19)**	**(€ 1.04)**	**(€ 1.33)**	**(€ 0.65)**	**(€ 0.76)**	**(€ 3.49)**	**(€ 0.77)**	**(€ 0.79)**	**(€ 0.36)**	**(€ 0.79)**	**(€ 2.71)**	**(€ 2.78)**
Diluted EPS	**(€ 6.19)**	**(€ 1.04)**	**(€ 1.33)**	**(€ 0.65)**	**(€ 0.76)**	**(€ 3.49)**	**(€ 0.77)**	**(€ 0.79)**	**(€ 0.36)**	**(€ 0.79)**	**(€ 2.71)**	**(€ 2.78)**

Source: RBC Capital Markets estimates and Company reports

Valuation

We use a sum-of-the-parts methodology to value BITI ($35/ADS), and estimate the probabilityadjusted NPV of the following: (1) tozadenant sales and royalties (55% probability of success) in Parkinson's disease ($21/ADS), (2) Selincro royalties (90% probability of success) ($5/ADS), and (3) the company's projected net cash position ($9/ADS). We have not assigned value to the SYN120 and BTT1023 programs in our price target due to both programs being early stage. We may revisit valuation for these early pipeline assets as they progress in the clinic.

Price target impediments

Factors that can negatively affect our valuation for Biotie include any delays in patient recruitment for the upcoming Phase III tozadenant trial or any preliminary safety signals that raise concerns about this clinical program. Moreover, a positive readout from one more Phase III istradefylline trial may resurrect its regulatory hopes with the FDA, which should in turn lead to more US competition in the field of A2A inhibitors. Factors that can positively affect our valuation include continued positive readouts from Biotie's pipeline programs, including SYN120 and BTT-1023. These assets offer upside potential, which we have not included in our valuation. Moreover, acceleration of Selincro sales in the EU and/or Japan may lead to more royalties for Biotie to fund its clinical programs.

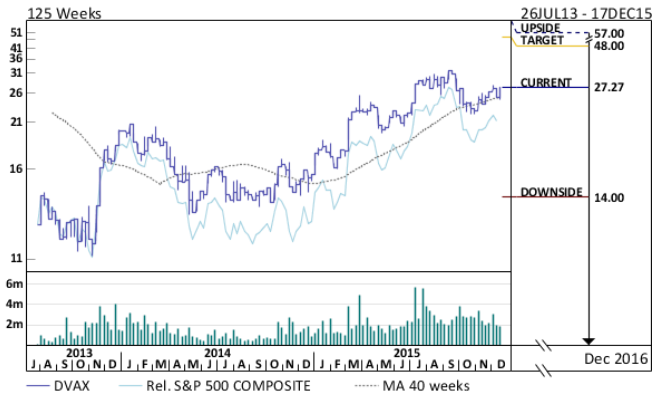
Dynavax Technologies Corp. (DVAX)

Outperform, Speculative Risk

Price Target USD $48.00

Target/Upside/Downside Scenarios

Exhibit 141: Dynavax Technologies Corp.



Source: RBC Capital Markets estimates

Target price/base case

We use a sum-of-the-parts methodology to value DVAX ($48/share) and estimate the probability-adjusted NPV of the following: 1) Heplisav sales and royalties in healthy individuals ($22/share); 2) Heplisav sales and royalties in Type 2 Diabetes patients ($11/share); 3) SD-101 sales ($6/share); and 4) the company's projected net cash position ($8/share).

Upside scenario

Our upside scenario assumes a faster than anticipated uptake of Heplisav in both healthy individuals and Type II diabetes patients, and successful readouts of the Phase I/II trials for SD-101. These in combination would increase our estimates to $34/share for Heplisav sales and royalties and to $15/share for SD-101. This leads to an upside scenario value for DVAX of $57/share.

Downside scenario

An unexpected minor safety signal in the data readout of the latest Heplisav Phase III trial could raise concerns as to the approvability of the BLA, as well as of the pipeline assets. This would lead us to cut Heplisav penetration rates by 50% and reduce the probability of success to 40%. This scenario would reduce the value of Heplisav to $5/share, the pipeline to $1/share, and the overall value for DVAX to $14/share.

Investment summary

Heplisav has achieved both non-inferiority and superiority over GSK's Engerix-B, the current standard-of-care Hepatitis B vaccine. Despite being generally accepted as an efficacious vaccine, Engerix-B has plenty of room for improvement in key areas such as efficacy within various patient subgroups and the length of time required to achieve seroprotection. In two successful Phase III trials, Heplisav provided a higher overall level of seroprotection in a shorter time frame and requiring fewer doses (2 doses over 4 weeks vs. 3 doses over 24 weeks) than Engerix-B. In addition, post-hoc analyses of the pooled Phase III data have shown that Heplisav has strong efficacy in four key subgroups in which Engerix-B has marginal efficacy: (i) males; (ii) BMI >30; (iii) smokers; and (iv) diabetics.

We believe Heplisav's superior profile can lead to widespread use. We expect Heplisav to gain a significant share of the $270M US market. Furthermore, in 2011 the CDC recommended that diabetes patients in the US receive a Hepatitis B vaccine. This could significantly expand the addressable population for Heplisav into the >20 million US adults with diabetes. Assuming a peak penetration of 70%, Heplisav could reach $400M in US sales in 2022, with peak WW sales of $651M in 2028.

SD-101, a novel TLR9 agonist, tested in combination with checkpoint inhibitors. Preclinical studies have demonstrated a synergistic anti-tumor effect when TLR9 agonists are used in combination with immune checkpoint inhibitors, such as antiPD-1 antibodies. Dynavax is aggressively pursuing the clinical development of SD-101, which will be in five Phase I/II trials by YE:15. Among these trials are two in partnership with Merck in combination with: (i) Keytruda (pembrolizumab) in metastatic melanoma; and (ii) the anti-IL-10 antibody MK-1966 in solid or hematological malignacies. Positive results from SD-101's trials would validate this compound and provide upside in DVAX shares.

Selected upcoming potential catalysts: 1) initiation of combination study with SD-101 and MK-1966 in solid or hematological malignancies, YE:15; 2) top-line data for Phase III Heplisav trial (HBV-23), January 2016; 3) submit amended BLA for Heplisav, 1Q:16; and 4) top-line data for SD-101 in Non-Hodgkin's Lymphoma (NHL) and melanoma trials, 4Q:16.

Risks: (1) safety signal in Heplisav Phase III trial; (2) regulatory delays for Heplisav; and (3) clinical setback in SD-101 development program. These risks, if they materialize, may result in significant volatility, and given that the majority of the value in the stock comes from a single product, lead to the Speculative Risk qualifier on our rating.

Key questions

	Our view
1. Will Heplisav's current Phase III *work*?	**While making a call ahead of any Phase III readout can be treacherous, we see this one as a relatively low-risk one to make.** With two successful Phase III trials already under its belt and the vaccine's efficacy already established, Dynavax is nearing completion of a third Phase III study, which was requested by FDA mainly to expand the Heplisav safety database. The FDA rejected Dynavax's previous BLA submission in February 2013, citing Heplisav's safety database (relatively small for a vaccine) as the reason for the CRL. The FDA requested that the Heplisav safety database be expanded from ~4K to ~10K patients in order to statistically exclude a causal relationship between Heplisav's novel TLR9 agonist adjuvant (1018) and the incidence of four autoimmune adverse events that were reported in the two Phase III trials. As the third and final DSMB occurred in July 2015 with no protocol changes requested, we expect the topline results anticipated in 1Q:16 to be positive and support a successful revised BLA submission based on Heplisav's already superior efficacy.
2. Heplisav vs. current standard of care, Engerix-B: do we *really* need a new HepB vaccine?	**In its first two Phase III trials, Heplisav achieved both non-inferiority and superiority over GSK's Engerix-B, the current standard-of-care Hepatitis B vaccine**. Despite being generally accepted as an efficacious Hepatitis B vaccine, Engerix-B leaves plenty of room for improvement in key areas such as efficacy within various patient subgroups and the length of time required to achieve seroprotection. In its two completed Phase III trials, Heplisav provided a higher overall level of seroprotection in a shorter time frame and required fewer doses (two doses over a month vs. three doses over six months) than Engerix-B. In addition, post-hoc analyses of the pooled Phase III data have shown that Heplisav has strong efficacy in four key subgroups in which Engerix-B shows marginal efficacy: (i) males; (ii) BMI >30; (iii) smokers; and (iv) diabetics.
3. How big of a drug can Heplisav be?	**This is a better and much more convenient vaccine: it will likely be widely used.** With a current market size of ~$270M in the US, we expect Heplisav's convenience, faster time-to-seroprotection and efficacy across multiple patient subgroups where the current standard-of-care doesn't offer satisfactory protection to enable Heplisav to gain a majority market share. Furthermore, following the 2011 CDC recommendation, diabetes patients in the US are now advised to receive a Hepatitis B vaccine. This increases the addressable population for Heplisav by moving into the >20 million US adults with diabetes. We expect its improvements in efficacy and convenience, combined with its comparable safety profile, to help Heplisav expand the market and establish it as the new standard-of-care Hepatitis B vaccine. We estimate $397M in US sales in 2022, with peak sales of $431M in 2027.
4. What is the potential for SD-101 as a cancer immunotherapy treatment?	**SD-101 is an intratumorally injected TLR9 agonist designed to enhance the responses seen with immune-based therapies in a wide range of cancers.** Preclinical studies have shown a synergistic anti-tumor effect when TLR9 agonists are used in combination with immune checkpoint inhibitors, such as anti-PD-1 antibodies. Dynavax is aggressively pursuing the clinical development of SD-101, which will be in five Phase I/II trials by YE15. Among these trials are two that have resulted from a partnership with Merck in which SD-101 will be tested: (i) in combination with Keytruda (pembrolizumab) in a metastatic melanoma trial funded by Dynavax; and (ii) in combination with the anti-IL-10 antibody MK-1966 in a Merck-funded trial in solid or hematological malignancies. Positive results for SD-101 in combination with immune checkpoint inhibitors would validate this approach clinically and create a new area of focus, outside of Heplisav, for DVAX investors.

Exhibit 142: Dynavax's pipeline

Drug	Target	Partner	Indication	Stage
Heplisav	**TLR9**	**None**	**Hepatitis B prevention**	**Phase III**
SD-101	TLR9	None	NHL, metastatic melanoma, other cancer types	Phase I/II
AZD1419	TLR9	AstraZeneca	Asthma	Phase II
DV1179	TLR7/9	None	Yet to be determined autoimmune disease	Phase I

Source: RBC Capital Markets, Dynavax

Exhibit 143: Dynavax's expected newsflow

Event	Drug	Timing
Select a target autoimmune indication for DV1179 clinical development	DV1179	4Q15
Initiation of combination study with MK-1966 in solid or hematological malignancies	SD-101	YE15
Top-line data for Phase III safety/diabetes trial (HBV-23)	**Heplisav**	**Jan. 2016**
Start Phase II trial for AZD1419 in asthma	AZD1419	1H16
Re-submit amended BLA for Heplisav	**Heplisav**	**1Q16**
Top-line data for Non-Hodgkin's Lymphoma (NHL), Keytruda in melanoma trials	SD-101	4Q16
Heplisav commercial launch	**Heplisav**	**2017**

Source: RBC Capital Markets, Dynavax

Exhibit 144: DVAX quarterly P&L ($MM)

($MM)	FY 2011A	FY 2012A	FY 2013A	FY 2014A	1Q:15A	2Q:15A	3Q:15A	4Q:15E	FY 2015E	1Q:16E	2Q:16E	3Q:16E	4Q:16E	FY 2016E	FY 2017E
Heplisav sales in Healthy people	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**50.2**
Heplisav royalties in Healthy people in EU				**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Heplisav sales in Type 2 Diabetes	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**42.7**
Heplisav royalties in Type 2 Diabetes in EU				**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Total Heplisav sales/royalties to Dynavax	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**92.9**
Collaboration revenue			4.9	7.9	0.5	0.9	0.8	0.0	2.2	0.0	0.0	0.0	0.0	0.0	50.0
EU Partner collaboration revenue															50.0
Grant revenue			5.1	2.7	0.1	0.1	0.4	0.0	0.6	0.0	0.0	0.0	0.0	0.0	0.0
Service and license revenue			1.2	0.4	0.0	0.5	0.0	0.0	0.5	0.0	0.0	0.0	0.0	0.0	0.0
Total Revenues			**11.3**	**11.0**	**0.6**	**1.6**	**1.2**	**0.0**	**3.4**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**142.9**
COGS	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**13.9**
R&D			**50.9**	**84.6**	**22.2**	**19.7**	**24.1**	**25.5**	**91.5**	**19.7**	**18.5**	**16.9**	**16.0**	**71.1**	**51.7**
SG&A			**25.9**	**17.4**	**4.9**	**5.1**	**5.5**	**5.3**	**20.8**	**5.3**	**5.2**	**5.4**	**15.3**	**31.2**	**64.4**
Unoccupied facility expense			0.9	0.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total Operating Expenses			**77.7**	**102.3**	**27.1**	**24.8**	**29.6**	**30.8**	**112.3**	**25.0**	**23.7**	**22.3**	**31.3**	**102.3**	**130.1**
Operating Income (loss)	**0.0**	**0.0**	**(66.5)**	**(91.3)**	**(26.5)**	**(23.2)**	**(28.4)**	**(30.8)**	**(108.9)**	**(25.0)**	**(23.7)**	**(22.3)**	**(31.3)**	**(102.3)**	**12.8**
Interest Expense/Income, Net			0.1	0.2	(0.2)	(0.2)	(0.0)	0.3	(0.2)	0.0	0.0	0.0	0.0	0.0	0.0
Other income, net			(0.3)	0.4	0.5	(0.1)	0.0	0.0	0.4	0.0	0.0	0.0	0.0	0.0	0.0
Loss on extinguishment of debt					0.0	0.0	(1.7)								
Net Income Before Taxes			**(66.7)**	**(90.7)**	**(26.2)**	**(23.6)**	**(30.1)**	**(30.5)**	**(110.4)**	**(25.0)**	**(23.7)**	**(22.3)**	**(31.3)**	**(102.3)**	**12.8**
Provision for Income Taxes				0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3
Net Income (Operations)			**(66.7)**	**(90.7)**	**(26.2)**	**(23.6)**	**(30.1)**	**(30.5)**	**(110.4)**	**(25.0)**	**(23.7)**	**(22.3)**	**(31.3)**	**(102.3)**	**12.6**
Non-recurring gains (charges)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net Income (Reported)			**(66.7)**	**(90.7)**	**(26.2)**	**(23.6)**	**(30.1)**	**(30.5)**	**(110.4)**	**(25.0)**	**(23.7)**	**(22.3)**	**(31.3)**	**(102.3)**	**12.6**
Basic EPS				**($3.45)**	**($0.97)**	**($0.78)**	**($0.82)**	**($0.83)**	**($3.38)**	**($0.67)**	**($0.56)**	**($0.52)**	**($0.73)**	**($2.47)**	**$0.30**
Diluted EPS				**($3.45)**	**($0.97)**	**($0.78)**	**($0.82)**	**($0.83)**	**($3.38)**	**($0.67)**	**($0.56)**	**($0.52)**	**($0.73)**	**($2.47)**	**$0.28**

Source: Company reports, RBC Capital Markets estimates

Valuation

To value DVAX shares, we use a sum-of-the-parts methodology and estimate the probability-adjusted NPVs of the following: 1) Heplisav sales and royalties in healthy individuals ($22/share); 2) Heplisav sales and royalties in Type 2 diabetes patients ($11/share); 3) SD-101 sales ($6/share); and 4) the company's projected net cash position ($8/share).

Price target impediments

Factors that can negatively affect our valuation for Dynavax include unexpected safety signals in the latest Phase III Heplisav trial, which could result in delays in filing for FDA approval or even lead to a Complete Response Letter. Moreover, negative readouts from the SD-101 Phase I/II trials in oncology indications would lead to a decrease in our Dynavax valuation. Factors that can positively affect our valuation include continued positive readouts from Dynavax's pipeline programs, including SD-101, AZD1419, and DV1179. We believe the last two assets can provide upside potential to DVAX shares; however, given their early-stage of development, we have not included them in our current valuation.

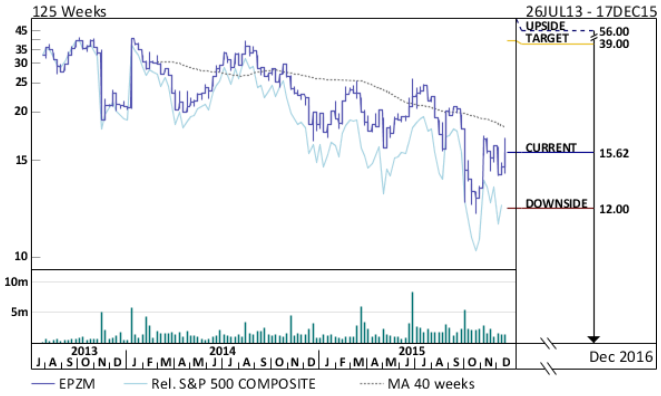
Epizyme, Inc. (DVAX)

Outperform, Speculative Risk

Price Target USD $39.00

Target/Upside/Downside Scenarios

Exhibit 145: Epizyme, Inc.



Source: RBC Capital Markets estimates

Target price/base case

We use a sum-of-the-parts methodology to value EPZM ($39/share), and we estimate the probability-adjusted NPV of the following: 1) tazemetostat sales in NHL ($35/share) at a 60% POS, 2) tazemetostat sales in solid tumors ($2/share) at a 50% POS, and 3) the company's projected net cash position ($2/share). Currently, we do not value Epizyme's platform; however, we may revisit in the future.

Upside scenario

Release of data from the 5-arm Phase II trial that continues to support the clinical efficacy of tazemetostat in DLBCL patients with non-GCB and with WT EZH2 tumors would lead us to increase penetrations in those patient populations as well as in FL patients with WT tumors. This would further increase our POS from 60% to 70%, resulting in an NPV of $47/share. This, coupled with continued collaboration interest in EPZM technology, would lead us to assign value to EPZM's platform ($6/share). This results in a total share price of $56.

Downside scenario

Our downside scenario assumes negative Phase II tazemetostat data that do not support its use in WT EZH2 FL and DLBCL patients, and DLBCL patients with non-GCB tumors. This would lead us to remove penetrations in these patient populations, and restrict tazemetostat use to the originally hypothesized patient populations (mutant EZH2 and GCB patients). Overall, this would also decrease our POS from 60% to 50% for the program, resulting in an NPV of $9/share. This net effect could result in EPZM being worth $12/share.

Investment summary

Tazemetostat demonstrates unexpected efficacy in additional NHL patient subpopulations. Originally hypothesized to demonstrate clinical utility only in NHL patients with mutated-EZH2 tumors and of the GCB subtype, tazemetostat has also shown promising clinical benefit in patients with WT EZH2 tumors and of the non-GCB subtype. If replicated in a larger clinical trial setting, these results can significantly expand the addressable NHL patient population. Given the promising results in the initial dataset, we believe tazemetostat has a good probability of doing so, in addition to validating the original hypothesis of targeting EZH2-mutated patients. We model initial sales in 2019 and $2B of peak 2032 sales, based off higher penetrations in mutant EZH2 patients than in WT/non-GCB patients.

The reacquisition of global (ex-Japan) rights from Eisai allows Epizyme to maximize the value of the tazemetostat asset. The unexpected efficacy in additional tumor subtypes provided the impetus for Epizyme to reacquire the global rights from Eisai. We like this strategic move since it provides Epizyme with significant upside, with the company shifting the economics favorably in its direction and also allowing it to transition from a developmental-stage company to a fully integrated oncology player.

Success of the EZH2 program bodes well for rest of HMT platform. Despite the fact that the company's first program, pinometostat (EPZ-5676), is only moving forward in pediatric patients after having been discontinued in adults, the compound has provided evidence of its biological activity. We view the combination of the results from the two programs as providing validation for Epizyme's platform, which also includes an earlier, preclinical pipeline, which will be moving into the clinic in the next few years. Finally, as a pure play in the HMT epigenetics arena, we view EPZM as a potential takeout candidate given its deep know-how and IP in the space.

Some upcoming potential catalysts: 1) Initiate tazemetostat Phase II trial of adult patients with INI1- and SMARCA4-negative tumors (synovial sarcoma, MRT, MRTO, etc), 4Q:15; 2) initiate tazemetostat Phase I trial of pediatric patients with INI1-deficient tumors (MRT), 4Q:15; 3) Initial data for Phase II tazemetostat trial in NHL, mid 2016.

Risks: 1) tazemetostat clinical setbacks; 2) competition in the EZH2 space; 3) unexpected safety signals in the tazemetostat trials. These risks, if they materialize, may result in significant volatility, and given that the majority of the value in the stock comes from a single product, lead to the Speculative Risk qualifier on our rating.

Key questions

	Our view
1. What is the addressable NHL patient population for tazemetostat?	**We believe that the base case scenario for tazemetostat includes the original hypothesis of GCB DLBCL patients with the EZH2 mutation (~8K patients WW), but based on the early efficacy data, there is significant *potential* upside in wild-type (WT) EZH2 patients, and in those with non-GCB disease (an additional ~40K patients).** The Phase I data shows unexpected activity in both WT EZH2 patients and in those with non-GCB DLBCL, which would significantly expand the target population for the compound. While the original hypothesis has – as of now – been assessed in only one patient with the mutation in the clinic (a second EZH2 mutant patient was on the food study and dosed below the Phase II tazemetostat dose), preliminary efficacy in WT EZH2 patients suggests that EZH2 signaling (even with WT protein) may also be an oncogenic driver in NHL. The eventual addressable population for tazemetostat should become clearer following Phase II data.
2. What patient populations could tazemetostat target outside of NHL?	**Despite the small number of evaluable patients with INI1- or SMARCA4-negative tumors who have been treated with tazemetostat to date, we believe the compound also has potential in this indication.** A total of 30 patients with solid tumors have now been treated with tazemetostat, including 11 patients with INI1-negative or SMARCA4-negative tumors. Nine of these 11 patients have been treated at or above the recommended Phase II dose of 800 mg BID. Six of these 11 patients (6/11; 55%) with INI1- or SMARCA4-negative tumors experienced a reduction in tumor size as best response, including four patients achieving >30% tumor reduction. Inhibition of EZH2 activity, which becomes misregulated as a result of INI1 or SMARCA4 loss, therefore provides a compelling case for treatment with tazemetostat in these cancer types.
3. What's the impact of the renegotiated deal with Eisai for Eisai?	**While the tazemetostat data to date are preliminary, we believe the reacquisition of worldwide rights from Eisai is a significant positive for Epizyme.** The enthusiasm over the recently updated Phase I data reinforces two commercial applications for the drug: 1) inhibition of EZH2 as an initial therapeutic application in EZH2-mutant tumors; and 2) a source of significant potential upside from an expanded population of WT EZH2 tumors in NHL, as mentioned in Question 1, and a range of solid tumors in which EZH2 activity is elevated by various mechanisms, such as INI1 deficiency. We believe the renegotiated deal is a significant positive for Epizyme, especially given the potential commercial opportunities and shift in economics, from co-promote option in the US and flat mid-single digit royalties ex-US, to the current deal where Epizyme owns the majority of US and ex-US sales outside of Japan.
4. How heavily does the rat lymphoma safety signal weigh on tazemetostat's prospects?	**Despite the worrisome finding of lymphoma in one animal (rat) in a 13-week preclinical safety study, we believe a number of reasons lessen concerns about this issue**. 1) The rat strain (Sprague-Dawley) in question is prone to developing tumors. 2) Only one animal developed lymphoma, and that was at a dose level much higher than tested in human trials. 3) In addressing relapsed/refractory patients who have few other options, we believe the risk/benefit calculation swings in the direction of tazemetostat. 4) Ongoing clinical trials in Europe do not indicate a similar safety signal, and further preclinical testing may be able to mitigate these concerns.

Exhibit 146: Epizyme's pipeline

Drug	Target	Indication	Stage
tazemetostat (EPZ-6438)	EZH2	DLBCL, FL	Phase II
pinometostat (EPZ-5676)	DOT1L	MLL-r AML and ALL	Phase I

Source: Company Reports

Exhibit 147: Epizyme expected newsflow

Event	Drug	Timing
Initiate Phase II trial of adult patients with INI1 or SMARCA4-deficient tumors	tazemetostat	4Q15
Initiate Phase I trial of pediatric patients	tazemetostat	4Q15
Complete enrollment in ongoing Phase I trial in pediatric MLL-r patients	pinometostat	4Q15
Initiate combo studies of tazemetostat in NHL with R-CHOP and with B-cell signaling inhibitor	tazemetostat	1H16
Initial data for Phase II tazemetostat trial in NHL	tazemetostat	mid 2016
Data from Phase I pediatric pinometostat trial	pinometostat	2H16

Source: Company Reports and RBC Capital Markets estimates

Exhibit 148: EPZM quarterly P&L ($MM)

($MM)	2012A	2013A	2014A	Q1:15A	Q2:15A	Q3:15A	Q4:15E	2015E	Q1:16E	Q2:16E	Q3:16E	Q4:16E	2016E	2017E
Total WW tazemetostat sales (EZH2, Eisai)	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Total tazemetostat revenue to EPZM	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Total US/EU pinometostat sales (DOT1L, Celgene)	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Total pinometostat revenue to EPZM	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Collaboration revenue	**45.2**	**68.5**	**41.4**	**0.9**	**0.7**	**0.4**	**0.0**	**2.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Total Revenue	**45.2**	**68.5**	**41.4**	**0.9**	**0.7**	**0.4**	**0.0**	**2.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
COGS	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
R&D	**38.5**	**57.6**	**75.6**	**57.1**	**20.6**	**16.8**	**30.7**	**125.1**	**30.0**	**32.0**	**35.2**	**46.8**	**144.0**	**129.2**
SG&A	**7.5**	**14.0**	**20.9**	**5.2**	**6.0**	**6.7**	**6.5**	**24.4**	**6.7**	**6.6**	**6.8**	**6.6**	**26.7**	**26.5**
Total Operating Expenses	**46.0**	**71.6**	**96.5**	**62.3**	**26.5**	**23.5**	**37.2**	**149.5**	**36.7**	**38.6**	**42.0**	**53.4**	**170.7**	**155.7**
Operating Income (Loss)	**(0.8)**	**(3.1)**	**(55.1)**	**(61.4)**	**(25.8)**	**(23.1)**	**(37.2)**	**(147.5)**	**(36.7)**	**(38.6)**	**(42.0)**	**(53.4)**	**(170.7)**	**(155.7)**
Interest income	0.1	0.1	0.1	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.1	0.0
Interest expense	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Other income (expense)	(0.1)	(0.0)	0.1	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.1	0.0
Pretax income	(0.7)	(3.1)	(54.9)	(61.3)	(25.8)	(23.1)	(37.2)	(147.3)	(36.7)	(38.6)	(42.0)	(53.4)	(170.5)	(155.7)
Income tax expense	0.0	0.3	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Accretion of redeemable convertible preferred stock to redemption value	0.5	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net Income (Loss)	**(1.2)**	**(3.747)**	**(55.0)**	**(61.3)**	**(25.8)**	**(23.1)**	**(37.2)**	**(147.3)**	**(36.7)**	**(38.6)**	**(42.0)**	**(53.4)**	**(170.5)**	**(155.7)**
Basic EPS	**($0.72)**	**($0.22)**	**($1.67)**	**($1.75)**	**($0.63)**	**($0.56)**	**($0.89)**	**($3.57)**	**($0.87)**	**($0.90)**	**($0.97)**	**($1.22)**	**($3.97)**	**($3.49)**
Diluted EPS	**($0.72)**	**($0.22)**	**($1.67)**	**($1.75)**	**($0.63)**	**($0.56)**	**($0.89)**	**($3.57)**	**($0.87)**	**($0.90)**	**($0.97)**	**($1.22)**	**($3.97)**	**($3.49)**

Source: Company reports and RBC Capital Markets estimates

Valuation

We use a sum-of-the-parts methodology to value EPZM ($39/share), and we estimate the probability-adjusted NPV of the following: 1) tazemetostat sales in NHL ($35/share) at a 60% POS, 2) tazemetostat sales in solid tumors ($2/share) at a 50% POS, and 3) the company's projected net cash position ($2/share). Currently, we do not value Epizyme's platform; however, we may revisit in the future, depending on further collaborations and clinical development.

Price target impediments

Factors that can negatively influence our valuation include negative clinical trials results for tazemetostat, the inability to file an IND for tazemetostat in the US due to concerns relating to the rat toxicity in a preclinical study, and increased competition from Constellation's EZH2 inhibitor, GSK's GSK2816126 or other HMT inhibitor competitors.

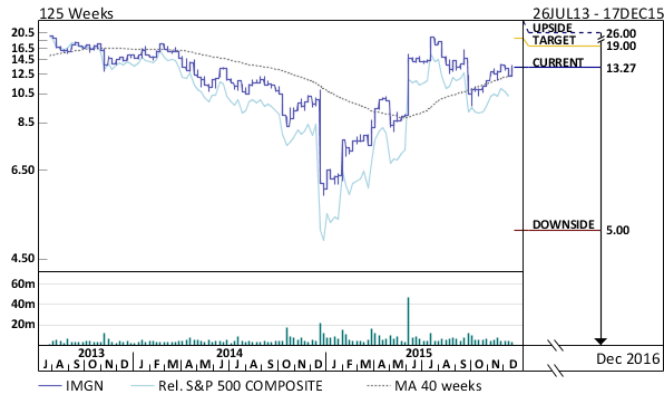
ImmunoGen, Inc. (IMGN)

Outperform, Speculative Risk

Price Target USD $19.00

Target/Upside/Downside Scenarios

Exhibit 149: ImmunoGen, Inc.



Source: RBC Capital Markets estimates

Target price/base case

We use a sum-of-the-parts methodology to value IMGN ($19/share), and we estimate the probability adjusted NPV of the following: 1) the remainder of the Kadcyla royalty stream (~$2.35/share); 2) the sales of IMGN853 in platinumresistant ovarian cancer and endometrial cancer (~$12/share); 3) the three wholly owned compounds (IMGN529, IMGN779, and SAR3419) in the clinic (~$1.50/share); 4) the portfolio of eleven partnered compounds (~$1.40/share); and 5) the company's projected net cash position (~$1.40/share).

Upside scenario

Release of updated positive data from the mirvetuximab/ IMGN853 program at the 2016 ASCO would further increase the probability of success from 70% in our base case to 80%. This in conjunction with continued data supporting a higher percentage (~80%) of FRalpha positive PROC patients would increase the value of the '853 program to ~$19/share. This would lead to a share price of $26.

Downside scenario

Our downside scenario includes negative data out of the mirvetuximab/IMGN853 program, which would lead us to also lower the value of the pipeline products. This net effect could push IMGN shares down to approximately $5/share.

Investment summary

Majority of focus is on mirvetuximab (IMGN853), but IMGN offers a diversified mix of assets. The majority of investor focus is currently on IMGN853, but we believe IMGN offers a diversified mix of assets through the Kadcyla outlicensing and the potential upside, the other three fully owned ADC programs, and the growing and advancing partnered pipeline.

Nothing on our radar screen yet from the partnered pipeline, but these are eleven clinical shots on goal: IMGN is currently partnered with six companies (SNY, AMGN, BAY, NVS, LLY and Biotest) in eleven clinical compounds. Two of them have early Phase II hematology data, with mixed reception from investors. It is tough to differentiate at this early stage among these clinical agents. Nonetheless, they, along with the numerous preclinical molecules partnered with NVS, AMGN, LLY, CytomX and Takeda, provide a diversified basket of ADCs that could end up resulting in one or more drugs.

Kadcyla currently in three Phase III trials: Sentiment on Kadcyla has soured, from both the flattening of US sales and the unexpected data announcements about MARIANNE and GATSBY. However, there are three more Kadcyla trials reading out: KRISTINE in neoadjuvant; and KATHERINE and KAITLIN in the adjuvant breast cancer setting. We view the chances of success in these three Phase III trials as fairly independent of what happened in MARIANNE and GATSBY.

Risks: 1) IMGN853 clinical/regulatory setbacks; 2) failure in ongoing trials of other pipeline programs; 3) unexpected safety signal from Kadcyla's clinical use. These risks, if they materialize, may result in significant volatility, and given that the majority of the value comes from a single product, lead to the Speculative Risk qualifier on our rating.

Key questions

Our view

1. Will the mirvetuximab soravtansine (IMGN853) development program succeed?

Updated data at 2015 AACR-NCI-EORTC "triple meeting" in Boston continue to look good. The data presented at the recent meeting updated and expanded on the previous data released at ASCO. Specifically, the updated ORR is 50% (10/20; 2 CR, 8 PR) based on 20 evaluable patients compared to the previously reported ORR of 53% (9/17; 1 CR, 8 PR), based on 17 evaluable patients. This response rate, well above the 15–20% response rate typically seen in platinum-resistant ovarian cancer (approved Avastin + chemo combo, 29% ORR, but in less heavily pre-treated pts), combined with the relatively benign safety profile, remains very encouraging for an agent used as monotherapy.

2. What about the eye toxicity seen with mirvetuximab soravtansine?

Blurred vision still there, but reversible and Grade 1 and 2 only: To date, the eye toxicity (blurred vision) associated with the drug has been mild to moderate (Grade 1 and 2, no Grade 3), and according to a study investigator we spoke to, reversible, usually resulting in "delaying the next dose by a couple of weeks". The company is currently evaluating the use of lubricating eye drops and/or corticosteroids as ways of helping with this AE and will also test a q4w schedule in the Phase II to evaluate whether the extra week between doses lessens the incidence of eye toxicity.

3. What about IMGN's partnered pipeline?

Nothing on our radar screen yet, but these are eleven clinical shots on goal: IMGN is currently partnered with six companies (SNY, AMGN, BAY, NVS, LLY and Biotest) in eleven clinical compounds. Two of them have early Phase II hematology data, with mixed reception from investors. It is tough to differentiate at this early stage among these clinical agents. Nonetheless, they, along with the numerous preclinical molecules partnered with NVS, AMGN, LLY, CytomX and Takeda, provide a diversified basket of ADCs that could end up resulting in one or more drugs.

Exhibit 150: ImmunoGen's pipeline

Drug (target)	Indication	Stage
Kadcyla (HER2)	HER2+ Breast Cancer	Marketed
Mirvetuximab soravtansine (FRα)	Ovarian, Endometrial Cancer	Phase I
Coltuximab (CD19)	NHL	Phase II
IMGN529 (CD37)	NHL	Phase I
IMGN779 (CD33)	AML	Pre-clinical

Source: RBC Capital Markets and Company reports

Exhibit 151: ImmunoGen expected newsflow

Event	Drug	Timing
Start IMGN529 + Rituxan Phase II trial	IMGN529	4Q15
Pre-clinical findings of Mirvetuximab in combination regimens	IMGN853	4Q15
Initiate Phase II trial of Mirvetuximab in FRα+ ovarian or endometrial cancer	IMGN853	4Q15
Data from Mirvetuximab Ph I study for ovarian cancer biopsy and endometrial cohorts	IMGN853	2Q16
Start Phase 1 trial with IMGN779 in AML	IMGN779	1H2016
Regulatory meeting with FDA for Mirvetuximab	IMGN853	1H2016
Mirvetuximab data from 40-patient expansion cohort at ASCO	IMGN853	June 3-7, 2016
Initiate Phase II testing of Coltuximab in combination regimen	Coltuximab	2016
Data from the two adjuvant studies of Kadcyla	Kadcyla	2018

Source: RBC Capital Markets and Company report

Exhibit 152: IMGN quarterly P&L ($MM)

($MM)	FY 2011A	FY 2012A	FY 2013A	FY 2014A	FY 2015A	Q1: 16A	Q2: 16E	Q3: 16E	Q4: 16E	FY 2016E	Q1: 17E	Q2: 17E	Q3: 17E	Q4: 17E	FY 2017E
Kadcyla															
Total WW Breast Cancer Sales	**0.0**	**0.0**	**88.9**	**415.7**	**720.6**	**206.3**	**215.0**	**222.2**	**232.1**	**875.6**	**243.0**	**254.5**	**267.7**	**280.9**	**1046.1**
Total WW Gastric Cancer Sales	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Total WW Kadcyla sales	**0.0**	**0.0**	**88.9**	**415.7**	**720.6**	**206.3**	**215.0**	**222.2**	**232.1**	**875.6**	**243.0**	**254.5**	**267.7**	**280.9**	**1046.1**
Total WW Kadcyla royalties	**0.0**	**0.0**	**0.6**	**10.3**	**19.4**	**5.7**	**6.8**	**8.2**	**6.7**	**27.4**	**7.0**	**8.0**	**9.7**	**8.0**	**32.7**
Kadcyla royalties paid to TSSP	**0.0**	**0.0**	**0.0**	**0.0**	**5.5**	**5.7**	**6.8**	**8.2**	**6.7**	**27.3**	**7.0**	**8.0**	**9.7**	**8.0**	**32.7**
Kadcyla royalties to IMGN			**0.6**	**10.3**	**13.9**	**0.0**	**0.0**	**0.0**	**0.0**	**0.1**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Total WW IMGN853 sales	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Research and development revenue	7.3	4.5	7.9	7.2	2.8	0.8	1.5	1.5	2.2	6.0	1.5	1.5	1.5	1.5	6.0
License/Milestones payments	6.4	9.2	24.2	39.5	57.8	6.1	0.0	15.0	20.0	41.1	0.0	0.0	0.0	0.0	0.0
Non-cash royalty revenue					5.5	5.7	6.8	8.2	6.7	27.3	7.0	8.0	9.7	8.0	32.7
Clinical materials reimbursement	5.7	2.7	2.8	2.9	5.5	2.3	1.0	1.0	1.0	5.3	1.0	1.0	1.0	1.0	4.0
Total Revenue	**19.3**	**16.4**	**35.5**	**59.9**	**85.5**	**14.9**	**9.3**	**25.7**	**29.9**	**79.8**	**9.5**	**10.5**	**12.2**	**10.5**	**42.7**
COGS	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
R&D	**63.5**	**69.2**	**87.1**	**107.0**	**111.8**	**35.1**	**37.1**	**35.8**	**36.1**	**144.1**	**36.9**	**37.5**	**38.2**	**38.5**	**151.1**
SG&A	**16.0**	**20.4**	**21.5**	**24.5**	**28.2**	**8.3**	**8.4**	**8.3**	**8.4**	**33.4**	**8.5**	**8.4**	**8.5**	**8.6**	**34.0**
Total Operating expenses	**79.5**	**89.6**	**108.5**	**131.4**	**140.0**	**43.5**	**45.5**	**44.1**	**44.5**	**177.6**	**45.4**	**45.9**	**46.7**	**47.1**	**185.1**
Operating Income/Loss	**(60.2)**	**(73.3)**	**(73.0)**	**(71.5)**	**(54.5)**	**(28.6)**	**(36.2)**	**(18.4)**	**(14.6)**	**(97.7)**	**(35.9)**	**(35.4)**	**(34.5)**	**(36.6)**	**(142.4)**
Total other income	1.9	(0.1)	0.2	0.1	(6.3)	(5.1)	(6.8)	(8.2)	(6.7)	(26.8)	(7.0)	(8.0)	(9.7)	(8.0)	(32.7)
Pretax income	(58.3)	(73.3)	(72.8)	(71.4)	(60.7)	(33.7)	(43.0)	(26.6)	(21.3)	(124.5)	(42.9)	(43.4)	(44.2)	(44.6)	(175.1)
Income tax expense	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net Income (Loss)	**(58.3)**	**(73.3)**	**(72.8)**	**(71.4)**	**(60.7)**	**(33.7)**	**(43.0)**	**(26.6)**	**(21.3)**	**(124.5)**	**(42.9)**	**(43.4)**	**(44.2)**	**(44.6)**	**(175.1)**
GAAP EPS															
Basic	($0.85)	($0.95)	($0.87)	($0.83)	($0.71)	($0.39)	($0.49)	($0.30)	($0.24)	($1.41)	($0.47)	($0.48)	($0.48)	($0.48)	($1.91)
Diluted	($0.85)	($0.95)	($0.87)	($0.83)	($0.71)	($0.39)	($0.49)	($0.30)	($0.24)	($1.41)	($0.47)	($0.48)	($0.48)	($0.48)	($1.91)

Source: Company reports and RBC Capital Markets estimates

Valuation

We use a sum-of-the-parts methodology to value IMGN ($19/share), and we estimate the probability adjusted NPV of the following: 1) the remainder of the Kadcyla royalty stream (~ $2.35/share); 2) the sales of IMGN853 in platinum-resistant ovarian cancer and endometrial cancer (~$12/share); 3) the three wholly owned compounds (IMGN529, IMGN779, and SAR3419) in the clinic (~$1.50/share); 4) the portfolio of eleven partnered compounds (~ $1.40/share); and 5) the company's projected net cash position (~$1.40/share).

Price target impediments

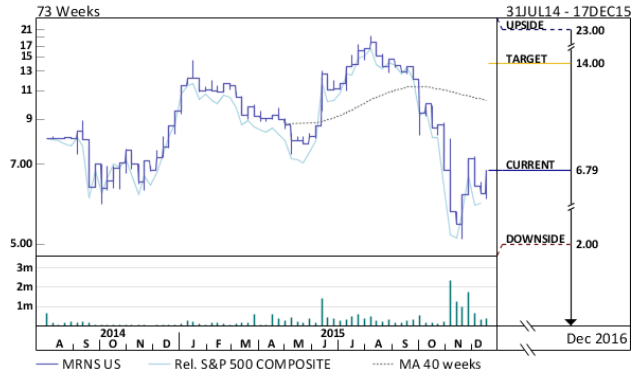
Factors that can negatively influence our valuation include discontinuation of any of ImmunoGen's wholly owned or partnered programs, negative outcomes from clinical trials of Kadcyla, and lower than projected penetrations for Kadcyla, especially for the second-line and later settings in metastatic breast cancer. Factors that can positively affect our valuation include setbacks for competition, positive data from other settings within HER2+ breast cancer, and positive data for its early-stage portfolio of therapeutic candidates that lead to more mature clinical development and testing

Marinus Pharmaceuticals, Inc. (MRNS)

Outperform, Speculative Risk
Price Target USD $14.00

Target/Upside/Downside Scenarios

Exhibit 153: Marinus Pharmaceuticals, Inc.



Source: RBC Capital Markets estimates

Target price/base case

We use a sum-of-the-parts methodology to value MRNS ($14/share), and estimate the probability-adjusted NPV of the following: 1) Ganaxolone sales and royalties in focal onset seizures (~$7.50/share), 2) Ganaxolone sales and royalties in status epilepticus (~$4.50/share), and 3) the company's projected net cash position ($2/share). We have not assigned value to the pediatric epilepsy or Fragile X Syndrome programs in our price target due to both programs being early stage. We will revisit valuation for these early pipeline assets as the development programs progress further in development and we get closer to more meaningful clinical data readouts.

Upside scenario

Positive data from either the Fragile X syndrome or the pediatric epilepsy program would add an additional $5/share to our current valuation and lead to an upside scenario of $19/share. We have not currently assigned any value to either one of these programs, since they're both early in development. In addition, positive data readouts from the first Phase III focal onset seizures trial in mid-2016 and from the Phase I status epilepticus trial in 2016 would add another $2/share and $3/share, respectively, bringing our upside scenario to $24/share.

Downside scenario

With the oral ganaxolone focal onset Phase II/III trial expected to read out in mid-2016, the first question investors would want to know would be what to happen to MRNS shares in the event of a negative trial result. We would expect shares to trade at around the company's cash position, or ~$2/ share, since a negative trial outcome in this pivotal Phase II/III trial would cast significant doubt on the broader ganaxolone development program, and not just the focal onset program.

Investment summary

Oral ganaxolone set for first Phase III readout in mid-2016 in focal onset, drug-resistant epilepsy. Marinus has completed a positive Phase II study evaluating oral ganaxolone as an adjunct treatment for refractory focal onset seizures. This study met its primary endpoint and showed a statistically significant mean seizure reduction from baseline of 19% over placebo. Marinus is currently conducting a Phase III study and based on the positive Phase II data, which yielded efficacy results that were comparable to approved anti-epileptic drugs (AEDs), we see a better than average chance for a positive trial. Assuming a 2020 launch, we model $200M in peak US sales and $355M in peak worldwide sales in 2030 based on 7% penetration assumptions and a 60% probability of success.

Intravenous ganaxolone formulation for orphan epilepsy setting: we model a 2021 launch in status epilepticus. Marinus is developing an IV formulation of ganaxolone for the treatment of refractory status epilepticus (RSE), an orphan disease setting. With a Phase I study set to begin in 1Q16, Marinus plans to initiate a Phase II/III study in 2H16. We model a 2021 launch and peak 2030 sales of $313M WW for IV ganaxolone in status epilepticus and have assigned a 30% probability of success, given its early stage of development.

SAGE-547 is the most serious competitive threat to ganaxolone IV success in status epilepticus. Sage Therapeutics has attracted investors' attention given its positive data with SAGE-547, an IV formulation of allopregnanolone, a compound with structural similarities to ganaxolone. These data came in super refractory status epilepticus (SRSE), the most advanced stage of the disease, which is one step after RSE, where Marinus is going to test ganaxolone. SAGE's head start in development certainly poses a risk to ganaxolone IV in SE. Marinus has based its decision to move into this disease setting on preclinical studies showing that ganaxolone may provide greater seizure reductions than allopregnanolone.

Risks: 1) Negative Phase II/III data from the ganaxolone focal onset trial; 2) Negative data from the FXS trial; 3) Development/regulatory delays in the ganaxolone IV program. These risks, if they materialize, may result in significant volatility, and given that the majority of the value in the stock comes from a single product, lead to the Speculative Risk qualifier on our rating.

Key questions

Our view

Will the ongoing trial of oral ganaxolone in focal onset seizures work?

Based on the positive Phase II data and the known mechanism of action, we think that despite the changes in formulation and the higher dose used in the Phase III, we see a better-than-average probability for a successful Phase III readout in mid-2016. Marinus has completed a positive Phase II placebo-controlled study in 147 patients testing oral ganaxolone as an adjunct treatment for refractory focal onset seizures in adults. This study met its primary endpoint and showed a statistically significant mean seizure reduction from baseline of 19% over placebo. The company is currently conducting a Phase III placebo-controlled study in 300 patients using a capsule formulation vs. the liquid formulation used in the Phase II. In the addition, the Phase III trial will test a higher dose (1800 mg/day) than the maximum dose used in Phase II (1500mg/day). Making changes between trials can make investors nervous, since it introduces additional elements of risk. However, based on the positive Phase II data, which were comparable to the ones from other anti-epileptic drugs (AEDs) approved in recent years, and the drug's known mechanism of action, we see a better-than-average chance for a positive trial.

What's next for the oral ganaxolone program and how much is it potentially worth?

Assuming a positive readout in the Phase III trial, Marinus plans to conduct a second Phase III trial, which is expected to start in 2H16 and would be required by FDA as part of ganaxolone's path to registration. And assuming a successful Phase III program for oral ganaxolone in focal onset seizures, we model $200M in peak US sales and $355M in peak worldwide sales in 2030 based on 7% peak penetration.

There are already numerous approved drugs for focal onset seizures: why do we need this one?

Despite numerous approved agents, there is still a significant unmet medical need in epilepsy, with a large number of treatment-refractory patients: we believe ganaxolone's novel mechanism of action and relatively benign safety profile can help it become a viable product as adjunctive therapy in focal onset seizures. Currently approved AEDs employ a variety of mechanisms of action such as potentiation of GABA receptors or modulation of voltage-activated sodium channels. However, ganaxolone, a synthetic analog of the naturally occurring neurosteroid allopregnanolone, differs from currently used GABA-targeted agents due to its ability to interact with unique binding sites on $GABA_A$ receptors located at both intrasynaptic and extrasynaptic locations, as opposed to only intrasynaptic. This mechanism of action is important because it provides the potential for patients who no longer derive benefit from their current treatment regimen of 2+ AEDs to gain additional clinical benefit from adding a new drug with a novel and differentiated approach. Furthermore, as opposed to currently approved AEDs, many of which are classified as Pregnancy Category C or D on their labels, Marinus is aiming for a Pregnancy Category B distinction for ganaxolone, which would indicate a lower risk of adverse effects for the fetus in women of child-bearing age. In combination with the drug's benign safety profile to date, this distinction may provide a competitive edge for ganaxolone in the AED space.

How much of a threat is SAGE-547 in status epilepticus?

The ganaxolone IV program could face potential competition from SAGE-547, a similar molecule and further ahead in development; preclinical studies point to ganaxolone's potentially greater potency. SAGE Therapeutics is currently developing an IV formulation of allopregnanolone (SAGE-547), for the *super refractory* stage of *status epilepticus* (SRSE). SAGE has positive Phase II data and has started a placebo-controlled Phase III study which is expected to be completed in 2H16. Marinus has just announced plans to develop an IV formulation of ganaxolone to be used for the treatment of *refractory status epilepticus* (RSE), one step before SRSE in the treatment paradigm. Marinus has based its decision to move into this disease setting on preclinical studies that showed that ganaxolone can provide significant seizure reductions. Although SAGE-547 is being developed for the treatment of SRSE (the most advanced and most serious form of SE), we believe it is theoretically possible for the drug to be moved upstream along the treatment continuum in SE where it would compete directly with ganaxolone and thus represent a potential competitive threat to the ganaxolone IV program. With a Phase I ganaxolone IV study set to begin in 1Q16, Marinus plans to initiate a Phase II/III study in 2H16. We are modeling a 2021 launch and peak 2030 sales of $326M WW for IV ganaxolone in the status epilepticus setting and have assigned a 30% probability of success, given its early stage of development.

Exhibit 154: Marinus' pipeline

Drug	Indication	Formulation	Stage
Ganaxolone	Adjunctive treament for focal onset seizures	Oral	Phase III
	Status epilepticus	IV	Phase I
	PCDH19 pediatric epilepsy	Oral	Phase II
	Fragile X syndrome	Oral	Phase II

Source: RBC Capital Markets, Company reports

Exhibit 155: Marinus' expected newsflow

Event	Drug	Timing
Top-line data from Phase II in Fragile X syndrome	Ganaxolone	1Q16
Initiate Phase I trial in status epilepticus		1Q16
Top-line data from Phase III trial in focal onset seizures		Mid-2016
Full data from Phase II trial in PCDH19		Mid-2016
Initiate 2nd Phase III trial in focal onset seizures		2H16
Initiate Phase II/III trial in status epilepticus		2H16

Source: RBC Capital Markets, Company reports

Exhibit 156: MRNS quarterly P&L ($MM)

($MM)	FY 2012A	FY 2013A	FY 2014A	Q1: 15A	Q2: 15A	Q3: 15A	Q4: 15E	FY 2015E	Q1: 16E	Q2:16E	Q3: 16E	Q4: 16E	FY 2016E	FY 2017E
Ganaxolone sales in focal onset seizures	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Ganaxolone royalties in focal onset seizures in EU	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Ganaxolone sales in status epilepticus	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Ganaxolone royalties in status epilepticus in EU	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Total ganaxolone sales/royalties to Marinus	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Milestone payments	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total Revenues	**0.1**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
COGS	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
R&D	**0.8**	**4.2**	**8.7**	**5.5**	**3.9**	**3.5**	**3.9**	**16.7**	**4.4**	**4.9**	**5.1**	**5.5**	**19.9**	**21.7**
SG&A	**0.7**	**1.2**	**3.2**	**1.4**	**1.3**	**1.4**	**1.5**	**5.6**	**1.6**	**1.5**	**1.7**	**1.6**	**6.4**	**6.6**
Total Operating Expenses	**1.5**	**5.4**	**11.9**	**6.9**	**5.2**	**4.9**	**5.4**	**22.3**	**6.0**	**6.4**	**6.8**	**7.1**	**26.3**	**28.3**
Operating Income	**-1.4**	**-5.4**	**-11.9**	**-6.9**	**-5.2**	**-4.9**	**-5.4**	**-22.3**	**-6.0**	**-6.4**	**-6.8**	**-7.1**	**-26.3**	**-28.3**
Change in fair value of warrant liability	0.3	0.2	1.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Interest income	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.1	0.1
Interest expense	-0.3	-0.1	-0.1	-0.2	-0.1	-0.1	-0.1	-0.5	-0.1	-0.1	-0.1	-0.1	-0.5	-0.5
Other income (expense)			0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Pretax Income	-1.4	-5.3	-10.8	-7.1	-5.3	-5.0	-5.5	-22.8	-6.1	-6.5	-6.9	-7.2	-26.8	-28.7
Benefit / provision for income taxes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Tax Rate	*0%*	*-1%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
NOLs			*-127.0*					*(149.8)*					*(176.5)*	*(205.2)*
Use of NOLs													*0.0*	*0.0*
Net Income	**(3.6)**	**(9.1)**	**(13.4)**	**(7.1)**	**(5.3)**	**(5.0)**	**(5.5)**	**(22.8)**	**(6.1)**	**(6.5)**	**(6.9)**	**(7.2)**	**(26.8)**	**(28.7)**
Basic EPS	**$ (8.00)**	**$ (19.60)**	**$ (2.17)**	**$ (0.50)**	**$ (0.37)**	**$ (0.35)**	**$ (0.28)**	**$ (1.47)**	**$ (0.31)**	**$ (0.33)**	**$ (0.34)**	**$ (0.29)**	**$ (1.26)**	**$ (1.34)**
Diluted EPS	**$ (8.00)**	**$ (19.60)**	**$ (2.17)**	**$ (0.50)**	**$ (0.37)**	**$ (0.35)**	**$ (0.28)**	**$ (1.47)**	**$ (0.31)**	**$ (0.33)**	**$ (0.34)**	**$ (0.29)**	**$ (1.26)**	**$ (1.34)**

Source: Company reports, RBC Capital Markets estimates

Valuation

To value MRNS shares, we use a sum-of-the-parts methodology, and estimate the probability-adjusted NPVs of the following: 1) Ganaxolone sales and royalties in focal onset seizures (~$7.50/share), 2) Ganaxolone sales and royalties in status epilepticus (~$4.50/share), and 3) the company's projected net cash position ($2/share).

Price target impediments

Factors that can negatively affect our valuation for Marinus include unexpected safety signals from ganaxolone, which could result in delays in filing for FDA approval or lead to a suspension of ganaxolone development. Additionally, increased competition from SAGE Therapeutics' SAGE-547 or other branded AEDs may lead to a reduction in market penetration and revenue.

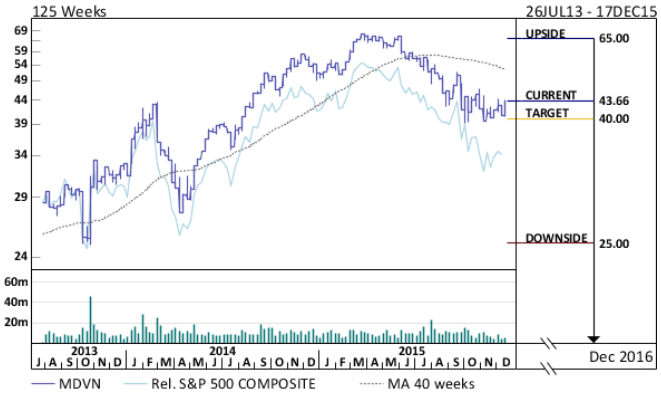
Medivation, Inc. (MDVN)

Sector Perform, Speculative Risk

Price Target USD $40.00

Target/Upside/Downside Scenarios

Exhibit 157: Medivation, Inc.



Source: RBC Capital Markets estimates

Target price/base case

We use a sum-of-the-parts methodology to value Medivation shares, at $40/share, and estimate the probability adjusted NPV of the following: 1) the XTANDI royalty stream in prostate cancer ($31.50/share); 2) the XTANDI royalty stream in breast cancer ($1/share); 3) the company's non-XTANDI pipeline ($6/ share); and 4) the company's projected net cash position ($1.50/share).

Upside scenario

Longer-than-expected duration of treatment following positive data from the STRIVE and TERRAIN trials would increase our peak sales estimates for XTANDI in prostate cancer to $12.4B, by increasing the estimated duration of therapy for patients receiving the drug in the pre-chemo setting. We are currently modeling 18 months of treatment for patients in that setting; if physicians end up using the drugs longer, in the 24-month range for XTANDI, that could drive MDVN shares to approximately $65/share.

Downside scenario

Slower-than-expected adoption of XTANDI in the pre-chemo space, following the STRIVE and TERRAIN data would limit potential upside. In the base case, we have modeled peak penetration of 50%, 20%, 38% and 5% in this setting in the US, EU, JPN and ROW, respectively; slower adoption following data from these trials would lead to lower peak penetrations in this setting (30%, 15%, 25%, 2%) and a $25/share NPV for MDVN.

Investment summary

We think XTANDI will be a big drug; we also think valuation already reflects that. XTANDI is now approved in both the pre- and post-chemo settings, where JNJ's incumbent Zytiga did $2.2B in 2014 WW sales. These drugs have "more or less the same efficacy" and docs currently use each "in about half their patients". However, we expect XTANDI to have the upper hand in the pre-chemo setting given Zytiga's need for concomitant steroid use, so we project that XTANDI will eventually become the dominant player in these settings. However, given that Medivation shares this asset with Astellas (gets 50% of US sales, low-teens to low-20s royalties ex-US), and despite projecting very generous sales for XTANDI, we think MDVN shares already reflect the drug's potential and we would look for a better entry point into this story. We rate MDVN Sector Perform, Speculative Risk.

TERRAIN and STRIVE successful: These two Phase II trials, comparing XTANDI to bicalutamide (Casodex) were designed with the goal of moving XTANDI upstream in the treatment paradigm. In the recently released TERRAIN study, XTANDI won handily in PFS. There were a few question marks, including the short time on treatment (11.7 months vs. PFS of 15.7 months), which may point to the drug's tolerability; the 31.1% incidence of SAEs in the trial, including 5.5% of Grade >3 cardiac AEs vs. 2.1% for Casodex. Finally, there were 2 seizures in the XTANDI arm vs. 1 in the Casodex arm. The STRIVE data were more clear cut, with the XTANDI showing a clear benefit over Casodex in terms of both efficacy and safety.

What about XTANDI in breast cancer and the anti-PD-1 drug? XTANDI is also tested in AR+ TNBC and MDVN recently presented data from a 118-patient, open-label, Phase II trial. The oncologists we spoke with described the data as "promising, but early, in a really tough disease setting". MDVN also recently in-licensed anti-PD1 antibody pidilizumab, from CureTech for $5M upfront and up to $85M in milestones. Pidilizumab was tested in three early hematology trials, two of which had read out. The data looked encouraging, but we could not draw strong conclusions from the limited, openlabel datasets or find any real differentiating factors from the multiple competitors further ahead in development.

Risks: 1) XTANDI sales not meeting expectations; 2) clinical/ reimbursement support for Zytiga ahead of XTANDI use in the pre-chemo setting; 3) failure of non-XTANDI early stage pipeline. These risks, if they materialize, may result in significant volatility, and given that the majority of the value comes from a single product, lead to the Speculative Risk qualifier on our rating.

Key questions

	Our view
1. XTANDI or Zytiga? Who wins the pre-chemo setting battle?	**We expect XTANDI to be the leader in the pre-chemo setting, over Zytiga.** Treatment sequencing in this setting is crucial to commercial success as the duration of treatment is significantly longer for whichever drug is used first. We view the two agents' efficacy as similar, with XTANDI having an edge in the pre-chemo setting, due to its overall safety, and due to the fact that it doesn't require the use of steroids. However, we note that in what could to be a new era of attempts for price controls by payers, there may be situations where the ultimate sequencing decision may not be made by the prescriber, by forced reimbursement and ability to make a co-pay. Our KOLs raised concerns regarding the high costs and reimbursement hurdles with XTANDI, indicating that it has been traditionally less burdensome to receive reimbursement with Zytiga than XTANDI, perhaps due to the fact that XTANDI was only recently approved in that setting.
2. How easy will it be for XTANDI to move up the treatment paradigm?	**MDVN's is to move XTANDI earlier and earlier in the prostate cancer (PC) treatment setting. While we acknowledge the large population of PC patients in these earlier settings, we believe that the low cost of the SOC drugs in these settings, in this new era of stricter price controls, coupled with urologists' historical comfort in prescribing them, will make it difficult for XTANDI to gain a significant foothold in these earlier settings.** The message from MDVN is to target urologists, who "*see PC patients for nearly 12 years out of the 14 years that patients receive treatment*", and to convert the >500k annual Casodex scripts into XTANDI scripts. The recently announced BCR trial is targeting even earlier patients who receive Lupron. The high cost and associated fatigue of XTANDI treatment may not justify the broad and long-term continued use in those patients, who mostly face no imminent threat of disease progression. Moreover, the long treatment durations in those early settings mean that investors will not see data read outs for a number of years. Another key question to also consider is whether by using XTANDI earlier in treatment, where you have a drug, like Lupron, for example, that controls disease very well, and is cheap, makes sense, versus reserving it, for later, when you are running out of good options to use.
3. Was TERRAIN a success?	**We view the TERRAIN data as mixed.** Even though XTANDI won handily in PFS, this was expected. There were a few question marks, including the low time on treatment (11.7 months vs. PFS of 15.7 months), which may point to the drug's tolerability; the 31.1% incidence of SAEs in the trial, including 5.5% of Grade >3 cardiac AEs vs. 2.1% for Casodex. Finally, there were two seizures in the XTANDI arm vs. one in the Casodex arm.
4. Is there another XTANDI in the pipeline?	**Too early to tell.** Outside of XTANDI, MDVN's pipeline does not include another late-stage asset. Recent efforts to boost the pipeline include in-licensing of a preclinical BET bromodomain program and early clinical stage PD-1 inhibitor (pidilizumab) from OncoFusion Therapeutics and CureTech, respectively. Anti-PD1 antibody pidilizumab was tested in three early hematology trials, two of which had read out. The data looked encouraging, but we could not draw strong conclusions from the limited, open-label datasets or find any real differentiating factors from the multiple competitors further ahead in development.

Exhibit 158: Medivation's pipeline

Drug	Trial	Indication	Stage
XTANDI (AR antagonist)	PLATO	post-XTANDI progression	Phase IV
	PROSPER	non-metastatic CRPC	Phase III
	NEOADJUVANT	neoadjuvant	Phase II
		biochemical recurrence	Phase III
	STRIVE/TERRAIN	asymptomatic mCRPC	Phase II
		AR+ TNBC	Phase II
		HER2-normal BC	Phase II
		AR+, HER2+ metastatic BC	Phase II
Pidilizumab (PD-1 antibody)		DLBCL	Phase II

Source: RBC Capital Markets and Company reports

Exhibit 159: Medivation expected newsflow

Event	Drug	Timing
Start Phase II trial for XTANDI in heptocellular carcinoma	XTANDI	4Q15
Start Phase III trial for MDV9300 (pidilizumab) in DLBCL	pidilizumab	YE15
Update on development of talazoparib (BMN-673)	talazoparib	Early 2016

Source: RBC Capital Markets and Company reports

Exhibit 160: MDVN quarterly P&L ($MM)

($MM)	FY 2011A	FY 2012A	FY 2013A	FY 2014A	Q1: 15A	Q2: 15A	Q3: 15A	Q4: 15E	FY 2015E	Q1: 16E	Q2: 16E	Q3: 16E	Q4: 16E	FY 2016E	FY 2017E
XTANDI															
Total US XTANDI Sales	**0.0**	**71.5**	**392.4**	**679.8**	**224.0**	**298.4**	**313.0**	**323.6**	**1159.0**	**335.0**	**348.0**	**361.0**	**371.8**	**1415.8**	**1668.3**
Total Ex-US XTANDI Sales	**0.0**	**0.0**	**52.5**	**376.7**	**133.0**	**188.0**	**205.0**	**183.3**	**709.3**	**187.1**	**190.8**	**196.6**	**202.2**	**776.7**	**919.8**
Total WW XTANDI Sales	**0.0**	**71.5**	**444.9**	**1056.5**	**357.0**	**486.4**	**518.0**	**506.9**	**1868.3**	**522.1**	**538.8**	**557.6**	**573.9**	**2192.4**	**2588.0**
Total US royalties	**0.0**	**35.8**	**196.2**	**338.6**	**112.0**	**149.2**	**156.5**	**161.8**	**579.5**	**167.5**	**174.0**	**180.5**	**185.9**	**707.9**	**834.1**
Total Ex-US royalties	**0.0**	**0.0**	**6.3**	**49.5**	**15.8**	**25.6**	**33.6**	**34.4**	**109.4**	**22.5**	**27.3**	**32.6**	**41.2**	**123.6**	**156.5**
Total WW royalties	**0.0**	**35.8**	**202.5**	**388.1**	**127.8**	**174.8**	**190.1**	**196.2**	**688.9**	**190.0**	**201.3**	**213.1**	**227.1**	**831.5**	**990.7**
Astellas collaboration revenue	24.4	109.7	272.9	710.5	129.2	175.7	260.7	371.2	936.7	190.0	201.3	213.1	227.1	831.5	990.7
Royalties from US XTANDI Sales	0.0	35.8	196.2	339.9	112.0	149.2	156.5	161.8	579.5	167.5	174.0	180.5	185.9	707.9	834.1
Royalties from Ex-US XTANDI sales	0.0	0.0	6.3	49.5	15.8	25.6	33.6	34.4	109.4	22.5	27.3	32.6	41.2	123.6	156.5
Upfront and milestone payments	24.4	73.9	70.4	321.1	1.4	0.8	70.6	175.0	247.8	0.0	0.0	0.0	0.0	0.0	0.0
GAAP Total Revenue	**60.4**	**181.7**	**272.9**	**710.5**	**129.2**	**175.7**	**260.7**	**371.2**	**936.7**	**190.0**	**201.3**	**213.1**	**227.1**	**831.5**	**990.7**
non-GAAP Total Revenue	**36.0**	**107.8**	**202.5**	**389.378**	**127.8**	**174.8**	**190.1**	**196.2**	**688.9**	**190.0**	**201.3**	**213.1**	**227.1**	**831.5**	**990.7**
R&D - GAAP	**73.4**	**95.6**	**119.0**	**189.6**	**44.7**	**47.3**	**45.9**	**70.0**	**207.8**	**82.0**	**83.0**	**90.0**	**91.0**	**346.0**	**370.1**
R&D stock-based compensation	8.1	12.0	16.5	17.9	5.8	6.1	5.7	8.4	26.0	9.0	9.1	9.9	10.0	38.1	40.7
R&D - non-GAAP				**134.0**	**37.9**	**41.3**	**40.0**	**61.6**	**180.7**	**73.0**	**73.9**	**80.1**	**81.0**	**307.9**	**329.4**
SG&A - GAAP	**29.9**	**112.3**	**176.2**	**239.1**	**83.9**	**74.7**	**75.8**	**92.0**	**326.5**	**74.3**	**74.2**	**75.7**	**75.2**	**299.4**	**307.8**
SG&A Stock-based compensation	5.8	11.7	20.6	27.2	7.6	8.0	7.7	8.9	32.1	8.9	8.9	8.3	8.3	34.4	33.9
SG&A - non-GAAP				**200.4**	**67.4**	**57.5**	**58.8**	**62.6**	**246.4**	**65.4**	**65.3**	**67.4**	**67.0**	**265.0**	**274.0**
Total GAAP Operating Expenses	**103.3**	**207.9**	**295.2**	**428.7**	**128.6**	**122.0**	**121.7**	**162.0**	**534.3**	**156.3**	**157.2**	**165.7**	**166.2**	**645.4**	**677.9**
GAAP Operating Income (Loss)	**(42.9)**	**(26.2)**	**(22.2)**	**281.8**	**0.6**	**53.7**	**139.0**	**209.2**	**402.4**	**33.7**	**44.2**	**47.4**	**60.9**	**186.1**	**312.7**
Total other income (expense), net	(0.2)	(15.0)	(20.3)	(21.7)	(5.5)	(13.2)	(14.1)	(5.0)	(37.8)	(5.1)	(5.1)	(5.1)	(5.1)	(20.2)	(6.8)
GAAP Pretax income	(43.2)	(41.3)	(42.5)	260.2	(4.9)	40.4	124.9	204.2	364.6	28.6	39.1	42.3	55.8	165.9	306.0
GAAP Income tax (expense) benefit	4.3	(0.0)	(0.1)	16.3	1.8	(14.6)	(45.3)	(71.5)	(129.6)	(10.0)	(13.7)	(14.8)	(19.5)	(58.1)	(107.1)
GAAP Net Income (Loss)	**(38.8)**	**(41.3)**	**(42.6)**	**276.5**	**(3.1)**	**25.8**	**79.5**	**132.7**	**235.0**	**18.6**	**25.4**	**27.5**	**36.3**	**107.8**	**198.9**
non-GAAP Net Income (Loss)				**34.6**	**13.4**	**48.7**	**58.4**	**46.1**	**166.6**	**33.0**	**39.8**	**42.0**	**50.6**	**165.4**	**247.8**
GAAP Basic EPS	($1.11)	($0.56)	($0.57)	$3.59	($0.04)	$0.33	$0.49	$0.81	$1.95	$0.11	$0.16	$0.17	$0.22	$0.88	$1.58
GAAP Diluted EPS	($1.11)	($0.56)	($0.57)	$3.42	($0.04)	$0.31	$0.47	$0.79	$1.84	$0.11	$0.15	$0.16	$0.21	$0.83	$1.50
non-GAAP Basic EPS				$0.45	$0.17	$0.61	$0.36	$0.28	$1.38	$0.20	$0.24	$0.26	$0.31	$1.34	$1.97
non-GAAP Diluted EPS				$0.43	$0.17	$0.58	$0.35	$0.28	$1.36	$0.20	$0.24	$0.25	$0.31	$1.32	$1.94

Source: Company reports and RBC Capital Markets estimates

Valuation

We use a sum-of-the-parts methodology to value Medivation shares, at $40/share, and estimate the probability adjusted NPV of the following: 1) the XTANDI royalty stream in prostate cancer ($31.50/share); 2) the XTANDI royalty stream in breast cancer ($1/share); 3) the company's non-XTANDI pipeline ($6/share); and 4) the company's projected net cash position ($1.50/share).

Price target impediments

Factors that can negatively influence our valuation include negative updates with the University of California regarding their legal proceedings with Medivation, XTANDI sales growth that do not meet our projections, delays in trial recruitment and readout for XTANDI trials in earlier prostate cancer disease settings, and increased competition from either Zytiga or the host of new therapeutics currently in advanced clinical programs. Factors that can positively influence our valuation include positive readouts from non-XTANDI clinical programs (including MDVN's BET bromodomain program and newly acquired PD-1 program), greater than projected sales growth for XTANDI upon pre-chemo launch, and negative readouts from other therapeutic candidates for prostate cancer.

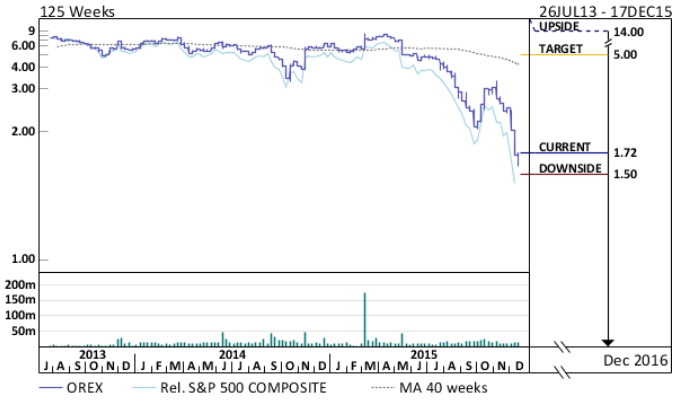
Orexigen Theraputics, Inc. (OREX)

Outperform, Speculative Risk

Price Target USD $5.00

Target/Upside/Downside Scenarios

Exhibit 161: Orexigen Therapeutics, Inc.



Source: RBC Capital Markets estimates

Target price/base case

In order to value OREX ($5/share), we use a sum-of-theparts methodology and estimate the probability-adjusted NPV of the following: (1) Contrave royalties ($4.50/share) and (2) Orexigen's projected net cash position ($0.50/share).

Upside scenario

Our upside scenario includes newsflow regarding life cycle management strategies that involve Contrave with Takeda's diabetes therapeutics, such as a fixed-dosed combination treatment for weight management and diabetes. This could add another $9 to our base case valuation and our price target on OREX to $14/share.

Downside scenario

Our downside scenario involves flattening of sales in the US and slower than expected launch in the EU. The combination of these two scenarios could lead shares to approximately the $1.50/share level.

Investment summary

No first-mover advantage here; this is a case where later may actually be better: In our view, the obesity market was not ready for the arrival of the first two players, Vivus' Qsymia and Arena's BELVIQ, with sales of both drugs disappointing investors. It looks like it ended up actually being an advantage for Orexigen's Contrave to come in after these first two obesity drugs had paved the way. Even though Contrave's launch is not a home-run by any stretch of the imagination, the silver lining is that not only is the obesity market more prepared to receive Contrave, in terms of physician and patient awareness and reimbursement, but investor expectations have also now been appropriately adjusted to a more realistic, lower level.

Commercial effort: Advantage Contrave... The obesity market is a primary care disease area and therefore, commercial success in it is determined not only by a drug's clinical profile, but also by the resources put behind it. Given the current competitive landscape in the obesity space, we believe that Takeda's 900-member sales team gives Contrave a significant advantage. Finally, Contrave is the only one of the three currently approved oral agents for obesity that can offer free samples to patients.

...but could the Takeda partnership be at risk? Contrave scripts in 3Q:15 grew 11% Q/Q (even though there was month-to-month TRx decline in the quarter), but net sales were down 20% Q/Q, indicating that the script growth came at the expense of very significant discounts. Despite being supported by a 900-rep sales force, Contrave is being hit with the same harsh realities of the obesity market facing its competitors in the space. As a reference to the $12.8M in net sales that were reported for Contrave in 3Q:15, OREX's competitor VVUS reported $14M in net sales last night. The key difference is that these sales came from the efforts (and the expense) of 900 Takeda reps vs. the 50 reps used by Vivus. The obvious question for us is at which point is Takeda starting to think that Contrave may not get to where they thought it would before they signed on to promote it.

Risks: (1) Contrave launch disappointment in the EU, (2) safety signal arising from clinical practice, and (3) slow down in obesity drug reimbursement progress. These risks, if materialized, may result in significant volatility, and the fact that the majority of the value comes from a single product leads to the Speculative Risk qualifier on our rating.

Key questions

Our view

1. Will this be the first successful obesity launch of its generation?

We believe the answer is Yes: Even though it is clear that the obesity market is still not established, and thus, do not yet see a dollar-for-dollar correlation between detailing and revenue, we believe that Takeda's significant investment in Contrave, with 900 sales reps, will result in making Contrave's launch the most successful of the three obesity drugs thus far. The launch has already gotten off to a great start and given the amount of resourcing Takeda has employed, the goal is not to just surpass the Qsymia and Belviq launches, but to actually make this a successful primary care drug launch.

2. Why will Contrave succeed where the other two failed?

It comes down to the level of commercial support; but coming in after the other two helps, also: The obesity market was clearly not ready for the arrival of Qsymia and Belviq. There were low levels of physician and patient awareness of the new pharmacotherapies, physician unwillingness, lack of experience and exposure with treating obesity with pharmacotherapy in general, and lack of reimbursement. However, two years later, even though things are far from perfect, there is a lot of improvement, mainly due to the efforts of the first two companies in the space. Thus, now that Takeda arrived with its 900 sales reps, with established relationships in the metabolic disease space, a lot of the work had already been done. In addition, they are promoting the only one of the three approved obesity agents that can offer free samples; Qsymia and Belviq are Schedule IV drugs and cannot be sampled. Finally, Contrave's mechanism of action is differentiated, addressing hunger via two separate pathways, by combining a widely used antidepressant and a drug to fight cravings. This potentially makes Contrave uniquely suited for a number of obese sub-populations, including the obese-depressed, which according to different literature sources, account for 20-40% of the overweight and obese population.

3. What will Orexigen do in Europe?

On their 3Q:15 earnings call, management outlined a number of general plans for a potential EU strategy. These included multiple possibilities for selling Mysimba, except for the most obvious and simple one, and the one that they had spent the previous year discussing: having a large pharma partner with established relationships and capabilities. At this point we have limited confidence in management's new plans for EU commercialization. We expect that it will be even more of an uphill battle than in the US for a small company to successfully execute a primary care launch in Europe.

Exhibit 162: Orexigen's pipeline

Drug	Indication	Stage
Contrave/Mysimba	**Chronic weight management**	**Marketed (US)**
Empatic	Chronic weight management	Phase II

Source: RBC Capital Markets and Company reports

Exhibit 163: Orexigen expected newsflow

Event	Drug	Timing
Dose first patient in post-marketing CVOT trial	Contrave	YE15
Potential EU launch of Mysimba	Contrave	2H16
Potential SK launch of Contrave	Contrave	2H16

Source: RBC Capital Markets and Company report

Exhibit 164: OREX quarterly P&L ($MM)

($MM)	FY 2012A	FY 2013A	FY 2014A	Q1: 15A	Q2: 15A	Q3: 15A	Q4: 15E	FY 2015E	Q1: 16E	Q2:16E	Q3: 16E	Q4: 16E	FY 2016E	FY 2017E
Product Sales														
US Contrave sales	0.0	0.0	6.5	11.5	16.0	12.8	14.9	55.2	17.0	18.0	19.5	21.2	75.7	117.7
EU Mysimba sales	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	10.7	10.7	35.8
SK Contrave sales	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.9	2.9	6.8
Total Contrave/Mysimba sales	**0.0**	**0.0**	**6.5**	**11.5**	**16.0**	**12.8**	**14.9**	**55.2**	**17.0**	**18.0**	**19.5**	**34.8**	**89.3**	**160.3**
Royalties on US Contrave sales	0.0	0.0	1.3	2.3	3.1	2.6	3.0	11.0	3.4	3.6	3.9	4.2	15.1	24.2
Royalties on EU Mysimba sales	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.7	2.7	9.0
Royalties on SK Contrave sales	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.9	0.9	2.5
Total Contrave/Mysimba revenue to OREX	**0.0**	**0.0**	**1.3**	**2.3**	**3.1**	**2.6**	**3.0**	**11.0**	**3.4**	**3.6**	**3.9**	**7.8**	**18.7**	**35.7**
Milestones/License Fees - Takeda	3.4	3.4	54.2	2.1	2.1	0.0	17.1	21.2	2.1	2.1	2.1	37.1	43.2	118.2
Milestones/License Fees - EU partners/distributors	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Milestones/License Fees - Kwang Dong (SK)				0.0	0.0	7.4	0.0	7.4	0.0	0.0	0.0	0.0	0.0	0.0
Others	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total Revenues	**3.4**	**3.4**	**55.5**	**4.4**	**5.2**	**10.0**	**20.1**	**39.6**	**5.5**	**5.7**	**6.0**	**44.9**	**62.0**	**154.0**
COGS	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
R&D	**73.7**	**56.7**	**57.4**	**11.2**	**15.1**	**8.8**	**9.1**	**44.3**	**12.6**	**12.6**	**13.6**	**13.6**	**52.3**	**46.3**
SG&A	**20.0**	**23.9**	**28.6**	**8.6**	**10.8**	**12.1**	**12.0**	**43.5**	**12.1**	**11.9**	**16.0**	**18.1**	**58.1**	**68.6**
Total Operating Expenses	**93.7**	**80.6**	**86.1**	**19.8**	**25.9**	**20.9**	**21.1**	**87.8**	**24.7**	**24.5**	**29.6**	**31.7**	**110.4**	**114.9**
Operating Income	**(90.2)**	**(77.2)**	**(30.5)**	**(15.5)**	**(20.7)**	**(10.9)**	**(1.0)**	**(48.1)**	**(19.2)**	**(18.8)**	**(23.6)**	**13.2**	**(48.5)**	**39.1**
Total Non-Operating Income	0.1	(0.5)	(7.0)	(1.8)	(1.8)	(0.2)	(1.8)	(5.5)	(1.7)	(1.7)	(1.7)	(1.7)	(6.7)	(6.8)
Pretax Income	(90.1)	(77.7)	(37.5)	(17.2)	(22.5)	(11.1)	(2.8)	(53.7)	(20.9)	(20.5)	(25.3)	11.5	(55.2)	32.3
Income tax expense	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.3
Net Income - Operations	**(90.1)**	**(77.7)**	**(37.5)**	**(17.2)**	**(22.5)**	**(11.1)**	**(2.8)**	**(53.7)**	**(20.9)**	**(20.5)**	**(25.3)**	**11.5**	**(55.2)**	**31.0**
Non-Recurring Gains (Losses)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net Income - Reported	**(90.1)**	**(77.7)**	**(37.5)**	**(17.2)**	**(22.5)**	**(11.1)**	**(2.8)**	**(53.7)**	**(20.9)**	**(20.5)**	**(25.3)**	**11.5**	**(55.2)**	**31.0**
Basic EPS	**($1.27)**	**($0.80)**	**($0.32)**	**($0.14)**	**($0.18)**	**($0.09)**	**($0.02)**	**($0.42)**	**($0.16)**	**($0.16)**	**($0.19)**	**$0.09**	**($0.42)**	**$0.23**
Diluted EPS	**($1.27)**	**($0.80)**	**($0.32)**	**($0.14)**	**($0.18)**	**($0.09)**	**($0.02)**	**($0.42)**	**($0.16)**	**($0.16)**	**($0.19)**	**$0.07**	**($0.42)**	**$0.18**

Source: RBC Capital Markets estimates

Valuation

In order to value OREX ($5/share), we use a sum-of-the-parts methodology and estimate the probability-adjusted NPV of the following: (1) Contrave royalties ($4.5/share) and (2) Orexigen's projected net cash position ($0.5/share).

Price target impediments

A slowdown in Contrave's US launch will negatively affect our price target. Other factors that can negatively influence our valuation include increased competition (considering that a fourth obesity drug, Saxenda, will now also enter the market), further delays in the EU launch, and unanticipated safety signals from use post-approval. Factors that can positively affect our valuation include increased investment in commercial infrastructure from Takeda that can lead to increased Contrave sales, and passing of any legislation that enforces Medicare reimbursement for obesity therapeutics.

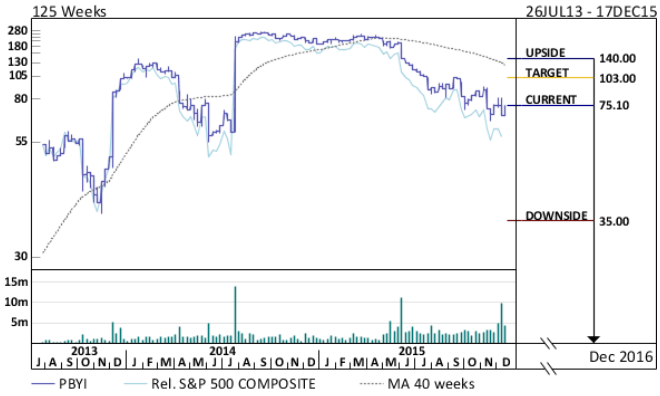
Puma Biotechnology, Inc (PBYI)

Outperform, Speculative Risk

Price Target USD $103.00

Target/Upside/Downside Scenarios

Exhibit 165: Puma Biotechnology, Inc



Source: RBC Capital Markets estimates

Target price/base case

We use a sum-of-the-parts methodology to value Puma shares at $103, and we estimate the probability adjusted NPV of the following: 1) the neratinib sales in HER2+ breast cancer ($101/ share); and 2) the company's projected net cash position ($2/ share). We have modeled neratinib to reach peak sales of $2.6B in 2026, with the majority of its sales coming from the extended adjuvant setting.

Upside scenario

Our upside scenario of $140 includes negative data from the ongoing APHINITY trial of pertuzumab, which is expected in 2016. We believe that a pertuzumab failure in the adjuvant setting in APHINITY would remove a significant overhang from the shares and could lead to more widespread adoption for neratinib in the extended adjuvant setting.

Downside scenario

Our downside scenario of $35 assumes significantly lower adoption of neratinib due to either higher than expected tolerability issues or Perjeta's approval in the adjuvant setting. Under these scenarios, we have modeled ~8% of the penetration rates of our base case scenario and reach peak WW sales of neratinib of $700MM.

Investment summary

Loperamide prophylaxis expected to help with neratinib's diarrhea issues: Despite investor concerns over the high incidence of Grade 3 diarrhea in the Phase III ExteNet trial, we believe that data from the Phase II loperamide prophylaxis trial, which are expected in 4Q:15, will show a significant decrease in the incidence of diarrhea to more acceptable levels.

This drug has a bad diarrhea profile, but prophylaxis seems to take care of that. Neratinib has an issue with diarrhea (~30% Grade 3) and seems to have been poorly developed by Pfizer. However, when high-dose loperamide prophylaxis is used, the incidence of Grade 3 diarrhea declines significantly. Moreover, the loperamide prophylactic regimen is only really in play for the first month of neratinib use, with patients taking loperamide thereafter as necessary. Oncologists we spoke with view it as "very manageable", especially for this patient population, which is "young and very motivated."

If approved, neratinib would be used, regardless of APHINITY. A lot has been made of Perjeta's upcoming APHINITY data. We believe that if approved, neratinib would be widely used, regardless of what happens with Perjeta, since neratinib would be the only drug approved for year 2 of adjuvant therapy, and thus not competing with Perjeta, which would only be used in year 1.

Other settings provide more upside to neratinib. Puma originally positioned neratinib as a contender for later lines of metastatic breast cancer. In addition to the third line, in which we believe neratinib to be a stronger agent than currently approved lapatinib, Puma is also testing neratinib in HER2- mutated breast cancer and other solid tumors with HER2 mutations. We believe these indications continue the neratinib story beyond the adjuvant HER2+ setting.

We think Alan goes 2-for-2 with his big cats and makes money for his investors. Alan Auerbach's strategy of developing underappreciated assets and selling companies is well underway at Puma. Based on what we've seen from Puma's first two years, we view an acquisition by a big biopharma as the most likely outcome, making it a successful second act for Puma's CEO.

Risks: 1) negative data from Phase II loperamide prophylaxis trial in 4Q:15; 2) regulatory setbacks; and 3) failure in ongoing trials. These risks, if they materialize, may result in significant volatility, and given that the majority of the value comes from a single product, lead to the Speculative Risk qualifier on our rating.

Key questions

	Our view
1. Will prophylactic loperamide lessen safety concerns?	**We believe that the drug's improved AE profile from the use of prophylactic loperamide, coupled with the unmet medical need in this space, will make diarrhea concerns less of an issue for neratinib.** Since Puma acquired the rights to neratinib, it has installed a prophylactic Imodium regimen to reduce the rate of Grade 3 diarrhea, from a historical incidence of around 30% in non-Puma-led trials to ~5-10% of patients, according to Puma now. If this reduction is consistently maintained in other Puma-led trials, we believe that this can adequately mitigate these safety concerns. Moreover, our KOLs indicate that the prophylactic regimen is "tough, but entirely extreme" and can make the diarrhea "manageable." Additionally, the high-dose 16 mg Imodium portion of the regimen only occurs on the first day of neratinib treatment, with Imodium tapering to 4 mg a day by the end of the first month.
2. What about the "upcoming competition" in the adjuvant setting?	**We do not foresee a serious issue if and when new therapies are approved for the adjuvant setting.** Data from the ongoing APHINITY and KAITLIN trials of Perjeta and Kadcyla in the adjuvant settings, with positive data questioned by some to pose a threat to neratinib, are expected in the next few years. However, the goal of these trials is to replace Herceptin as the only biologic agent used in the *first* year of adjuvant therapy. Neratinib is currently positioned to target the *second* year of adjuvant therapy. Therefore, we believe that neratinib would still be used in the second year of adjuvant treatment, even with the entry of Perjeta and Kadcyla into the first year treatment, since it would be the only drug approved for that setting, even if the treatment paradigm were to begin to shift.
3. How much is neratinib worth outside of the adjuvant breast cancer setting?	**Instead of focusing on 1st or 2nd line metastatic patients, where trials would be longer and where Perjeta and Kadcyla may be difficult to unseat, Puma is addressing later disease settings, starting with the 3rd line.** Here, the only major competition is Tykerb (lapatinib), which we do not view as much of a competitor, given its toxicity and weaker efficacy. We believe the 3rd line setting is worth around $580MM in peak WW sales, with another $230MM coming from the 4th line.
4. So, will Alan Auerbach do it again?	Puma has been mentioned in the press as a takeover target essentially since its founding, given the success President and CEO Alan Auerbach had with his previous company, Cougar, which was sold to J&J in 2009 for $1B. **Given the size of the market and the scarcity of active oncology assets, we would not be surprised to see him make biotech history and go 2-for-2 with his big cats.**

Exhibit 166: Puma's pipeline

Drug		Indication	Stage
Neratinib	Monotherapy	Extended adjuvant breast cancer (ExteNET)	Phase III
	Combo with Xeloda	Metastatic breast cancer (3rd-line) (PUMA-NER-1301)	Phase III
	Combo with Torisel	Metastatic breast cancer (4th-line)	Phase III
	Combo with chemo	Neoadjuvant breast cancer (NSABP FB-7)	Phase II
	Combo +/- Xeloda	Metastatic BC with brain metastases	Phase II
	Monotherapy	HER2 mutated solid tumors (Basket trial)	Phase II
	Combo +/- Torisel	HER2-mutated NSCLC	Phase II
	Monotherapy	HER2-mutated breast cancer	Phase II

Source: Company reports and RBC Capital Markets estimates

Exhibit 167: Puma's expected newsflow

Event	Drug	Timing
Publish Phase III ExteNET trial data	neratinib	4Q15
Publish results to date on use of loperamide prophylaxis	neratinib	4Q15
Expand additional cohorts in Basket Trial	neratinib	4Q15
Initial data from Ph II loperamide prophylaxis study	neratinib	4Q15
US/EU filing for regulatory approval	neratinib	1Q16
Complete Phase II trial in mBC patients with brain mets	neratinib	1H16
Ph III results of neratinib combo with Xeloda	neratinib	2H16
FDA decision on approval for neratinib	neratinib	YE16
Launch neratinib in US/EU	neratinib	2017

Source: Company reports and RBC Capital Markets estimates

Exhibit 168: PBYI quarterly P&L ($MM)

($MM)	FY 2011A	FY 2012A	FY 2013A	FY 2014A	Q1: 15A	Q2: 15A	Q3: 15A	Q4: 15E	FY 2015E	Q1: 16E	Q2: 16E	Q3: 16E	Q4: 16E	FY 2016E	FY 2017E
Neratinib															
Total WW Neratinib Sales	**0.0**	**0.0**	**0.0**	**0.0**	0.0	0.0	0.0	0.0	**0.0**	0.0	0.0	0.0	0.0	**0.0**	**375.7**
Total Revenue	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**375.7**
Cost of product sales	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**78.9**
SG&A	**9.3**	**24.8**	**9.8**	**19.4**	**7.9**	**5.5**	**8.8**	**8.4**	**30.6**	**8.0**	**8.3**	**8.4**	**8.3**	**33.0**	**88.7**
R&D	**0.8**	**49.6**	**45.0**	**122.9**	**44.7**	**59.4**	**51.9**	**59.0**	**215.0**	**58.0**	**59.0**	**57.0**	**57.8**	**231.8**	**215.0**
Total Operating Expenses	**10.2**	**74.5**	**54.8**	**142.3**	**52.6**	**64.9**	**60.7**	**67.4**	**245.6**	**66.0**	**67.3**	**65.4**	**66.1**	**264.8**	**382.6**
Operating income (loss)	**(10.2)**	**(74.5)**	**(54.8)**	**(142.3)**	**(52.6)**	**(64.9)**	**(60.7)**	**(67.4)**	**(245.6)**	**(66.0)**	**(67.3)**	**(65.4)**	**(66.1)**	**(264.8)**	**(6.8)**
Total other income	(0.1)	0.1	0.2	0.3	0.1	0.2	0.3	0.0	0.7	0.0	0.0	0.0	0.0	0.2	0.2
Pretax income	(10.2)	(74.4)	(54.7)	(142.0)	(52.5)	(64.7)	(60.4)	(67.4)	(245.0)	(66.0)	(67.3)	(65.4)	(66.1)	(264.6)	(6.7)
Income tax expense	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	(1.0)
Net income (loss)	**(10.2)**	**(74.4)**	**(54.7)**	**(142.0)**	**(52.5)**	**(64.7)**	**(60.4)**	**(67.4)**	**(245.0)**	**(66.0)**	**(67.3)**	**(65.4)**	**(66.1)**	**(264.6)**	**(5.7)**
Basic EPS	**($1.32)**	**($3.42)**	**($1.90)**	**($4.73)**	**($1.66)**	**($2.01)**	**($1.87)**	**($2.07)**	**($7.62)**	**($2.01)**	**($2.03)**	**($1.95)**	**($1.95)**	**($7.93)**	**($0.16)**
Diluted EPS	**($1.32)**	**($3.42)**	**($1.90)**	**($4.73)**	**($1.66)**	**($2.01)**	**($1.87)**	**($2.07)**	**($7.62)**	**($2.01)**	**($2.03)**	**($1.95)**	**($1.95)**	**($6.59)**	**($0.14)**

Source: Company reports and RBC Capital Markets estimates

Valuation

We use a sum-of-the-parts methodology to value Puma shares at $103, and we estimate the probability adjusted NPV of the following: 1) the neratinib sales in HER2+ breast cancer ($101/share); and 2) the company's projected net cash position ($2/share). We have modeled neratinib to reach peak sales of $2.6B in 2026, with the majority of its sales coming from the extended adjuvant setting. We also modeled its opportunities in the later settings of metastatic breast cancer to approach $800MM in peak sales.

Price target impediments

As the majority of Puma's value lies with the neratinib asset, and particularly in the adjuvant HER2+ breast cancer setting, any further delays to the filing timeline for neratinib would negatively affect our valuation. Other factors that can negatively influence our valuation include increased competition (from other HER2-targeted agents), regulatory setbacks, and lower than projected penetrations for neratinib. Factors that can positively affect our valuation include more favorable pricing, setbacks for competition, positive data from other settings within HER2+ breast cancer or other tumors, and M&A, which we have not included in our valuation.

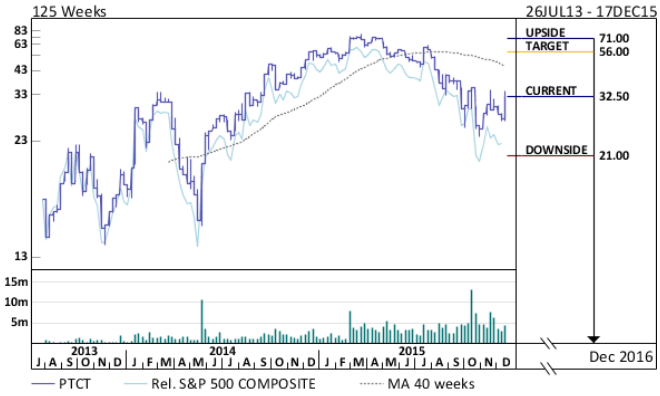
PTC Therapeutics, Inc. (PTCT)

Outperform, Speculative Risk

Price Target USD $56.00

Target/Upside/Downside Scenarios

Exhibit 169: PTC Therapeutics, Inc.



Source: RBC Capital Markets estimates

Target price/base case

We use a sum-of-the-parts methodology to value PTC Therapeutics shares at $56/share and estimate the probability-adjusted NPV of the following: (1) Translarna sales in DMD ($35/share); (2) Translarna sales in CF ($15/share); (3) RG7800 royalties in SMA ($3/share); and (4) the company's projected net cash position ($3/share).

Upside scenario

Our upside scenario of $71/share assumes 100% probability that ataluren is approved in the US and the drug remains on the market in Europe. We thus get to a $50/share value for the DMD program, $15/share value for the CF program, $3/share for the SMA program and $3/share in cash.

Downside scenario

Our downside scenario of $21/share assumes that the FDA does not approve Translarna for DMD in 2016. With the ACT CF trial still ongoing, there are slim, but still plausible chances that the confirmatory trial in CF works. By assigning a 20% probability of success for the Phase III trial in CF, we get to a $15/share value for the CF program, $3/share for the SMA program and $3/share in cash.

Investment summary

Translarna for DMD: approved in the EU, confirmatory trial fails. Translarna (ataluren), PTC Therapeutics' lead drug, has received conditional approval in the EU for DMD patients with nonsense mutations (nmDMD), and the initial launch got under way in December 2014. Translarna's confirmatory Phase III trial in nmDMD failed to meet its primary endpoint, but given the unmet medical need, we believe the FDA and EMA may still allow the drug on the market.

Larger CF opportunity for Translarna in question following Phase III failure in DMD. In addition to DMD, Translarna had also produced promising Phase III data in CF patients with nonsense mutations (nmCF). It is currently in the confirmatory Phase III ACT CF trial, with data expected YE:16. If positive, we expect the drug to be approved and see rapid adoption in the ~7,000 CF patients with nonsense mutations in the US/EU. We estimate peak US/EU sales in nmCF of ~$1.3B. However, ataluren's failure in the confirmatory Phase III trial in DMD makes us less hopeful that the drug will work in CF.

SMA program early but promising; currently on hold due to preclinical eye toxicity: RG7800 is an internally discovered small molecule in development for SMA (Spinal Muscular Atrophy) for which PTC has licensed WW rights to Roche. After promising POC data from a Phase I healthy subject trial, RG7800 entered the Phase Ib/IIa MOONFISH trial in November 2014. Dosing is currently on hold while eye toxicity observed in a preclinical study is being investigated. In addition to royalties and up to $450M in milestones, positive data here would provide further validation for PTC's research engine.

Risks: (1) slower than expected EU launch of Translarna in DMD; (2) delayed filing of Translarna in CF for conditional approval in the EU; (3) negative FDA news in DMD. These risks, if they materialize, may result in significant volatility, and given that the majority of the value comes from a single product, lead to the Speculative Risk qualifier on our rating. trials.

Key questions

Our view

1. If approved in the US, how restrictive will the Translarna labels for DMD be?

We believe the FDA will not restrict DMD patients based on ambulatory status or age. We also do not believe that caregivers or physicians will be willing to wait until a specific age indicated on the label to treat DMD patients, as physicians we have spoken with believe that earlier treatment is better. Additionally, we expect the DMD patient community to exert pressure on the FDA not to restrict based on ambulatory status, as there could be potential treatment benefits even after the loss of ambulation. In contrast, the current conditional approval for Translarna in the EU comes with label restrictions (patients ≥5 years old and who are still ambulatory). Considering that there are no other available treatments for DMD that is caused by nonsense mutations, we believe that EMA will eventually expand the label to include all nmDMD patients, regardless of age or ambulatory status, especially after safety results are available in pediatric DMD patients.

2. What will the competition be for Translarna in cystic fibrosis patients who have one nonsense mutation allele?

From our discussions with CF KOLs, we believe that most nonsense mutation CF patients would receive combination therapy, therefore removing the potential threat of competition for overlapping patient subpopulations. An estimated 10% of CF patients harbor a nonsense mutation, but that subpopulation can be further broken down into additional categories based on the mutation on the *second* allele. These combinations include another nonsense mutation (homozygous nonsense, ~10%), F508Δ (~70%), and G551D (~4%). The heterozygous G551D/nonsense CF patients may already be treated by Kalydeco. Although this assumes a direct competition, the CF doctors we spoke with indicate they would prefer to use both therapies for these patients, if possible. The F508Δ/nonsense heterozygote patients present a bigger uncertainty, especially given that Vertex's VX-661 trials have not yet read out. If anything is approved in the much larger F508Δ heterozygote patient group, the nonsense mutation/F508Δ group could theoretically be treated with either the F508Δ drug, with Translarna, or with both. Again, the CF KOLs we spoke with indicated that they would prefer to treat these patients with two drugs. Of course, in the end, a lot would depend on the strength of the data of the potential F508Δ drug and on the cost of the combined therapy.

3. What's up next for Translarna?

A number of investigator-led preclinical studies have already started testing Translarna in models of a number of other orphan disorders. Translarna is a small molecule targeting the ribosome to allow for read-through of premature stop codons. It is not specific to just the treatment of DMD or CF, but could be applicable to any genetic disorder underlined by a mutation resulting in a premature stop codon. Currently, Translarna's third proposed indication is MPS I, which could be just the start in a list of rare disorders that could expand the "Translarna pipeline".

Exhibit 170: PTC's pipeline

Drug candidate	Indication	Stage
Translarna (ataluren)	Nonsense mutation Duchenne muscular dystrophy (nmDMD)	Marketed in EU
	Nonsense mutation cystic fibrosis (nmCF)	Phase III
	Mucopolysaccharidosis type I (MPS I)	Phase II
RG7800	Spinal muscular atrophy (SMA)	Phase Ib/IIa
PTC596	Oncology (target: BMI1)	Phase I

Source: Company reports and RBC Capital Markets estimates

Exhibit 171: PTC expected newsflow

Event	Drug	Timing
Continue launch of Translarna for DMD in major EU countries	Translarna	4Q15
Complete enrollment in the Phase III nmCF trial	Translarna	YE15
Complete rolling NDA submission to FDA for Translarna in DMD	Translarna	YE15
Present ACT DMD trial data to EMA	Translarna	YE15
Initiate Phase II trial in aniridia	Translarna	YE15
Safety data for anti-bacterial gonorrhea program	anti-bacterial	4Q15
Resume clincal development in SMA program	SMA program	early 2016
EMA decision for Translarna in CF	Translarna	1H16
FDA regulatory decision for Translarna in DMD	Translarna	mid-2016
EU launch for Translarna in CF	Translarna	2H16
US launch for Translarna in DMD	Translarna	2H16
Top-line results from the Phase III ACT CF trial	Translarna	YE16
Results from the MPS I trial	Translarna	2016

Source: Company reports and RBC Capital Markets estimates

Exhibit 172: PTCT quarterly P&L ($MM)

($MM)	FY 2011A	FY 2012A	FY 2013A	FY 2014A	1Q:15A	2Q:15A	3Q:15A	4Q:15E	FY 2015E	1Q:16E	2Q:16E	3Q:16E	4Q:16E	FY 2016E	FY 2017E
Translarna sales in DMD	**0.0**	**0.0**	**0.0**	**0.7**	**5.1**	**6.2**	**9.8**	**12.6**	**33.6**	**15.0**	**18.0**	**21.7**	**34.9**	**89.6**	**164.4**
% increase (y/y)														*140%*	*31%*
Translarna sales in CF	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**4.0**	**11.7**	**15.7**	**144.4**
Total Translarna sales	**0.0**	**0.0**	**0.0**	**0.7**	**5.1**	**6.2**	**9.8**	**12.6**	**33.6**	**15.0**	**18.0**	**25.7**	**46.6**	**105.3**	**308.9**
Total RG7800 sales	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Total Royalties on RG7800 sales	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Collaboration revenue	99.0	28.8	31.3	22.2	0.3	0.2	0.0	0.0	0.5	0.0	0.0	0.0	30.0	30.0	25.0
Grant revenue	6.5	5.2	3.4	2.3	2.1	0.4	0.0	2.0	4.5	0.0	0.0	0.0	0.0	0.0	0.0
Total Revenues	**105.4**	**33.9**	**34.7**	**25.2**	**7.5**	**6.8**	**9.8**	**14.6**	**38.6**	**15.0**	**18.0**	**25.7**	**76.6**	**135.3**	**333.9**
COGS	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**1.3**	**1.3**	**1.5**	**1.8**	**2.6**	**4.7**	**10.5**	**30.9**
R&D	**58.7**	**46.1**	**54.9**	**79.8**	**27.9**	**28.2**	**30.6**	**31.6**	**118.4**	**32.4**	**34.1**	**32.9**	**34.4**	**133.8**	**147.7**
SG&A	**16.2**	**14.6**	**25.2**	**44.8**	**17.6**	**17.2**	**21.4**	**22.2**	**78.4**	**22.3**	**22.6**	**35.7**	**36.6**	**117.2**	**216.0**
Total Operating Expenses	**74.8**	**60.8**	**80.2**	**124.7**	**45.6**	**45.4**	**52.0**	**55.1**	**198.0**	**56.2**	**58.5**	**71.2**	**75.7**	**261.5**	**394.6**
Operating Income (loss)	**30.6**	**(26.8)**	**(45.5)**	**(99.4)**	**(38.1)**	**(38.6)**	**(42.2)**	**(40.5)**	**(159.4)**	**(41.2)**	**(40.5)**	**(45.5)**	**0.9**	**(126.3)**	**(60.8)**
Interest Expense/Income, Net	(2.4)	(1.2)	(6.1)	1.18	0.5	0.5	(0.9)	1.4	1.6	1.1	1.1	1.1	1.1	4.5	4.5
Other income, net	0.5	1.8	0.0	(0.2)	(0.4)	(0.1)	(0.1)	0.0	(0.5)	0.0	0.0	0.0	0.0	0.0	0.0
Net Income Before Taxes	**28.6**	**(26.2)**	**(51.6)**	**(98.4)**	**(37.9)**	**(38.2)**	**(43.1)**	**(39.1)**	**(158.3)**	**(40.1)**	**(39.4)**	**(44.3)**	**2.0**	**(121.8)**	**(56.3)**
Provision for Income Taxes	(2.3)	0.0	0.0	(4.7)	0.0	0.1	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net Income (Operations)	**30.9**	**(26.2)**	**(51.6)**	**(93.8)**	**(37.9)**	**(38.4)**	**(43.2)**	**(39.1)**	**(158.5)**	**(40.1)**	**(39.4)**	**(44.3)**	**2.0**	**(121.8)**	**(56.3)**
Non-recurring gains (charges)	0.0	159.6	(14.9)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net Income (Reported)	**30.9**	**133.3**	**(66.4)**	**(93.8)**	**(37.9)**	**(38.4)**	**(43.2)**	**(39.1)**	**(158.5)**	**(40.1)**	**(39.4)**	**(44.3)**	**2.0**	**(121.8)**	**(56.3)**
Basic EPS	**$23.95**	**$219.76**	**($5.18)**	**($2.97)**	**($1.15)**	**($1.14)**	**($1.27)**	**($1.14)**	**($4.70)**	**($1.16)**	**($1.13)**	**($1.26)**	**$0.06**	**($3.47)**	**($1.53)**
Diluted EPS	**$4.55**	**$42.50**	**($5.18)**	**($2.97)**	**($1.15)**	**($1.14)**	**($1.27)**	**($1.14)**	**($4.70)**	**($1.16)**	**($1.13)**	**($1.26)**	**$0.05**	**($3.47)**	**($1.53)**

Source: Company reports and RBC Capital Markets estimates

Valuation

We use a sum-of-the-parts methodology to value PTC Therapeutics shares at $56/share and estimate the probability-adjusted NPV of the following: (1) Translarna sales in DMD ($35/share); (2) Translarna sales in CF ($15/share); (3) RG7800 royalties in SMA ($3/share); and (4) the company's projected net cash position ($3/share).

Price target impediments

Slower than expected EU launch of Translarna in DMD. Ataluren is currently approved in the EU on a conditional basis. PTCT anticipates being granted full approval based upon results from the second Phase IIb trial. However, the recent failure of the Phase III trial in DMD may raise concerns about Translarna's efficacy with the EMA. Any delay in full approval and launch in the EU is likely to exert downwards pressure on shares of PTCT.

Negative FDA news in DMD. The Phase III DMD trial of Translarna missed its primary endpoint and showed significant treatment effects only in a subgroup of patients. This raises the possibility that the FDA may express concerns about the efficacy of Translarna. Moreover, if the FDA requests more data from either Sarepta or BioMarin regarding their NDA submission, or declines to approve either of their drugs, it would appear that the regulatory environment is changing, which could affect PTC in a negative way.

SMA Phase II trial continues to show safety signals. The Phase II trial (MOONFISH) would test the safety and tolerability of RG7800 in SMA patients. Preclinical studies of RG7800 showed effects on only a very small number of genes other than SMN2. The Phase I study demonstrated a good safety profile for the drug candidate. However, this trial is currently on clinical hold due to a pre-clinical occular toxicity safety signal arising in monkeys. If this hold continues it will likely exert negative pressure on PTC's collaboration with Roche and limit RG7800's potential.

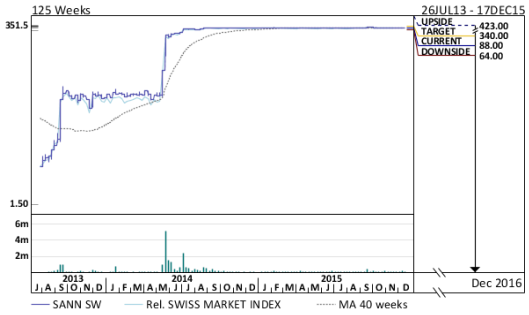
Santhera Pharmaceuticals Holding AG (SANN)

Outperform, Speculative Risk

Price Target CHF 340.00

Target/Upside/Downside Scenarios

Exhibit 173: Santhera Pharmaceuticals Holding AG



Source: RBC Capital Markets estimates

Target price/base case

We use a sum-of-the-parts methodology to value Santhera shares (CHF340/share) and estimate the probability adjusted NPV of the following: 1) the idebenone sales in DMD (CHF298/ share); 2) the idebenone sales in LHON (CHF30/share); and 3) the company's projected net cash position (CHF12/share). We model peak US/EU sales in 2025 of $873MM for idebenone in DMD and a probability of success of 75%.

Upside scenario

Our upside scenario of CHF423/share assumes that the market for idebenone/Raxone in DMD is higher than we had estimated. We have assumed that 40% of patients are currently not using steroids and would thus constitute the addressable DMD population for idebenone. If, however, this number turns out to be higher (50%) either by difference in actual steroid use or due to use of idebenone in patients that are currently taking steroids, the value of the DMD revenue stream would be CHF380 and the PT would move to CHF423.

Downside scenario

Our downside scenario of CHF64/share assumes that the FDA and EMA would request additional data and/or trials before Santhera can submit its applications for idebenone for DMD. This would delay its launch by two years and negatively affect its penetration rate. We have also reduced the probability of success of idebenone in DMD to 30% in both regions. We estimate that the probability adjusted NPV of the idebenone sales in DMD would be CHF41/share in this scenario.

Investment summary

The first pill to delay pulmonary decline in DMD patients, regardless of mutational status. Idebenone is an oral small molecule that targets the mitochondria and has been developed as a treatment for the respiratory dysfunction in DMD. It has produced positive Phase III data in DMD and Santhera plans to file for FDA approval in 4Q:15. If approved, it would be the first oral treatment applicable to all DMD patients, regardless of mutational status. This would allow idebenone to be used by a significantly larger patient population, without directly competing against other therapies. We estimate that it could reach ~$873MM in peak 2025 US/EU sales in this high unmet medical need space.

LHON market opportunity appears small but may have upside potential. In addition to DMD, idebenone has produced positive data in an additional disease setting. It was tested in the pivotal Phase II RHODOS trial in patients suffering from Leber's Hereditary Optic Neuropathy (LHON), which is a mitochondrial disease that leads to the loss of central vision, a form of blindness. The drug is currently being used in Europe under an Expanded Access Program and had received temporary approval in France. Santhera received EU marketing authorization in September 2015 following a positive CHMP opinion in June 2015. The company plans to market the drug on its own in the EU. The LHON experts we have spoken with believe that there could possibly be significantly more patients than the 500 new annual cases we have modeled. We view this scenario, of a higher than expected LHON market opportunity, as one way of providing upside to our current estimates. Finally, idebenone's mechanism of action on the mitochondria could potentially lend itself to applications in additional rare disease settings that may share similar mitochondrial-derived etiology.

An attractive takeover candidate: We believe that due to idebenone's EU approval for LHON and/or if it receives positive regulatory news in DMD, M&A may be a likely outcome. Santhera's very lean corporate structure may facilitate a potential takeover. Given the company's European presence and ties, we see an EU pharma as the most likely acquirer, but we would not exclude a company from the US or Japan.

Risks: 1) Delays to filing idebenone in DMD in US/EU; and 2) changing climate in DMD regulatory environment. These risks, if they materialize, may result in significant volatility, and given that the majority of the value comes from a single product, lead to the Speculative Risk qualifier on our rating.

Key questions

	Our view
1. As pulmonary function trials typically focus on FVC (forced vital capacity), will demonstrating significance in its primary endpoint (peak expiratory flow, PEF) be enough for idebenone in the eyes of the FDA?	**Although idebenone did not reach statistical significance in the FDA's preferred pulmonary endpoint, we expect Santhera to highlight that it met the primary endpoint and the totality of the data on improvements in all pulmonary endpoints to support its filing.** These would include the primary endpoint (PEF), FEV_1, FVC, and reduction in respiratory tract infection data that altogether demonstrate the benefit of idebenone on pulmonary functions in DMD patients. Since idebenone's 52-week Phase III trial showed a statistically significant treatment effect on FVC at intermediate time points, but not *at* 52 weeks, this strategy may be necessary as the FDA's industry guidance for DMD therapeutics views idebenone's primary endpoint, PEF, as a "*potentially useful measure*" and an "*exploratory pulmonary biomarker*" for DMD.
2. What other data will the FDA/EMA require? What regulatory paths are available for DMD?	**We expect Santhera to apply for FDA accelerated approval using PEF as an intermediate clinical endpoint.** However, this strategy entails concomitant data regarding either published or provided natural history studies examining PEF or other pulmonary endpoints. We believe idebenone can receive accelerated approval with its current dataset; however, a future natural history study of lung function in DMD patients may be a post-approval requirement. Under this scenario, company management indicates that a three- to five-year study looking at both respiratory and cardiac endpoints may be needed.
3. How big can the addressable DMD population be?	**We estimate the DMD population addressable by idebenone is at least 30% of all DMD patients.** Unlike other candidate DMD therapeutics, idebenone will not be restricted based on the patient's dystrophin mutation genotype. Instead, its only exclusion may be just patients who take steroids. We do not expect idebenone to replace steroids treatment in younger DMD patients, as steroids have other benefits outside of pulmonary function in that age group. However, in adolescents, steroids become less widely used due to side effects, and we believe idebenone can be beneficial for this patient population. We have initial estimates of 40% of current DMD patients not on steroids, but, we do see upside if a greater number of older patients switch from steroids to idebenone. We also expect patients ranging from 8-22 years of age to receive treatment, in order to preemptively treat (in the case of younger patients) and prolong any residual treatment benefit (in the case of older patients). We estimate this age group to comprise ~75% of the DMD population, by age. Therefore, we estimate idebenone can address at least 30% (=40%*75%) of DMD patients.

Exhibit 174: Santhera's pipeline

Drug candidate	Indication	Stage
Idebenone	Duchenne muscular dystrophy (DMD)	Phase III
	Leber's hereditary optic neuropathy (LHON)	Marketed in EU
	Primary progressive multiple sclerosis (PPMS)	Phase I/II
Omigapil	Congenital muscular dystrophy (CMD)	Phase I

Source: RBC Capital Markets and Company reports

Exhibit 175: Santhera's expected newsflow

Event	Drug	Timing
Next NDA meeting with FDA for idebenone	Idebenone	1Q16
Submit NDA for idebenone in DMD to FDA	Idebenone	1Q16
Submit application for idebenone in DMD to EMA	Idebenone	1Q16
EMA decision on idebenone DMD application	Idebenone	2H16
FDA decision on idebenone DMD NDA	Idebenone	2H16

Source: RBC Capital Markets and Company reports

Exhibit 176: SANN quarterly P&L (CHF MM)

(CHF MM)	FY 2011A	FY 2012A	FY 2013A	FY 2014A	1H:15A	2H:15E	FY 2015E	1H:16E	2H:16E	FY 2016E	FY 2017E
Total idebenone sales in DMD	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**51.4**	**51.4**	**208.8**
EU idebenone sales in LHON	**0.0**	**0.0**	**0.0**	**2.6**	**1.5**	**3.9**	**5.4**	**6.5**	**27.9**	**34.4**	**52.6**
Total idebenone sales	**3.3**	**3.5**	**1.3**	**2.6**	**1.5**	**3.9**	**5.4**	**6.5**	**79.3**	**85.8**	**261.5**
Other Revenue	0.0	0.0	0.0	0.0		0.3	0.3	0.2	0.2	0.4	0.3
Total Revenue	**3.3**	**3.5**	**1.3**	**2.6**	**1.5**	**4.2**	**5.6**	**6.7**	**79.5**	**86.2**	**261.8**
Other Operating Income	0.4	0.4	0.3	0.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0
COGS	**0.3**	**0.3**	**0.1**	**0.2**	**0.2**	**0.4**	**0.6**	**0.7**	**13.1**	**13.7**	**43.4**
R&D	**18.1**	**28.7**	**4.7**	**5.7**	**2.8**	**4.2**	**7.1**	**4.2**	**3.7**	**7.9**	**8.5**
SG&A	**12.3**	**5.9**	**4.0**	**4.7**	**4.5**	**6.0**	**10.5**	**17.0**	**21.3**	**38.3**	**42.6**
Other Operating Expenses - Total	0.1	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total Operating Expenses	**30.5**	**34.7**	**8.6**	**10.6**	**7.52**	**10.6**	**18.1**	**21.9**	**38.1**	**59.9**	**94.5**
Operating Income (Loss)	**(26.9)**	**(30.8)**	**(7.1)**	**(7.5)**	**(6.043)**	**(6.4)**	**(12.4)**	**(15.2)**	**41.4**	**26.3**	**167.2**
Financial Income	3.3	0.4	1.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Financial Expenses	(3.7)	(0.6)	(0.2)	(0.0)	(0.2)	0.0	(0.2)	0.0	0.0	0.0	0.0
Net Income Before Taxes	(27.5)	(31.3)	(5.8)	(7.5)	(6.2)	(6.4)	(12.6)	(15.2)	41.4	26.3	167.2
Provision for Income Taxes	0.3	0.2	(0.0)	0.002	(0.0)	0.0	(0.0)	0.0	0.0	0.0	13.4
effective tax rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*8%*
Net Income (Loss)	**(27.8)**	**(31.4)**	**(5.8)**	**(7.5)**	**(6.2)**	**(6.4)**	**(12.6)**	**(15.2)**	**41.4**	**26.3**	**153.9**
Basic EPS	**CHF -7.60**	**CHF -8.55**	**CHF -1.55**	**CHF -1.60**	**CHF -1.24**	**CHF -1.25**	**CHF -2.48**	**CHF -2.93**	**CHF 7.88**	**CHF 5.04**	**CHF 28.71**
Diluted EPS	**CHF -7.60**	**CHF -8.55**	**CHF -1.55**	**CHF -1.60**	**CHF -1.24**	**CHF -1.25**	**CHF -2.48**	**CHF -2.93**	**CHF 6.78**	**CHF 4.33**	**CHF 24.03**

Source: RBC Capital Markets estimates and Company reports

Valuation

We use a sum-of-the-parts methodology to value Santhera shares (CHF340/share) and estimate the probability adjusted NPV of the following: 1) the idebenone sales in DMD (CHF298/share); 2) the idebenone sales in LHON (CHF30/share); and 3) the company's projected net cash position (CHF12/share). We model peak US/EU sales in 2025 of $873MM for idebenone in DMD and a probability of success of 75%.

Price target impediments

The EMA or FDA requests more data before Santhera can submit its application for DMD. Although idebenone is the only drug so far to have met its primary endpoint in a Phase III

trial in DMD, questions regarding regulatory approval remain, as Santhera has just started conversations with the FDA. In its industry draft guidance, the FDA considers peak expiratory flow, the primary endpoint used in idebenone's Phase III trial, as an exploratory endpoint without contemporary natural history data. If either the EMA or FDA requests more data, it would delay the timeline for idebenone approval and launch.

Commercial launch of idebenone in DMD is delayed or not as successful as expected. Santhera only has limited sales experience in marketing therapeutics. To successfully launch idebenone in DMD without a partnership, significant investment, commercial infrastructure, and industry experience are required, which Santhera needs to establish quickly. A slower uptake in DMD would impact the largest revenue stream for Santhera.

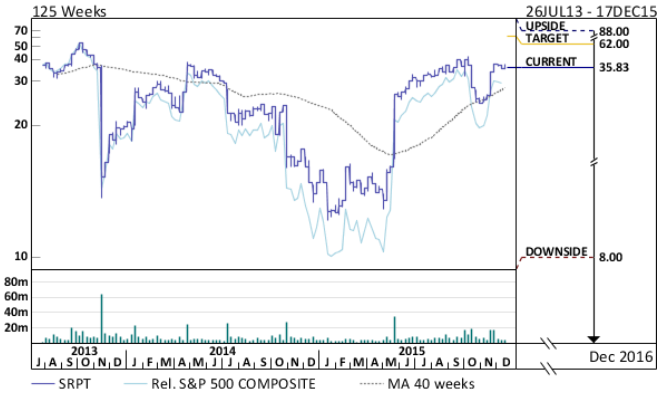
Sarepta Therapeutics, Inc. (SRPT)

Outperform, Speculative Risk

Price Target USD $62.00

Target/Upside/Downside Scenarios

Exhibit 177: Sarepta Therapeutics, Inc.



Source: RBC Capital Markets estimates

Target price/base case

We use a sum-of-the-parts methodology to value Sarepta shares at $62, and we estimate the probability adjusted NPV of the following: (1) the eteplirsen sales DMD ($19/share); (2) SRP-4053 sales DMD ($10/share); (3) SRP-4045 sales DMD ($10/share); (4) follow-on exons sales DMD ($16/share); and (5) the company's projected net cash position ($7/share).

Upside scenario

Our upside scenario of $88/share assumes positive clinical trial results for Sarepta's exon-skipping DMD drugs. Our upside scenario assumes approval in the US and the EU for eteplirsen ($25/share). It also assumes an 80% POS in both the US and EU for SRP-4053 ($13/share) and an 80% POS in both the US and EU for SRP-4045 ($16/share). For the follow-on exons, our upside scenario assumes a 70% POS in both the US and EU ($28/share).

Downside scenario

Our downside scenario of $8/share assumes that the FDA would issue a CRL and request more data in order to approve eteplirsen. Thus, Sarepta would have to wait for readout from the eteplirsen Phase III trial and push commercial launch out to 2018. This would give drisapersen, if approved, more opportunity to gain market share and limit the market potential of eteplirsen. Our downside scenario also assumes negative clinical trials results for SRP-4053, SRP-4045, and the follow-on exon DMD drugs.

Investment summary

We believe the NDA dataset revealed at World Muscle Society (WMS), albeit not perfect, is a significant improvement over prior iterations and should lead to eteplirsen's accelerated approval: DMD is a devastating disease affecting young boys and their families, and the FDA has been working closely with companies, including Sarepta, and we believe the agency is under significant pressure to approve a drug for these patients soon. Despite the known question marks, especially around the drug's efficacy, given the small dataset and questions about the reliability and reproducibility of dystrophin as an endpoint, given the dataset that Sarepta has put together in the NDA, including eteplirsen's apparent benign safety profile and the significant pressure by patient advocacy groups, we believe the eteplirsen NDA will end up getting approved.

Sarepta vs. BioMarin: who has the better drug? BioMarin's acquisition of Sarepta's direct competitor, Prosensa, is a key point to consider. Among the many similarities between the two drugs are their mechanisms of action and the fact that both companies have looked at different cuts of the data where their drug looks better. Sarepta points to drisapersen's failed Phase III trial and AE profile and argues that "they don't make dystrophin". Prosensa countered by pointing to the small size of Sarepta's most advanced trial and that the FDA recently casted doubts on its dystrophin measurement methodology. Additional issues include IP, regulatory expertise, commercial execution, first to market, etc. In most of these, the nod would have to go to BioMarin, given its track record and reputation as one of the top rare disease companies. On the other hand, despite a lot of the controversy, Sarepta has garnered a lot of institutional expertise on DMD, especially in dealing with FDA. So, we don't necessarily see a clear winner between the two yet and believe a lot of this could play out at the FDA AdComs, where we will get a clearer understanding of the FDA's views on these agents and where a lot of the clinical questions will have to be addressed.

Risks: (1) Additional data requested by FDA for approval; (2) Competitor's milestone in regulatory filing, approval, and launch. These risks, if they materialize, may result in significant volatility, and, given that the majority of the value comes from a single product, lead to the Speculative Risk qualifier on our rating.

Key questions

		Our view
1.	**In light of drisapersen's recent advisory committee, what are eteplirsen's odds with the FDA?**	**FDA panel clearly not convinced drisapersen works: this could open the door for eteplirsen to get through based on its impact on dystrophin and its clean safety profile.** The recent FDA panel on drisapersen raised serious questions about the drug's approvability, including about its mechanism of action, based on the lack of an impact on dystrophin. In addition, the well-designed and executed but failed Phase III trial, cast serious doubt on the data seen in the first, smaller Phase II trial. Finally, the drug's safety profile was highlighted as a serious issue for the drug. At the very least, we believe this leaves the door open for Sarepta's eteplirsen to get to the market as a drug which may have not met the traditional burden of clinical proof for approval (i.e. a successful large randomized clinical trial), but with enough evidence, mainly in the form of its dystrophin data, coupled with a benign safety profile, to allow it to get to the market.
2.	**Can eteplirsen really get approved with only 12 patients worth of data?**	**The mixed quality of drisapersen's dataset, coupled with the agency's willingness to be flexible, can help eteplirsen get there.** New Sarepta management has been very smart to listen to the agency and "respect the process": they have used a historical control to match their 12-patient study, they followed the FDA's guidance regarding dystrophin, and they have started their confirmatory trial. We believe there's many ways that the FDA can poke holes in the 201/202 6MWT dataset if they want to (small, uncontrolled, etc). However, we believe that the efficacy, and more importantly, the safety and dystrophin data from 201/202 dataset is what can help make the difference for eteplirsen. Finally, even though many investors think of just the 12-patient 201/202 study, Sarepta actually submitted 114 patients worth of safety data in its NDA, many coming from its ongoing confirmatory trial.
3.	**How will the FDA view Sarepta's dystrophin data?**	**We believe this could be the key factor to eteplirsen's approval, especially given the obvious absence of a large clinical dataset.** We believe that the FDA understands the unmet medical need in DMD and wants to give this patient community a treatment option. We also believe that the FDA is unconvinced drisapersen really works (failed trials, lack of impact on dystrophin). Some of the discussion at the recent adcom focused on the small % changes in dystrophin expression (single digits). This is a favorable comparison for eteplirsen, whose dystrophin dataset appears significantly more robust, in terms of number of methods tested (RT-PCR, dystrophin-positive fibers, western blot; rescoring of prior biopsies; following FDA's guidance in every step along the way) and fold-difference between treated/untreated samples etc.
4.	**How will the IP dispute with Prosensa/BioMarin play out?**	**In the EU, we do not expect Sarepta to win its appeal of the prior decision to grant Prosensa/BioMarin's patent claims on exon 51 skipping agents.** Under this scenario, we expect Sarepta to seek a licensing deal from and pay royalties to Prosensa/BioMarin in order to launch eteplirsen in the EU. In the US, Sarepta is in similar IP interference proceedings with Prosensa. Before a final decision from the patent appealing process is reached, Sarepta can still market eteplirsen in the US. However, losing the US court decision and appeal would leave it in the same IP predicament as it is in the EU.

Exhibit 178: Sarepta's pipeline

Drug candidate	Indication	Stage
Eteplirsen	DMD Exon 51 skipping	Phase III
SRP-4053	DMD Exon 53 skipping	Phase III
SRP-4045	DMD Exon 45 skipping	Phase III
SRP-4050	DMD Exon 50 skipping	Preclinical
SRP-4044	DMD Exon 44 skipping	Preclinical
AVI-7288	Marburg virus	Phase I
AVI-7537	Ebola virus	Phase I
AVI-7100	H1N1 Influenza virus	Phase I

Source: RBC Capital Markets and Company reports

Exhibit 179: Sarepta expected newsflow

Event	Drug	Timing
Meet with EMA to discuss 4th biopsy and 192-wk eteplirsen data	eteplirsen	4Q15
Full enrollment of Study 301 (PROMOVI) confirmatory trial	eteplirsen	4Q15
Complete enrollment for both phases of Study 4053-101 in EU	SRP-4053	4Q15
Tentatively scheduled FDA advisory panel	eteplirsen	January 22, 2016
Eteplirsen PDUFA date	eteplirsen	Feburary 26, 2016
Start Phase 3 study 4045-301	SRP-4045 and SRP-4053	Early 2016
Launch eteplirsen in the US	eteplirsen	1H16
Submit MAA for eteplirsen	eteplirsen	2016
Data from eteplirsen Phase III PROMOVI trial	eteplirsen	2016

Source: RBC Capital Markets estimates and Company reports

Exhibit 180: SRPT quarterly P&L ($MM)

($MM)	FY 2011A	FY 2012A	FY 2013A	FY 2014A	1Q:15A	2Q:15A	3Q:15A	4Q:15E	FY 2015E	1Q:16E	2Q:16E	3Q:16E	4Q:16E	FY 2016E	FY 2017E
Eteplirsen sales in US	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	28.0	78.8	106.8	201.3
Eteplirsen sales in EU	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	41.0
Total product sales	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**28.0**	**78.8**	**106.8**	**242.3**
Revenue from research contracts and other sources	47.0	37.3	14.2	9.8	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total Revenue	**47.0**	**37.3**	**14.2**	**9.8**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**28.0**	**78.8**	**106.8**	**242.3**
COGS	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**5.6**	**15.8**	**21.4**	**52.6**
R&D	**66.9**	**52.4**	**72.9**	**94.2**	**39.2**	**29.2**	**36.7**	**35.8**	**140.8**	**35.6**	**36.6**	**35.2**	**35.8**	**143.1**	**153.1**
SG&A	**16.1**	**14.6**	**31.6**	**49.3**	**22.7**	**12.9**	**15.1**	**13.0**	**63.7**	**13.6**	**19.8**	**21.0**	**21.2**	**75.6**	**100.0**
Total Operating Expenses	**82.9**	**67.0**	**104.5**	**143.5**	**61.9**	**42.1**	**51.8**	**48.8**	**204.5**	**49.2**	**56.4**	**61.8**	**72.8**	**240.1**	**305.6**
Operating Income (Loss)	**(35.9)**	**(29.7)**	**(90.3)**	**(133.8)**	**(61.9)**	**(42.1)**	**(51.8)**	**(48.8)**	**(204.5)**	**(49.2)**	**(56.4)**	**(33.8)**	**6.1**	**(133.3)**	**(63.3)**
Interest income and other, net	0.6	0.4	0.3	0.8	0.3	0.3	(0.2)	(0.1)	0.3	(0.2)	(0.2)	(0.2)	(0.2)	(0.8)	(0.8)
Loss on change in warrant valuation	33.0	(91.9)	(22.0)	(2.8)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net Income Before Taxes	(2.3)	(121.3)	(112.0)	(135.8)	(61.6)	(41.9)	(51.9)	(48.9)	(204.2)	(49.4)	(56.5)	(34.0)	5.9	(134.0)	(64.1)
				(0.1)											
Other comprehensive income	0.0	0.0	0.0	(0.1)	0.0	0.0	0.0	0.0	0.0	(0.2)	(0.2)	(0.2)	(0.2)	(0.8)	(0.8)
Provision for Income Taxes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net Income After Taxes	**(2.3)**	**(121.3)**	**(112.0)**	**(135.9)**	**(61.6)**	**(41.9)**	**(51.9)**	**(48.9)**	**(204.2)**	**(49.6)**	**(56.7)**	**(34.2)**	**5.7**	**(134.8)**	**(64.9)**
Basic EPS	**($0.11)**	**($5.14)**	**($3.31)**	**($3.40)**	**($1.49)**	**($1.01)**	**($1.25)**	**($1.09)**	**($4.83)**	**($1.10)**	**($1.25)**	**($0.75)**	**$0.12**	**($2.96)**	**($1.38)**
Diluted EPS	**($0.11)**	**($5.14)**	**($3.31)**	**($3.40)**	**($1.49)**	**($1.01)**	**($1.25)**	**($1.09)**	**($4.83)**	**($1.10)**	**($1.25)**	**($0.75)**	**$0.10**	**($2.96)**	**($1.38)**

Source: Company reports and RBC Capital Markets estimates

Valuation

We use a sum-of-the-parts methodology to value Sarepta shares at $62, and we estimate the probability adjusted NPV of the following: (1) the eteplirsen sales DMD ($19/share); (2) SRP-4053 sales DMD ($10/share); (3) SRP-4045 sales DMD ($10/share); (4) follow-on exons sales DMD ($16/share); and (5) the company's projected net cash position ($7/share).

Price target impediments

FDA continues to question the validity of dystrophin expression measurement. In October 2014, due to concerns about the reproducibility of the dystrophin positive fibers, the FDA requested an independent assessment, among other things. If the FDA continues to question Sarepta's dystrophin expression data, then the likelihood of approval for eteplirsen would be greatly reduced.

Royalty cost to be paid by Sarepta is significantly higher. The licensing negotiation between Sarepta and Prosensa/BioMarin could yield a higher royalty rate, forcing Sarepta to pay more. In addition, the patent interference proceedings and appealing process in the US between Sarepta and Prosensa/BioMarin regarding exon 51 skipping products could end earlier, which would require Sarepta to pay royalties earlier as well.

High manufacturing cost of eteplirsen continues to take its toll on finances. Company management has commented that the manufacturing cost of eteplirsen is high and has accounted for a large proportion of overall operation expenses. Because Sarepta has started or is going to start 5 trials (3 for eteplirsen) with more than 200 patients in those trials, the cost of making drugs needed in the trials will significantly increase, compared to current drug expenses. This could consume Sarepta's cash reserve quickly and exert pressure on its cash flow

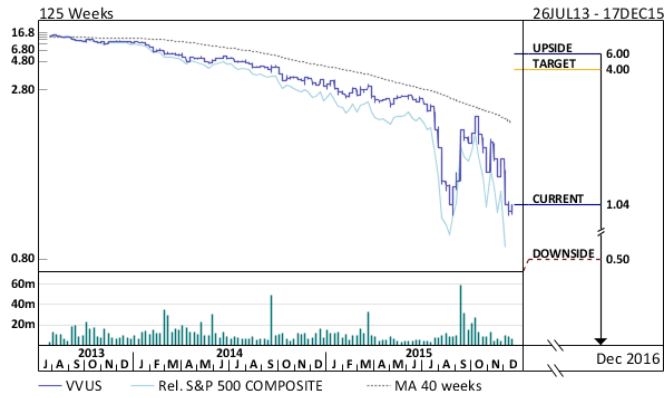
Vivus, Inc. (VVUS)

Outperform, Speculative Risk

Price Target USD $4.00

Target/Upside/Downside Scenarios

Exhibit 181: Vivus, Inc.



Source: RBC Capital Markets estimates

Target price/base case

In order to value VVUS shares at $4, we use a sum-of-the-parts methodology, and estimate the probability-adjusted NPV of the following: 1) the value of Qsymia's revenues ($2/share), 2) the value of the Stendra royalties ($2/share), and 3) the company's projected net cash position ($0/share). Our base case assumes that Vivus will enter into a partnership to copromote Qsymia, starting in 2016, and Qsymia to enter the EU market in 2018.

Upside scenario

Our upside scenario of $6/share includes more favorable economics on the US and EU commercialization collaboration agreements than what we have conservatively modeled. In addition, incremental positive news from the European regulatory process for Qsiva would increase the probability of success to 60%. Combined with increases in royalty rates and lower tiers to achieve the modeled rates in our base case, this would add $2/share to VVUS value.

Downside scenario

Lower than expected sales of Qsymia and/or Stendra, in addition to the lack of commercial partner for US marketing of Qsymia could lead to further price erosion. Continued overhang without any solution to the CVOT, the generic threat, and an additional year without a large pharma partner would lead to a slower ramp in sales, resulting in a valuation of $0.50/ share for VVUS.

Investment summary

Qsymia has great efficacy, but it gets minimal commercial support, and the obesity space is taking much longer than expected to develop. The consensus from our work in the obesity space is that Qsymia has very strong efficacy and an acceptable safety profile. We believe that VVUS can benefit from the changing dynamics of the obesity market: the doubling of the number of drugs on the market and the more-than-doubling in the number of sales reps, as increasing physician and patient awareness eventually should benefit the best drugs in the space.

Promoting a drug with 50 sales reps in an arena where it's hard to get traction with 900 reps is clearly not sustainable. In contrast to the former regime, the new board and management team, which really understand pharma detailing, appear more open to a partnership. The recent decision to settle with J&J simultaneously removed at least a part of the IP overhang for investors and should also help on the partnership front. However, there is either no partner out there for Qsymia or none at acceptable terms.

Stendra/Spedra is still early in its launch phase, but hoping it can do better: Vivus has partnered Stendra with Endo (US), Menarini (EU) and Sanofi (some ROW regions). The $4.5B WW ED space is split between Viagra and Cialis, with Levitra getting 10% of the market. We view Stendra as the only one of these agents with a differentiated profile, given the recent 15 min onset of action label expansion, which should help it capture ~$500MM in WW sales by 2018 and worth ~$2/share in royalties for Vivus.

Despite all the problems and the risk, current levels appear attractive. Despite the multiple issues facing the company, we consider shares at current levels as undervalued. Vivus has faced and continues to face a number of issues and hurdles. However, we believe that: 1) these are mostly in the stock, and 2) current levels represent a decent entry point into the story, with an attractive risk/reward ratio.

Risks: 1) Lack of recovery in Qsymia sales; 2) slowdown in reimbursement progress; 3) inability to secure a pharma partner; 4) negative news on IP front. These risks, if they materialize, may result in significant volatility, and the fact that the majority of the value comes from a single product, leads to the Speculative Risk qualifier on our rating.

Key questions

Our view

1. Is there a *real* obesity market out there?

We believe that the answer is Yes, but the market is still in the process of being built. To say that the first two years of sales for Qsymia have been a disappointment would be both stating the obvious and a major understatement. However, we believe that judging the obesity market opportunity by what has transpired thus far would be premature. This is a market that *not only* did not exist two years ago, but in its prior iteration was inhabited by drugs that were subsequently pulled off the market due to serious safety concerns.

2. What will it take to get Qsymia scripts up?

Partnership, partnership, partnership…and more time for the market to develop (i.e., physician and patient awareness/education and reimbursement). We believe in this agent, but also see the need for a commercial partner for Qsymia. Qsymia scripts have been flat, and we do not expect them to grow meaningfully near term. The market needs time to grow and Qsymia would significantly benefit by the commercial presence provided by a pharma partner.

3. Well, then….is there a partner out there for Qsymia and if yes, why hasn't Vivus done a partnership yet?

Yes, we expect a pharma partner for Qsymia to eventually step up. A number of factors have contributed to the lack of a partnership, including the following: **1)** the historical issues of the obesity space; **2)** Vivus' prior management team was not willing to do a partnership, and throughout 2013 Vivus management was either defending itself from a takeover or was just getting used to their new role; and **3)** questions around Qsymia's IP, especially regarding the Shank patents. We view the pick-up in Belviq scripts in response to the increases in Eisai's sales force and the effective-thus-far Contrave launch as positive signals that the obesity market can respond to extra detailing.

4. How will the increased competition from Contrave and Saxenda affect Qsymia?

We expect this type of "competition" to be good for Qsymia. Takeda recently launched Contrave with 900 reps. We believe that even though some patients may initially be "taken away", two key factors make the Contrave threat less of an issue. First, Takeda is targeting a lot of non-obesity writers. This isn't the case for the Vivus salesforce, since its strategy is to initially focus on high prescribers of obesity agents. Second, we believe that the flooding of the space with sales reps educating physicians about Contrave and Saxenda, but also about the benefits of pharmacotherapy, will eventually help Qsymia, albeit with a short lag period, since it will help raise awareness about the obesity space overall, and will help "crack the door open" for the Vivus reps to come in with their pitch, especially after a patient has failed to lose weight with one of the other therapies.

Exhibit 182: Vivus' pipeline

Drug (Target)	Indication	Stage
Qsymia	Chronic weight management	Marketed
Stendra (PDE5)	Erectile dysfunction (ED)	Marketed

Source: RBC Capital Markets and Company reports

Exhibit 183: Vivus expected newsflow

Event	Drug	Timing
Initiate AQCLAIM CVOT trial	Qsymia	2016
Partnership for Qsymia	Qsymia	2016
Interim results from AQCLAIM CVOT trial	Qsymia	2017

Source: RBC Capital Markets estimates and Company reports

Exhibit 184: VVUS quarterly P&L ($MM)

($MM)	FY 2012A	FY 2013A	FY 2014A	Q1: 15A	Q2: 15A	Q3: 15A	Q4: 15E	FY 2015E	Q1: 16E	Q2: 16E	Q3: 16E	Q4: 16E	FY 2016E	FY 2017E
Total Qsymia revenue to VVUS	**2.0**	**23.7**	**45.3**	**12.6**	**14.0**	**14.0**	**13.6**	**54.3**	**14.5**	**15.5**	**16.5**	**16.7**	**63.2**	**58.5**
Stendra revenues	**0.0**	**57.4**	**68.9**	**19.5**	**9.0**	**10.9**	**5.6**	**45.0**	**3.8**	**4.6**	**5.5**	**46.8**	**60.6**	**80.5**
Total Qsymia and Stendra revenues	**2.0**	**81.1**	**114.2**	**32.2**	**23.0**	**24.9**	**19.2**	**99.3**	**18.3**	**20.1**	**22.0**	**63.6**	**123.9**	**139.0**
Milestones/License Fees - Qsymia - US partner	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	50.0
Milestones/License Fees - Qsymia - EU partner	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	50.0
Net product revenue	2.0	25.2	45.3	12.6	14.0	14.0	13.6	54.3	14.5	15.5	16.5	16.7	63.2	48.8
License and milestone revenue	0.0	55.8	38.6	11.6	0.0	0.0	0.0	11.6	0.0	0.0	0.0	40.0	40.0	145.0
Supply revenue	0.0	0.0	26.5	8.5	8.1	10.1	2.0	28.7	0.0	0.0	0.0	0.0	0.0	0.0
Royalty revenue	0.0	0.0	3.8	(0.5)	0.9	0.9	3.6	4.8	3.8	4.6	5.5	6.8	20.6	45.2
Total Revenues	**2.0**	**81.1**	**114.2**	**32.2**	**23.0**	**24.9**	**19.2**	**99.3**	**18.3**	**20.1**	**22.0**	**63.6**	**123.9**	**239.0**
Cost of Goods Sold	**0.2**	**4.9**	**33.4**	**9.9**	**9.9**	**11.8**	**6.5**	**38.1**	**5.0**	**5.8**	**6.6**	**7.6**	**25.0**	**21.8**
R&D	**32.1**	**29.7**	**13.8**	**2.7**	**2.6**	**1.5**	**2.8**	**9.6**	**6.3**	**7.2**	**6.3**	**6.3**	**26.1**	**32.0**
SG&A	**109.7**	**158.2**	**111.5**	**26.4**	**22.2**	**17.1**	**16.5**	**82.2**	**16.0**	**16.0**	**16.4**	**15.7**	**64.1**	**62.0**
Total Operating Expenses	**141.9**	**235.7**	**164.9**	**39.0**	**64.2**	**33.0**	**25.8**	**161.9**	**27.3**	**29.0**	**29.3**	**29.6**	**115.2**	**115.8**
Operating Income	**(139.9)**	**(154.6)**	**(50.7)**	**(6.8)**	**(41.2)**	**(8.0)**	**(6.6)**	**(62.6)**	**(9.0)**	**(8.9)**	**(7.3)**	**33.9**	**8.7**	**123.2**
Total Non-Operating Income	0.2	(20.2)	(32.6)	(8.6)	(8.1)	(8.1)	(8.6)	(33.5)	(4.0)	(4.0)	(4.0)	(4.0)	(15.8)	(15.8)
Pretax Income	(139.7)	(174.8)	(83.3)	(15.5)	(49.3)	(16.1)	(15.2)	(96.1)	(13.0)	(12.8)	(11.3)	30.0	(7.1)	107.4
Income tax expense (benefit)	0.0	0.1	(0.6)	0.0	0.0	0.0	0.0	0.0	0.0	(0.4)	0.0	1.5	1.1	4.3
Net Income - Operations	**(139.7)**	**(174.9)**	**(82.6)**	**(15.5)**	**(49.4)**	**(16.1)**	**(15.2)**	**(96.1)**	**(13.0)**	**(12.4)**	**(11.3)**	**28.5**	**(8.2)**	**103.1**
Non-Recurring Gains (Losses)	(0.1)	0.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net Income - Reported	**(139.9)**	**(174.5)**	**(82.6)**	**(15.5)**	**(49.4)**	**(16.1)**	**(15.2)**	**(96.1)**	**(13.0)**	**(12.4)**	**(11.3)**	**28.5**	**(8.2)**	**103.1**
Basic EPS	**($1.42)**	**($1.72)**	**($0.80)**	**($0.15)**	**($0.48)**	**($0.15)**	**($0.15)**	**($0.92)**	**($0.12)**	**($0.12)**	**($0.11)**	**$0.27**	**($0.08)**	**$0.95**
Diluted EPS	**($1.42)**	**($1.72)**	**($0.80)**	**($0.15)**	**($0.48)**	**($0.15)**	**($0.15)**	**($0.92)**	**($0.12)**	**($0.12)**	**($0.11)**	**$0.25**	**($0.08)**	**$0.89**

Source: Company reports and RBC Capital Markets estimates

Valuation

In order to value VVUS shares at $4, we use a sum-of-the-parts methodology, and estimate the probability-adjusted NPV of the following: 1) the value of Qsymia's revenues ($2/share), 2) the value of the Stendra royalties ($2/share), and 3) the company's projected net cash position ($0/ share). Our base case assumes that Vivus will enter into a partnership to co-promote Qsymia, starting in 2016, and Qsymia to enter the EU market in 2018.

Price target impediments

Any further delay to secure a commercial partner to co-promote Qsymia would negatively affect our price target. Other factors that can negatively influence our valuation include increased competition (considering that a fourth obesity drug Saxenda has now entered the market); lower than projected penetrations for Qsymia; and unanticipated safety signals coming from the CVOT trial. Factors that can positively affect our valuation include increased investment in commercial infrastructure that can lead to more Qsymia sales, better than anticipated upfront payment and economics for the co-promote partnership for Qsymia program, and passing of any legislation that enforces Medicare reimbursement for obesity therapeutics.

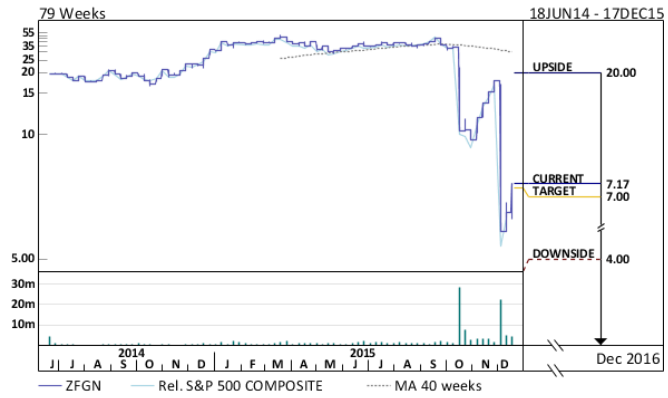
Zafgen, Inc. (ZFGN)

Sector Perform, Speculative Risk

Price Target USD $7.00

Target/Upside/Downside Scenarios

Exhibit 185: Zafgen, Inc.



Source: RBC Capital Markets estimates

Target price/base case

We currently value ZFGN shares at $7/share, which are around the company's net cash position. We expect shares to remain range-bound near-term ahead of Phase III data as investors will not assign significant value to the beloranib program given the recent deaths in the Phase III PWS trial until the drug's safety profile has been cleared by the data.

Upside scenario

Our upside scenario of $20/share assumes the lifting of the partial clinical hold, which would lessen investors' concerns about the drug's role in contributing to the thromboembolic events observed in the trial.

Downside scenario

The downside scenario of $4/share assumes that the company decides to terminate development of beloranib and wind down operations.

Investment summary

With the recent safety concerns notwithstanding, beloranib has been a really impressive injectable drug for obesity… Beloranib acts via a novel mechanism of action to lead to rapid and impressive weight loss in the obese patients it has been tested on in early stage Phase I and II trials. Using a novel mechanism different from the ones used by other drugs currently on the market, this methionine aminopeptidase 2 (MetAP2) inhibitor leads to significant weight loss (up to 10% of body weight) in just 12 weeks.

…but it is not intended to get to the market for obesity first: Despite beloranib's impressive efficacy, Zafgen has decided to try a different approach and not go with obesity as its lead indication for this drug. If successful, this would possibly allow the drug to reach market faster, in addition to gaining other benefits along the way, including premium pricing.

Prader-Willi Syndrome (PWS): a rare, genetic, obesity-related disease. There are an estimated 21,000 PWS cases in the US, with 7,500 of them identified. PWS patients are characterized by hyperphagia, the inability to feel satiety, which leads them to overeat and (most) to become obese. After promising data from a 17-patient Phase II trial, Zafgen is testing the drug in the bestPWS Phase III trial, with data expected 1Q:16. A second trial to be conducted in Europe is expected to start after completion of bestPWS, and will be required for US and EU approval. Based on the efficacy observed thus far, we expect the drug to be approved. Zafgen plans to market beloranib on its own, via a specialty salesforce, and we project that it can become a significant product in PWS alone, reaching $750MM in peak US/EU 2029 sales.

HIAO doubles beloranib's commercial potential: In early 2015, Zafgen reported positive data from a 14-patient, Phase II trial of beloranib in patients with hypothalamic injuryassociated obesity (HIAO). These patients develop obesity due to uncontrollable hunger, somewhat akin to an "acquired PWS", following surgery to remove craniopharyngiomas. Positive data in this setting would make HIAO the 2nd rare disease indication for beloranib, doubling its market potential.

Risks: 1) Sustained clinical hold leading to extended delays in PWS trials; 2) negative data in Phase III PWS trials; and 3) additional beloranib safety signals. These risks, that if materialized, may result in significant volatility, and the fact that the majority of the value comes from a single product leads to the Speculative Risk qualifier on our rating.

Key questions

		Our view
1.	**Will Phase III work?**	**We continue to believe that the Phase III could be positive.** So, even though we don't want to be in front of a potential negative FDA action, or any additional potential safety disclosures between now and Phase III data, we continue to view the drug's efficacy as strong. The Phase III data will have to be evaluated within the context of a serious disease without any options and with an annual death rate of ~3%; at this point, the two deaths that have occurred in the PWS program fall within that range.
2.	**What if Phase III is positive? What does FDA do then?**	**We believe that will depend on two factors:** 1) how strong the Phase III data will be in terms of efficacy and 2) what else may happen in terms of safety. If all we have is the two deaths and no other safety concerns, and the Phase III meets its primary endpoints, we believe the drug is on its way to approval and the stock on its way to significant recovery.
3.	**What is the market opportunity in HIAO?**	**We view the market opportunity in HIAO as roughly equivalent to that in PWS. This would essentially double the revenue that can be generated by beloranib**. Our estimates place the number of existing craniopharyngioma patients who develop obesity (HIAO patients) to around 3,000 and 5,000 in the US and EU, respectively. This is in comparison with nearly 3,700 and 6,000 addressable PWS patients in the US and EU that we believe beloranib can initially target. We project beloranib could bring in an additional ~$630MM in peak US/EU HIAO sales.
4.	**So, what is the plan for beloranib in general obesity?**	**Our understanding of management's current plan is that beloranib, if the Phase III program in PWS is successful, will be (p)reserved for the treatment of orphan diseases (like PWS and HIAO).** However, management remains interested in continuing to develop the drug in the general obese population. So, if the data continue to support the use of MetAP2 inhibitors in obesity (as in positive data from the Phase IIb ZAF-203 trial that will read out YE15), we expect ZFGN to use beloranib for rare diseases and develop its own proprietary MetAP2 inhibitor program for the treatment of weight management. Some of the advantages of this strategy include better economics to the future asset and the potential to adjust some of beloranib's properties, including avoiding penetration of the placenta and being brain impermeable—perhaps to offset any CNS and/or hypothalamus effects on sleep and/or circadian rhythms for the general population.

Exhibit 186: Zafgen's pipeline

Drug	Indication	Stage
beloranib	Prader-Willi Syndrome (PWS)	Phase III
	hypothalamic injury-associated obesity (HIAO)	Phase II
	severe and complicated obesity	Phase II
ZGN-839	nonalcoholic steatohepatitis (NASH)	Preclinical

Source: Company reports

Exhibit 187: Zafgen expected newsflow

Event	Drug	Timing
Submit IND for oral ZGN-839 program	ZGN-839	4Q15
6 month Ph III bestPWS readout	beloranib	1Q16
Ph II ZAF-203 data	beloranib	1Q16
Initiate second PWS trial (ZAF-312) in EU	beloranib	2016
Initiate Phase III trials in HIAO	beloranib	2016
Submit IND for 2nd Gen MetAP2 inhibitor	2nd Gen MetAP2 inhib.	2016

Source: RBC Capital Markets estimates and Company reports

Exhibit 188: ZFGN quarterly P&L ($MM)

($MM)	FY 2013A	FY 2014A	Q1: 15A	Q2: 15A	Q3: 15A	Q4: 15E	FY 2015E	Q1: 16E	Q2: 16E	Q3: 16E	Q4: 16E	FY 2016E	FY 2017E
US beloranib PWS sales	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
US beloranib HIAO sales	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total US beloranib sales	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
EU beloranib PWS sales	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
EU beloranib HIAO sales	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total EU beloranib sales	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Total US/EU beloranib sales	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Total revenue	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
COGS	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
R&D	**9.6**	**27.4**	**10.2**	**12.5**	**14.2**	**14.3**	**51.2**	**10.7**	**10.6**	**10.9**	**14.7**	**46.9**	**53.7**
SG&A	**4.2**	**8.1**	**3.0**	**5.1**	**5.5**	**5.4**	**19.1**	**5.3**	**5.1**	**5.0**	**5.7**	**21.1**	**22.6**
Total Operating Expenses	**13.8**	**35.5**	**13.2**	**17.6**	**19.7**	**19.7**	**70.3**	**16.0**	**15.7**	**15.9**	**20.4**	**68.0**	**76.3**
Operating Income (loss)	**(13.8)**	**(35.5)**	**(13.2)**	**(17.6)**	**(19.7)**	**(19.7)**	**(70.3)**	**(16.0)**	**(15.7)**	**(15.9)**	**(20.4)**	**(68.0)**	**(76.3)**
Total other expenses, net	(0.2)	(0.9)	(0.2)	(0.1)	(0.2)	(0.1)	(0.7)	(0.1)	(0.1)	(0.1)	(0.1)	(0.5)	(3.8)
Net loss and comprehensive loss	(14.0)	(36.5)	(13.5)	(17.8)	(19.9)	(19.8)	(70.9)	(16.1)	(15.8)	(16.0)	(20.5)	(68.5)	(80.1)
Accretion of redeemable convertible stock	(0.2)	(0.1)	0.0	0.0	0.0	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.1)	(0.1)
Pretax income	(14.2)	(36.6)	(13.5)	(17.8)	(19.9)	(19.8)	(71.0)	(16.2)	(15.9)	(16.1)	(20.6)	(68.6)	(80.1)
Income tax expense	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net income (loss)	**(14.2)**	**(36.6)**	**(13.5)**	**(17.8)**	**(19.9)**	**(19.8)**	**(71.0)**	**(16.2)**	**(15.9)**	**(16.1)**	**(20.6)**	**(68.6)**	**(80.1)**
GAAP EPS													
Basic	($19.53)	($3.00)	($0.53)	($0.66)	($0.73)	($0.73)	($2.65)	($0.59)	($0.57)	($0.58)	($0.50)	($2.22)	($2.51)
Diluted	($19.53)	($3.00)	($0.53)	($0.66)	($0.73)	($0.73)	($2.65)	($0.59)	($0.57)	($0.58)	($0.50)	($2.22)	($2.51)

Source: Company reports and RBC Capital Markets estimates

Valuation

We currently value ZFGN shares at $7/share, which is the company's net cash position. We expect shares to remain range-bound near-term ahead of Phase III data as investors will not assign significant value to the beloranib program given the recent deaths in the Phase III PWS trial until the drug's safety profile has been cleared by the data.

Price target impediments

As the majority of Zafgen's value lies with the beloranib asset, and particularly in the rare disease indications, any additional concerns about safety, particularly thrombotic events, would negatively affect our valuation. Other factors that can negatively influence our valuation include increased competition, regulatory setbacks, and lower than projected penetrations for beloranib. Factors that can positively affect our valuation include more favorable pricing, positive data from other early-stage Zafgen programs (such as ZGN-839 or a new compound for general obese individuals), and M&A, which we have not included in our valuation.

Company profiles – (Butt)

Aerie Pharmaceuticals (AERI)

Outperform, Speculative Risk

Price Target USD $50.00

Target/Upside/Downside Scenarios

Exhibit 189: Aerie Pharmaceuticals.

Source: RBC Capital Markets estimates

Target price/base case

We value AERI at $50 per share, which includes US/EU sales of Rhopressa and Roclatan. We assign a 75% probability of success and a value of ~$39 per share to the US and ~$11 per share to the EU opportunity. We assume a US launch in 2017 and an EU launch in 2019. We forecast peak Roclatan sales of ~$1.6B and ~$0.8B and Rhopressa sales of ~$282M and ~$205M in the US and EU, respectively. Finally, we assume patent protection through 2030 and include a terminal value based on a discount rate of 15% and a growth rate of -50%.

Upside scenario

Our upside scenario of $88 includes ~$64 per share in value for the US opportunity and ~$24 per share in value for the EU opportunity. We forecast peak Roclatan sales of $2.3B in the US and $1.8B in the EU and Rhopressa sales of ~$377MM in the US and ~$403MM in the EU. We assign products in the pipeline and 60% probability of success, a discount rate of 15%, and a terminal growth rate of -50%.

Downside scenario

Our downside scenario of $6 assumes that Roclatan and Rhopressa may not be successful commercially due to a perceived lack of efficacy. Under this scenario, we assume that AERI will be valued at cash per share of $6 in this scenario.

Investment summary

We believe AERI shares offer the potential for significant upside as both products in development, Rhopressa and Roclatan, use a new mechanism of action for the treatment of glaucoma, a blockbuster potential market. Rhopressa and Roclatan will enter Phase III trials based on positive Phase IIb data. Results from these and additional studies are expected 2015–2017. Millions of patients worldwide suffer from glaucoma, most need multiple medications, and we forecast peak sales of AERI's products at ~$1B.

AERI owns 100% of the rights to Rhopressa and Roclatan worldwide and patent protection extends into 2030, which means the company is free to partner or be acquired. Given that ophthalmology remains an attractive therapeutic area and AERI's product candidates could have a convenient, one drop once per day efficacy and safety profile, progress through clinical and regulatory milestones, as well as a partnership, could all be upside catalysts.

Potential catalysts for the stock

Our investment view is driven by:

- **Phase III data for Roclatan in 2016:** Key catalyst as clean safety and efficacy beyond latanoprost could make Roclatan the first-line drug of choice.
- **Potential partnership for Rhopressa and Roclatan:** AERI owns worldwide rights to both product candidates, and a partnership is likely after Phase III data, in our view.
- **Potential approvals and launches in 2017 in the US and in 2018 in the EU** following regulatory filings in 2016.

Risks to our investment thesis

- **Pivotal Phase III and earlier-stage studies could fail:** Rhopressa must show non-inferiority to a comparator over a longer period, and Roclatan must show a benefit in patients, which raise the risk of failure.
- **AERI could fail to find a partner** for Rhopressa and Roclatan outside the US.
- **Sales ramp of Rhopressa and Roclatan could lag expectations** as clinicians fail to take up AERI's drugs, payers put up hurdles for reimbursing branded drugs, and cheaper generic drugs with other mechanisms hamper market penetration.

Key questions and debates for AERI

1. Is Rhopressa approvable based on Rocket 1 and Rocket2 trials?	While Rocket 1 did not meet its primary endpoint, Rocket 2, the second Phase III study did. Based on multiple FDA interactions, an end of Phase II meeting, and meeting minutes, AERI believes it can use Rocket 2 and Rocket 1 data to file an IND for Rhopressa in 3Q:16. The FDA also has a history of being permissive when it comes to glaucoma approvals.
2. Will Roclatan Phase III study work?	Phase IIb study was positive and demonstrated a stat sig benefit from the combo over the individual agents Rhopressa (AR-13324) and latanoprost. While this outcome was achieved at 1 month, the ongoing Phase III study measures efficacy at 3 months hence the clinical risk and uncertainty. KOLs tell us they are comfortable with the durability questions and longer term Rhopressa Phase III studies hint at synergy with a prostaglandin as well as show benefit out to 3 months.
3. Will AERI be acquired?	While AERI has sufficient capital to see Rhopressa and Roclatan through to approval and launch in the US, we believe chances are high that AERI could be acquired given the potential blockbuster indication addressed. Furthermore, while a partnership is not needed, regional partnerships are also possible, especially in Asia.
4. Can Rhopressa be a standalone product?	Rhopressa, a rho-kinase and norepinephrine transporter inhibitor that also lowers episcleral venous pressure, could demonstrate similar or better efficacy and better safety than any second-line drug for glaucoma. The comparator in the Phase III trial is timolol. Given that 10-20% of patients either do not want to or cannot tolerate first-line drugs and the significant limitations of current second-line drugs, we believe Rhopressa can have significant sales in both the second- and first-line glaucoma markets.

Exhibit 190: Expected news flow for AERI

Timing	Expected News Flow	Program
YE:15	Rocket 1, 2 and 3 safety data update	Rhopressa (AR-13324)
2015/ 2016	Potential ex-US partnership(s)	
2016	Initiate Phase I trials	AR-13533
2016	Pre-clinical combination data with anti-VEGFs	AR-13154
1H:16	Initiate Phase III trials in glaucoma (Mercury 2)	Roclatan (PG324)
Mid/ 2H:16	Initiate Phase III trials in glaucoma (Mercury 3)	Roclatan (PG324)
Mid/ 2H:16	Potential Rocket 4 data	Rhopressa (AR-13324)
Mid/ 2H:16	Efficacy results from Phase III studies (Mercury 1)	Roclatan (PG324)
2H/ YE:16	File NDA	Rhopressa (AR-13324)
2016/ 2017	Further disease modification pre-clincal data	Rhopressa (AR-13324)
2016/ 2017	Initiate Phase I study	AR-13154
1H:17	Phase III efficacy and safety results in glaucoma (Mercury 2)	Roclatan (PG324)
Mid/ 2H:17	Phase III efficacy and safety results in glaucoma (Mercury 3)	Roclatan (PG324)
2H:17	File NDA	Roclatan (PG324)
2H/ YE:17	File MAA	Roclatan (PG324)
2H/ YE:17	Expect approval and launch	Rhopressa (AR-13324)
2H:18	Expect approval and launch	Roclatan (PG324)

Source: Company reports and RBC Capital Markets estimates

Exhibit 191: AERI pipeline

Product	Mechanism	Stage	Indication
Rhopressa (AR-13324)	Dual-action ROCK / NET inhibitor	Phase III	Glaucoma
Roclatan (PG324)	Triple-action ROCK / NET inhibitor and latanoprost, a PGA	Phase III planned	Glaucoma
AR-13154	ROCK/ JAK/ PDGFR-beta inhibitor	Pre-clinical	wet AMD
AR-13533	Dual-action ROCK / NET inhibitor	Pre-clinical	Glaucoma

Source: Company reports and RBC Capital Markets estimates

Exhibit 192: Income statement for AERI

(in MM; except per share)	2014A	1Q:15A	2Q:15A	3Q:15A	4Q:15E	2015E	1Q:16E	2Q:16E	3Q:16E	4Q:16E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E
REVENUES																		
AR-13324												2.1	21.9	46.7	74.6	106.1	141.3	180.8
PG324													13.2	56.4	180.4	320.5	546.6	801.2
Product Sales												2.1	35.1	103.1	255.0	426.5	687.9	982.0
Royalties														11.6	31.1	51.3	79.8	109.3
Other																		
Total Revenues												2.1	35.1	114.7	286.1	477.8	767.7	1,091.2
EXPENSES																		
COGS												0.2	3.5	10.3	25.5	42.7	68.8	98.2
R&D	29.9	11.6	10.6	9.9	19.9	52.0	11.6	10.6	13.4	19.4	55.0	42.5	20.5	12.5	12.5	12.5	12.5	12.5
SG&A	20.1	8.0	7.5	7.5	7.6	30.6	8.0	7.5	7.7	7.8	32.6	34.6	35.0	42.5	45.0	51.8	59.5	68.4
Other																		
Total Expenses	50.0	19.6	18.1	17.4	27.5	82.6	19.6	18.1	21.1	27.2	87.6	77.3	59.0	65.3	83.0	106.9	140.8	179.1
Operating Income (Expense)	(50.0)	(19.6)	(18.1)	(17.4)	(27.5)	(82.6)	(19.6)	(18.1)	(21.1)	(27.2)	(87.6)	(75.3)	(23.9)	49.4	203.1	370.9	626.9	912.1
OTHER																		
Interest income	0.0				0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.3	0.3	0.4	0.4	0.5	0.5	0.5
Interest expense	(0.5)		(0.5)	(0.5)	(0.5)	(1.6)	(0.5)	(0.5)	(0.5)	(0.5)	(2.2)	(2.2)	(2.2)	(2.2)	(2.2)	(1.6)		
Other	2.3	2.4																
Total Other Income (Expense)	1.8	2.4	(0.5)	(0.5)	(0.5)	(1.5)	(0.5)	(0.5)	(0.5)	(0.5)	(2.0)	(1.9)	(1.9)	(1.8)	(1.8)	(1.2)	0.5	0.5
Income before Tax	(48.1)	(17.2)	(18.6)	(17.9)	(28.0)	(84.1)	(20.1)	(18.6)	(21.5)	(27.7)	(89.6)	(77.2)	(25.8)	47.5	201.3	369.7	627.4	912.6
Taxes			0.2	0.1				0.2						16.2	68.5	125.7	213.3	310.3
Net income (loss)	(48.1)	(17.2)	(18.8)	(18.0)	(28.0)	(84.1)	(20.1)	(18.8)	(21.5)	(27.7)	(89.6)	(77.2)	(25.8)	31.4	132.9	244.0	414.1	602.3
EPS, Basic (GAAP)	($2.00)	($0.70)	($0.73)	($0.69)	($1.07)	($3.28)	($0.75)	($0.69)	($0.78)	($0.98)	($3.25)	($2.42)	($0.79)	$0.95	$3.92	$6.87	$10.36	$14.77
EPS, Diluted (GAAP)	($1.51)	($0.50)	($0.52)	($0.50)	($0.77)	($2.35)	($0.55)	($0.50)	($0.56)	($0.71)	($2.37)	($1.83)	($0.60)	$0.72	$3.00	$5.45	$9.09	$12.97
Shares outstanding, Basic	24.1	24.6	25.8	26.1	26.2	25.7	26.7	27.3	27.8	28.4	27.5	31.9	32.6	33.2	33.9	35.5	40.0	40.8
Shares outstanding, Diluted	31.4	34.6	35.9	36.2	36.4	35.7	36.9	37.5	38.2	38.8	37.8	42.2	42.9	43.6	44.4	44.8	45.6	46.4
EPS, Basic (Non-GAAP)	($1.62)	($0.59)	($0.62)	($0.58)	($0.95)	($2.83)	($0.65)	($0.59)	($0.67)	($0.87)	($2.62)	($1.87)	($0.25)	$1.47	$4.44	$7.37	$10.79	$15.20
EPS, Diluted (Non-GAAP)	($1.62)	($0.59)	($0.62)	($0.58)	($0.95)	($2.83)	($0.65)	($0.59)	($0.67)	($0.87)	($2.62)	($1.87)	($0.25)	$1.05	$3.09	$5.42	$9.47	$13.35

Source: Company reports and RBC Capital Markets estimates

Valuation

We value AERI at $50 per share, which includes US/EU sales of Rhopressa and Roclatan. We assign a 75% probability of success and a value of ~$39 per share to the US and ~$11 per share to the EU opportunity. We assume a US launch in 2017 and an EU launch in 2019. We forecast peak Roclatan sales of ~$1.6B and ~$0.8B and Rhopressa sales of ~$282M and ~$205M in the US and EU, respectively. Finally, we assume patent protection through 2030 and include a terminal value based on a discount rate of 15% and a growth rate of -50%.

Price target impediments

Our price target is dependent solely on the clinical, regulatory, and commercial success of Rhopressa and Roclatan. A Phase III study for Rhopressa and Roclatan is expected in 2015, and failure to demonstrate efficacy or safety in one or both of these studies would be a significant setback. Furthermore, any setbacks in regulatory approvals in the US or EU, delay in launch, failure to secure a partnership outside the US for Rhopressa and Roclatan, increased competition, or other limitations to the market potential of these products either due to better efficacy and/or safety outcomes or pricing pressure due to the availability of generic drugs for glaucoma could negatively impact.

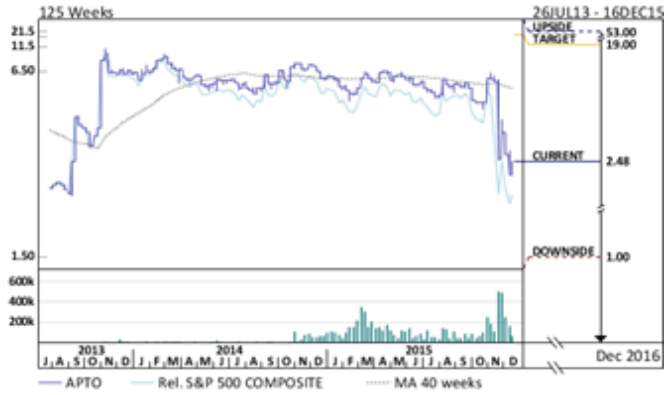
Aptose Biosciences Inc. (APTO)

Outperform, Speculative Risk

Price Target USD $19.00

Target/Upside/Downside Scenarios

Exhibit 193: Aptose Biosciences Inc.



Source: RBC Capital Markets estimates

Target price/base case

We value APTO at $19 per share, including US and EU sales of APTO-253. We assign a probability of success of 30% to APTO-253 given the early stage nature of the program. We assume a US and EU launch in 2022. We assume that APTO will sell APTO-253 in the US and a partner will commercialize these compounds outside the US. We forecast peak APTO-253 sales of more than $1B each in the US and EU for AML and MDS.

Upside scenario

Our upside scenario includes $53 per share in value for the US and EU opportunity. We forecast peak APTO-253 sales of ~$6B in the US and ~$3B in the EU. We currently assign no additional value to the earlier stage pipeline. We assign APTO-253 a 30% probability of success, a discount rate of 15%, and a terminal growth rate of -50%. The larger numbers are driven by a higher assumed market penetration for APTO-253.

Downside scenario

Our downside scenario assumes that APTO-253 will not be successful in clinical trials either due to a compelling efficacy benefit or an adverse event profile that we have not seen to date, especially in combination with other drugs. Under such a scenario, we expect the shares could trade at roughly cash per share, which is currently $1 per share.

Investment summary

Aptose is a cancer-focused biotechnology company that, in conjunction with a new management team and scientific advisory board, is re-focusing APTO-253 on the treatment of hematologic malignancies, specifically AML and MDS. Recent discoveries in the etiology of AML showed that APTO-253, a KLF4 inducer, could have a role as a broadly applicable therapeutic for AML. Since CDX2 expression is raised and KLF4 levels lowered in other blood cancers as well, development of a companion diagnostic and expansion into additional indications are also likely. Phase Ib trials are expected to begin in 2014, and the compound could move into Phase II by 2016 with data and/or updates likely in 2014 or 2015 and 2016 or 2017, respectively. Both AML and MDS are attractive markets with potential sales exceeding $1B, and Aptose owns all rights to APTO-253.

Potential catalysts for the stock

Our investment view is driven by:

- Phase Ib data updates for APTO-253 in 2015/2016. Important catalyst as it could show safety and efficacy for APTO-253.
- Phase II monotherapy data for APTO-253. Important catalyst as it could show signs of activity and safety for therapeutic doses for the first time.
- Phase II combo data for APTO-253. Important in demonstrating combinations with drugs on the market and in development as well as additional data on efficacy, safety, and biomarkers.
- Potential partnership for APTO-253. APTO owns worldwide rights and partnerships could be possible given the unique mechanism of action.

Risks to our investment thesis

- **Phase Ib and Phase II studies could fail**. Our assumption for success is based on pre-clinical data with APTO-253, and since it has not been tested in blood cancers before, evaluating it in patients for the first time is risky.
- **Companion diagnostic could fail to demonstrate clinical correlations.** This could affect the ability to develop a targeted therapeutic.
- **APTO could fail to find a partner** for APTO-253 outside the US.
- **Competitors could emerge that change the treatment paradigm**, as a number of companies are targeting drugs for AML and MDS.
- **Sales ramp of APTO-253 could lag expectations** as clinicians fail to take up APTO-253, payors put up hurdles for reimbursement, and competitors enter the market.

Key questions and debates for APTO

1. Why was Phase Ib study put on hold?

APTO was in the process of reviewing its manufacturing processes and procedures when it was informed of operational difficulty with an intravenous infusion pump at a clinical site. In reviewing APTO-253 manufacturing processes, the company discovered likely deficiencies in manufacturing documentation. APTO then instituted a voluntary suspension of dosing and the FDA put the trial on clinical hold.

2. Is APTO-253 still viable?

We expect trials to resume in 2016 although precise timing is a function of completing internal reviews and FDA sign-off. We do not believe this is a safety or tolerability issue. In fact, APTO completed a safety review of all patient files recently and there were no serious adverse events related to APTO-253.

3. How is patient enrollment going in APTO-253 trials?

Prior to the Phase Ib being put on hold, the Phase Ib was enrolling patients in four centers. An additional site is expected in 4Q:15 and another in 1Q:16 and more centers could continue to be added. APTO believes enrollment will complete in Phase Ib in 1H:16 and that it could start single agent expansion and Phase II combination studies in 2016. APTO is also assessing levels of KLF4 gene expression and Cdx2, which could be used to enrich patients in the Phase Ib expansion or Phase II combination studies.

4. When is APTO-253 in AML approaching therapeutic levels?

From 3Q:15 quarterly update, APTO disclosed that the next cohort would be 140 mg/m2. To date the company has dosed patients at 20 mg/m2, 40 mg/m2, 66 mg/m2 and 100 mg/m2. APTO also believes based on pre-clinical and prior data that 100 mg/m2 could be the therapeutic level. Therefore, activity could be seen soon or it is more likely that dosing would continue at 140 mg/m2 or possibly even higher.

5. What is the next value inflection point?

Set up for share is potentially high-risk and very high reward. However, given the current clinical hold the next inflection points will be 1) restarting Phase Ib, which will de-risk from a safety standpoint; 2) reaching therapeutic dose levels; 3) Phase Ib data, all of these could be 2016 events; 4) initiation of the expansion cohorts; and 5) advancement of the recently in-licensed pre-clinical candidates that could have applicability across blood tumors, including AML, which could be 2016 or 2017 events.

Exhibit 194: Expected news flow for APTO

Timing	Expected News Flow	Program
2H:15	Update on in vitro and in vivo data including data from the Beat AML initiative	APTO-253
YE:15	Phase Ib interim safety/efficacy - possibly at ASH	APTO-253
YE:15/ early 2016	Complete Phase Ib dose escalation	APTO-253
2015/ 2016	Possible strategic licensing deal	APTO-253
1H:16	Final Phase Ib data	
1H:16	Phase II trial designs: mono- and combination therapy	APTO-253
1H:16	Initiate Phase II monotherapy studies in AML/ MDS/lymphomas/ multiple myeloma	APTO-253
2016	Initiate Phase II combo studies in AML/ MDS/lymphomas/multiple myeloma	APTO-253
2016/2017	Potential Phase II mono data	APTO-253
2017/ 2018	Potential Phase II combo data	APTO-253
2017/ 2018	Potential Phase III/ pivotal study plans	APTO-253
2018	Initiate Phase III/ pivotal studies	APTO-253

Source: Company reports and RBC Capital Markets estimates

Exhibit 195: APTO pipeline

Product	Mechanism	Stage	Indication	Partner
APTO-253	Upregulate KLF4 Gene Expression	Phase Ib Phase I	AML & MDS Solid Tumors	
IL-17E	Immunomodulator	Pre-clinical	Oncology	Genentech
APTO-500	MELK inhibitor	Discovery	Oncology	
Small Molecule Program		Discovery	Various	Eli Lilly / Elanco
Early Discovery Program		Discovery	Various	

Source: Company reports and RBC Capital Markets estimates

Exhibit 196: Income statement for APTO

Fiscal Year Ends in Dec. *(CAD in MM; except per share)*	2010A	2011A	2012A	2013A	2014A	1Q:I-A	2Q:I-A	Interim	1Q:15A	2Q:15A	3Q:15A	4Q:15E	2015E	2016E	2017E	2018E	2019E	2020E
Revenue																		
APTO253 - US	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
APTO253 - EU Royalty	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Other revenue	0.1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Total Revenue	**0.1**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Operating expenses																		
COGS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
R&D	2.5	2.3	2.1	3.3	3.0	1.3	1.1	2.4	0.9	1.3	1.7	1.5	5.4	7.2	10.7	17.0	24.2	33.7
SG&A	3.1	2.7	2.4	2.3	7.4	3.0	2.6	5.6	2.8	2.8	2.2	2.3	10.1	9.7	10.5	11.3	9.0	9.5
Dep & Amort of fixed assets	0.1	0.0	0.0	0.0	0.0	-	-	-	-	-	-	-	-	0.0	0.0	0.0	0.0	0.0
Other expense	0.1	0.0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Total Costs	**5.7**	**5.1**	**4.6**	**5.6**	**10.4**	**4.3**	**3.7**	**8.0**	**3.7**	**4.1**	**4.0**	**3.8**	**15.5**	**16.9**	**21.2**	**28.3**	**33.2**	**43.2**
Operating Income (Expense)	**(5.6)**	**(5.1)**	**(4.6)**	**(5.6)**	**(10.4)**	**(4.3)**	**(3.7)**	**(8.0)**	**(3.7)**	**(4.1)**	**(4.0)**	**(3.8)**	**(15.5)**	**(16.9)**	**(21.2)**	**(28.3)**	**(33.2)**	**(43.2)**
Finance expense	(0.1)	(0.1)	(0.0)	(0.0)	(0.3)	(0.0)	(0.0)	(0.1)	(0.0)	(0.0)	(0.0)	(0.0)	(0.1)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)
Finance income	0.1	0.1	0.0	0.0	0.1	0.2	0.1	0.3	0.1	0.1	0.7	0.7	1.6	2.9	2.9	2.9	2.9	2.9
Other	11.0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Loss before income taxes	**5.3**	**(5.0)**	**(4.6)**	**(5.6)**	**(10.6)**	**(4.2)**	**(3.6)**	**(7.8)**	**(3.6)**	**(4.0)**	**(3.3)**	**(3.1)**	**(14.0)**	**(14.0)**	**(18.4)**	**(25.4)**	**(30.4)**	**(40.4)**
Income tax benefit	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Net income (loss)	**5.3**	**(5.0)**	**(4.6)**	**(5.6)**	**(10.6)**	**(4.2)**	**(3.6)**	**(7.8)**	**(3.6)**	**(4.0)**	**(3.3)**	**(3.1)**	**(14.0)**	**(14.0)**	**(18.4)**	**(25.4)**	**(30.4)**	**(40.4)**
Deemed dividend	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Accretion preferred stock	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Net loss to shareholder	**5.3**	**(5.0)**	**(4.6)**	**(5.6)**	**(10.6)**	**(4.2)**	**(3.6)**	**(7.8)**	**(3.6)**	**(4.0)**	**(3.3)**	**(3.1)**	**(14.0)**	**(14.0)**	**(18.4)**	**(25.4)**	**(30.4)**	**(40.4)**
EPS - Basic (GAAP)	**$6.90**	**($4.67)**	**($2.76)**	**($1.58)**	**($2.02)**	**($0.36)**	**($0.31)**	**($0.67)**	**($0.30)**	**($0.34)**	**($0.27)**	**($0.26)**	**($1.17)**	**($1.04)**	**($1.03)**	**($1.30)**	**($1.50)**	**($1.78)**
EPS - Diluted (GAAP)	**$1.66**	**($4.67)**	**($2.76)**	**($1.58)**	**($2.02)**	**($0.36)**	**($0.31)**	**($0.67)**	**($0.30)**	**($0.34)**	**($0.27)**	**($0.26)**	**($1.17)**	**($1.04)**	**($1.03)**	**($1.30)**	**($1.50)**	**($1.78)**
Shares (basic)	0.8	1.1	1.7	3.5	5.2	11.6	11.6	11.6	11.8	11.9	11.9	12.0	11.9	13.4	17.8	19.5	20.3	22.7
Shares (diluted)	3.2	3.5	4.1	6.0	7.8	13.3	13.3	13.3	13.5	13.5	13.6	13.6	13.5	14.9	19.3	21.1	21.9	24.4

Source: Company reports and RBC Capital Markets estimates

Valuation

We value APTO at US$19 per share, which includes US and EU sales of APTO-253. We assign a probability of success of 30% to APTO-253 given the early-stage nature of the clinical program. We assume a US and EU launch in 2022. Currently, we assume that APTO will sell APTO-253 in the US and a partner will commercialize these compounds outside the US. We forecast peak APTO-253 sales of more than $1B each in the US and EU for AML and MDS. We currently assign no additional value to the earlier-stage pipeline. Finally, we assume product sales extend through 2030 and include a terminal value based on a discount rate of 15% and a terminal growth rate of -50%. The probability of success could move up rapidly with positive pre-clinical and clinical data that could be generated in 2016.

Price target impediments

Our price target is dependent solely on the clinical, regulatory, and commercial success of APTO-253. Results from a Phase I study for APTO-253 are expected in 2015 and Phase II data are expected in 2016 or 2017 and need to show activity. Failure to demonstrate efficacy or safety in these and other studies would be a significant setback. Furthermore, any setbacks in regulatory approvals in the US or EU, delay in launch, failure to secure a partnership, or a change in competitive dynamics could all negatively affect our valuation.

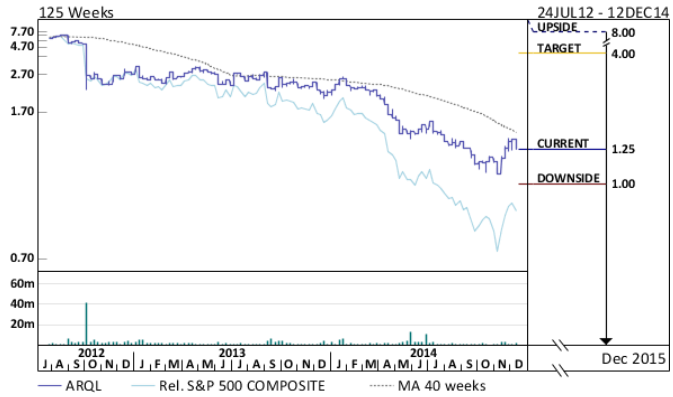
Arqule (ARQL)

Outperform, Speculative Risk

Price Target USD $4.00

Target/Upside/Downside Scenarios

Exhibit 200: Arqule Pharmaceuticals.



Source: RBC Capital Markets estimates

Target price/base case

We arrive at our $4 price target using a DCF and sum of the parts analysis probability adjusted for success in second-line HCC. For second-line HCC, we assume a 15% discount rate and a -50% terminal growth rate to arrive at a value of ~$4/share.

Upside scenario

Our $8 per share upside scenario assumes tivantinib approval in second-line HCC, NSCLC KRAS mutant, and c-MET high. For second-line HCC, our probability of success is 60%, and the value is reduced to ~5/share. The value of the NSCLC franchise and pipeline assets is ~$3/share, as we assume tivozanib treatment in KRAS mutant and c-MET high setting.

Downside scenario

Our downside scenario assumes that tivantinib pivotal trials do not succeed; in which case, our valuation approaches net cash balance or roughly ~$1/share

Investment summary

Our long-term thesis on ARQL is based on expected positive data for its main drug tivantinib in 2014 or 2015 for second-line HCC. We believe there are multiple shots at success for tivantinib with HCC and even NSCLC and the proprietary pipeline. However, timelines to Phase III data are long and uncertain given uncertainty regarding the tolerability of tivantinib in patients with liver cancer.

Potential catalysts for the stock

Our investment view is driven by:

- Update on the ability to dose and enroll patients in the ongoing Phase III second-line liver cancer study.
- Positive updates from non-ARQL sponsored tivantinib studies in 2016.
- Phase III data in second-line liver cancer patients by 2015 or 2016.
- Progress in the proprietary pipeline.

Risks to our investment thesis:

- Setbacks in the early or late-stage pipeline evaluating tivantinib in a number of cancers.
- Failure for tivantinib to secure approval in second-line liver cancer and/or finding a path forward in NSCLC.
- Setbacks in earlier-stage, proprietary programs.
- Greater than expected competition in the clinic or commercially.
- Higher than forecast cash burn.

Key questions and debates for ARQL

1. When do we expect to see Tivantinib Phase III data on HCC?

   Tivantinib Phase III data are more likely released in 2016. An interim analysis is anticipated in 1H:16 or sooner (at ~60% of events has an efficacy but no futility stop) and final data by YE:16/ 1H:17.

2. Why did ARQL choose to co-promote?

   By exercising the option, ARQL has the right to co-commercialize Tivantinib in the U.S, which will give ARQL an opportunity to form a sale force. The option does not change the current financials. ARQL will gain launching experience and the same medical sales can be deployed for the drugs in the pipeline, for example, ARQ -087 for intrahepatic cholangiocarcinoma, currently under Phase II trial. The physicians who would prescribe Tivantinib in second line HCC have quite some overlap with the physicians that could theoretically prescribe ARQ-087 in intrahepatic cholangiocarcinoma.

3. When does the Phase I Proteus syndrome study become a driver?

   Given that Proteus syndrome is driven by a mutation of the AKT1 gene, ARQ 092 could have a role in this rare disorder. Though the Phase I is being conducted in conjunction with the NIH, an update is likely in 2016 and could include AKT levels data.

4. What makes ARQL risk reward attractive?

   There are at least four ongoing programs and progress in any one or two could be upside to expectations, including a Phase III study of tivantinib in 2nd line liver cancer, Phase I ARQ 092 study in proteus syndrome, ARQ 092 Phase Ib especially in endometrial cancer, lymphoma, breast cancer, etc., and ARQ 087 Phase II in intrahepatic cholangiocarcinoma, especially as two or more programs have the potential to advance quickly if some of the earlier stage studies are positive.

Exhibit 201: Expected news flow for ARQL

Timing	Expected News Flow	Program
2H:15	Complete enrollment of Phase Ib trials	ARQ-087
2H:15	Complete enrollment of Phase Ib trials	ARQ-092
YE:15/ 1H:16	File IND	ARQ-751
2H:15/ 1H:16	Phase I data in solid tumors	ARQ-087
YE:15/ 1H:16	Potential Phase Ib update in endometrial cancer, lymphoma and other cancers with AKT1 mutation	ARQ-092
YE:15	Complete enrollment of Phase III METIV-HCC trial	Tivantinib
YE:15/ 1H:16	Phase I data	ARQ-761
1H:16	Potential interim Phase III METIV study results in 2nd line HCC	Tivantinib
2015/ 2016	Phase II data from IST/NCI studies: Head & Neck cancer, prostate and kidney cancers	Tivantinib
2016	Initiate Phase I studies	ARQ-751
2016	Phase III data in 2nd-lne HCC (Japanese patients)	Tivantinib
2016/ 2017	Phase III data in 2nd-lne HCC (METIV / Western)	Tivantinib
2016/ 2017	Phase I data in Proteus Syndrome	ARQ-092
2016/ 2017	Phase II data in cholangiocarcinoma	ARQ-087
2016/ 2017	Initiate additional Phase II studies	ARQ-092/ ARQ-087

Source: Company reports and RBC Capital Markets estimates

Exhibit 202: ARQL pipeline

Program	Target	Phase	Indication	Drug combinations
Tivantinib (ARQ-197)	c-MET	Phase III	Liver (HCC); 2nd-line (METIV-HCC Study)	Single agent
		Phase III	Non-small cell lung (NSCLC)	Tarceva (erlotinib)
		Phase II	Colorectal cancer (CRC)	Irinotecan/Erbitux
		Phase II	Gastric (Asia)	Single agent
		Phase II	Metastatic prostate cancer	Single agent
		Phase I	Breast, ovarian, uterine, pancreatic	Gemzar (gemcitabine)
		Phase I	HCC, RCC, breast, NSCLC, melanoma	Nexavar (sorafenib)
ARQ-087	FGFR	Phase II	Cholangiocarcinoma	
ARQ-092	AKT	Phase I	Proteus Syndrome; cancer	
		Phase I	Solid tumor	
ARQ-621	Eg5, KSP	Phase I	Solid or hematologic tumors	
ARQ-736	BRAF	Phase I	Solid tumors (BRAF and NRAS mutations)	
ARQ-761	NQ01/ beta-lapachone	Phase I	Solid tumor	

Source: Company reports and RBC Capital Markets estimates

Exhibit 203: Income statement for ARQL

($ in millions, except per share) Fiscal Year Ends December	2014A	Q1:15A	Q2:15A	Q3:15A	Q4:15E	2015E	Q1:16E	Q2:16E	Q3:16E	Q4:16E	2016E	2017E	2018E	2019E
Tivantinib royalties						0.0	**0.0**	**0.0**	**0.0**	**0.0**	0.0	3.7	21.0	128.8
Research and development revenue	11.3	2.8	3.0	2.7	2.2	10.7	2.0	2.2	2.4	2.6	9.2	10.0	7.5	5.0
Total revenue	11.3	2.8	3.0	2.7	2.2	10.7	2.0	2.2	2.4	2.6	9.2	13.7	28.5	133.8
Research and development	22.3	4.4	4.3	3.2	4.7	16.6	4.8	4.9	4.9	5.0	19.6	22.1	27.1	32.1
General and administrative	12.2	3.2	2.8	1.8	1.7	9.5	1.7	1.6	1.7	1.7	6.6	8.0	10.0	12.0
Other / Repayment to Daiichi	1.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	3.7	21.0	3.3
Total costs and expenses	35.5	7.6	7.1	5.0	6.4	26.1	6.5	6.5	6.6	6.7	26.2	33.7	58.0	47.4
Loss from operations	(24.3)	(4.8)	(4.1)	(2.4)	(4.1)	(15.4)	(4.5)	(4.3)	(4.2)	(4.1)	(17.0)	(20.1)	(29.6)	86.4
Sub-sum Other income (expense)	0.9	0.3	0.1	0.0	(0.0)	0.3	0.1	0.1	0.1	0.1	0.3	0.3	0.3	0.3
Loss before taxes	(23.4)	(4.6)	(4.0)	(2.4)	(4.2)	(15.1)	(4.3)	(4.1)	(4.0)	(4.0)	(16.6)	(19.7)	(29.2)	86.8
Income tax	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net Income (Loss)	(23.4)	(4.6)	(4.0)	(2.3)	(4.2)	(15.1)	(4.3)	(4.1)	(4.0)	(4.0)	(16.6)	(19.7)	(29.2)	86.8
EPS - Basic	($0.37)	($0.07)	($0.06)	($0.04)	($0.07)	($0.24)	($0.07)	($0.06)	($0.06)	($0.06)	($0.26)	($0.27)	($0.40)	$1.16
EPS - Diluted	($0.37)	($0.07)	($0.06)	($0.04)	($0.07)	($0.24)	$0.00	$0.00	$0.00	$0.00	($0.26)	($0.27)	($0.40)	$1.07
Shares outstanding (basic)	62.6	62.7	62.8	62.8	63.1	62.9	63.5	63.8	64.1	64.4	63.9	71.7	73.1	74.6
Shares outstanding (diluted)	67.4	68.7	68.7	68.8	69.1	68.8	69.6	69.9	70.2	70.5	70.1	77.8	79.3	80.7

Source: Company reports and RBC Capital Markets estimates

Valuation

We arrive at our $4 price target using a DCF/ sum of the parts analysis probability adjusted for success in second-line HCC. For second-line HCC, we assume a 15% discount rate, and a -50% terminal growth rate to arrive at a value of ~$4/share.

Price target impediments

Our price target is dependent primarily on the clinical, regulatory, and commercial success of tivantinib in hepatocellular carcinoma and KRAS mutant NSCLC. We expect Phase III results for tivantinib in 2015 or 2016 to show OS benefit in second-line liver cancer and Phase II results for tivantinib in KRAS mutant NSCLC to show a PFS benefit. Any clinical, regulatory, or commercial setbacks could negatively affect our valuation. Upside could come from better than anticipated market penetration, partnerships for the pipeline, and clinical success of programs not directly included in our valuation.

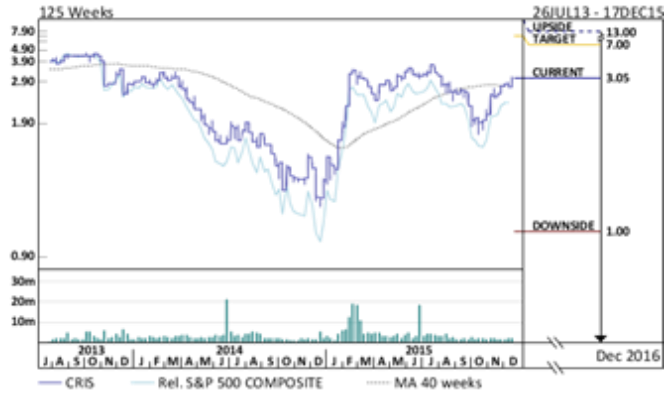
Curis, Inc. (CRIS)

Outperform, Speculative Risk

Price Target USD $7.00

Target/Upside/Downside Scenarios

Exhibit 204: Curis, Inc.



Source: RBC Capital Markets estimates

Target price/base case

We arrive at our $7 price target using a DCF/ sum of the parts analysis probability adjusted for the pipeline. For Erivedge in basal cell carcinoma, we value the royalties at ~$2/share. We also include ~$5 in value from the proprietary pipeline using a probability adjusted DCF based analysis and cash. We do not include the earlier-stage pre-clinical pipeline.

Upside scenario

Our $13 upside scenario assumes larger markets for CUDC-907, CUDC-427, anti-PD-L1, and the IRAK4 kinase inhibitor and also includes <$0.50 per share in value for CUDC-305.

Downside scenario

Our $1 downside scenario assumes Erivedge will see a flat ramp that is roughly under $200M in peak sales worldwide, which leads to a royalty value plus net cash of ~$1/share. We also ascribe no value to the pipeline.

Investment summary

Our Outperform, Speculative Risk rating is based on the expected news flow from at least four Phase I drug candidates (CUDC-907, CUDC-427, anti-PD-L1, IRAK4 kinase inhibitor) and downside support from royalties on commercial sales of Erivedge. We believe the proprietary pipeline remains underappreciated, especially with these assets being unique and differentiated. Recent progress includes advancement of CUDC-907 into Phase II and expected progression of anti-PD-L1 and the IRAK4 kinase inhibitor into Phase I. Data from CUDC-427 is also expected. Partnering activity from one or more candidates across one or more geographies could also occur.

Potential catalysts for the stock

Our investment view is driven by:

- Erivedge prescription data. TRx and NRx are growing and trends on a weekly and monthly basis should continue to go up.
- If CUDC-907 pivotal/ Phase II trial shows safty and activity, it could be an important value driver with data possible in 2017.
- Anti-PD-L1 and IRAK4 kinase inhibitor Phase I data are expected in 2016.
- Pipeline expansion with more oral checkpoint inhibitors added.

Risks to our investment thesis

- **Erivedge prescription, sales, and royalties** could lag our estimates.
- **Clinical, regulatory, and/or commercial setbacks** for CUDC-427, CUDC-907, and Debio 0932.
- **Competition from other agents** targeting similar indications or the same mechanism of action for marketed and pipeline products could be tougher than expected.

Key questions and debates for CRIS

1. Do CUDC-907 Phase I data appear competitive for the treatment of DLBCL?	Phase Ib data at ASH demonstrated an ORR of 44% in r/r DLBCL. KOLs tell us that a single agent response rate of 30-40% in r/r DLBCL is sufficient to warrant further development. What is even more notable is that CUDC-907 has activity against tumors that are driven by MYC, such as MYC copy number gain, MYC IHC+, BCL-2 translocation or IHC+ and/or GCB DLBCL, which are all typically hard to treat tumor types. Other agents are in development for the treatment of r/r DLBCL as well but what could make CUDC-907 unique, aside from its novel mechanism of action, is its ability to demonstrate efficacy in MYC+ DLBCL.
2. How did the Street view the Aurigene deal?	When announced the deal saw CRIS gain significant value. That is because CRIS is gaining a pipeline of oral checkpoint inhibitors whose clinical development CRIS will lead and fund. Since this is an approach not yet taken by bigger biopharma companies, there were questions around how CRIS were able to secure these assets if they are so promising and from what we understand it was a competitive process.
3. Why did the timelines for the start of Phase I studies for the immuno-oncology assets, such as CA-170 (anti-PD-L1/VISTA), slip?	CRIS had assumed that toxicology studies would complete sooner; however, dosing appears relatively safe so it continued beyond internal projections. Instead of starting a Phase I study by YE:15 for the anti-PD-L1/VISTA product candidate, also called CA-170, CRIS had to extend the pre-clinical evaluation period and now expects to start a Phase I in 2016.
4. Will Phase I data for oral checkpoint inhibitors or the IRAK4 inhibitor be a catalyst?	Though the debate around whether or not an oral checkpoint inhibitor could work, whether CRIS can fund development by itself, or if this is even a useful approach could continue, the fact remains that development of an oral checkpoint inhibitor let alone a variety of them would be unique and a first of its kind approach. For instance, CA-170 (anti-PD-L1 and VISTA) could: 1) potentiate therapeutic effects; 2) address tumors that relapse after PD-1/PD-L1 targeted treatments; 3) expanding indications beyond tumors currently targeted by anti-PD-1 and anti-PD-L1 antibodies; 4) offer easier combinability with other anti-cancer therapies, and, most importantly, 5) allow for a quicker 'off'. Other oral checkpoint inhibitors, such as the dual PD-L1 and TIM-3 antagonist, will follow. Given that Nimbus (private) announced a partnership with Roche (Genentech) for its pre-clinical IRAK4 inhibitor, we think positive Phase I data from CRIS' IRAK4 inhibitor could be a driver as well.
5. What is the outlook on Erivedge with increased competition?	Novartis could well be launching Odomzo but we think Erivedge has better data and an incumbent position. It remains to be seen if there could be price competition. CRIS' partner Roche is also starting a Phase Ib study in patients with myelofibrosis (Erivedge+ruxolitinib) and a previously planned Phase II (currently suspended) in IPF could restart with Esbriet (pirfenidone).

Exhibit 205: Expected news flow for CRIS

Timing	Expected News Flow	Program
YE:15	Potential Phase Ib update in heme onc and solid tumors	CUDC-907
YE:15/ 1H:16	Potential Phase II/ pivotal trial designs in blood and/or solid tumors	CUDC-907
YE:15/ 1H:16	Potential expansion cohort data in r/r DLBCL (combo with Rituxan)	CUDC-907
1H:16	Initiate Phase I in cancer	IRAK4 kinase inhibitor (oral)
1H:16	Initiate Phase I in cancer	Anti-PD-L1/VISTA (oral)
2015/ 2016	In-license further pipeline candidates from Aurigene	Aurigene
2H:16	Phase I update in cancer	Anti-PD-L1/VISTA (oral)
YE:16/ 1H:17	Pivotal Phase II update in r/r DLBCL	CUDC-907
YE:16/ 1H:17	Phase I data in cancer	Anti-PD-L1/VISTA (oral)
YE:16/ 1H:17	Phase I update in blood cancers	IRAK4 kinase inhibitor (oral)
YE:16/ 1H:17	Phase II data in untreated basal cell cancer with surgery	Erivedge
YE:16/ 1H:17	Phase II data in locally advanced/ metastatic basal cell cancer	Erivedge
2016/ 2017	Phase II 'go/ no-go' decision potentially in combination	Anti-PD-L1/VISTA (oral)
2016/ 2017	File IND	Anti-PD-L1/TIM-3 (oral)
2017	Phase I update in blood cancers	IRAK4 kinase inhibitor (oral)
Mid/ 2H:17	Pivotal Phase II data in r/r DLBCL	CUDC-907
Mid/ 2H:17	Phase I data in cancer	IRAK4 kinase inhibitor (oral)
2017	Phase II data in idiopathic pulmonary fibrosis	Erivedge

Source: Company reports and RBC Capital Markets estimates

Exhibit 206: CRIS pipeline

Product	Target(s)	Stage of Development	Indication(s)	Partner(s)
Erivedge (vismodegib)	Hedgehog signaling	Marketed	Basal cell carcinoma	Roche
			Basal cell nevus syndrome	Roche
		Phase II	Operable basal cell carcinoma	Roche
		Phase II	Multiple basal cell carcinomas	Roche
		Phase II	Previously untreated basal cell carcinoma	Roche
		Phase II	Locally advanced / metastatic basal cell carcinoma	Roche
CUDC-907	PI3K/HDAC	Phase II planned; Phase I ongoing	DLBCL	Proprietary
		Phase I	Lymphoma and multiple myeloma	Proprietary
		Phase I	Solid tumors	Proprietary
CUDC-427	IAP inhibitor	Phase I	Solid tumors and lymphoma	Proprietary
		Phase Ib/ II planned (capecitabine combination)	HER2-negative breast cancer	Proprietary
		Phase I planned (monotherapy)	Aggressive and indolent MALT lymphoma	Proprietary
Anti-PD-L1/VISTA (oral)	PD-L1/VISTA	Phase I planned (monotherapy)	TBD (solid tumors likely)	Aurigene
IRAK4 kinase inhibitor (oral)	IRAK4 kinase	Phase I planned (monotherapy)	TBD (lymphoma likely)	Aurigene
Anti-PD-L1/TIM-3 (oral)	PD-L1/TIM-3	Pre-IND	TBD (solid tumors likely)	Aurigene
CUDC-305 (Debio 0932)	Hsp90	Phase I/II	Advanced NSCLC	Proprietary
		Phase I/II	NSCLC (wild type EGFR)	
		Preclinical	Systemic mastocytosis	
CUDC-101	EGFR/Her2/HDAC	Preclinical	Head and neck cancer	Proprietary
n/a	HDAC/Bcr-Abl	Preclinical	Not determined	Proprietary
n/a	HDAC/Hsp90	Preclinical	Not determined	Proprietary

Source: Company reports and RBC Capital Markets estimates

Exhibit 207: Income statement for CRIS

($ in millions, except per share)	2014A	1Q15A	2Q15A	3Q15A	4Q15E	2015E	1Q16E	2Q16E	3Q16E	4Q16E	2016E	2017E	2018E	2019E	2020E
Revenues:															
Erivedge (vismodegib) royalty	6.8	1.7	2.0	2.3	2.8	8.8	2.2	2.4	2.6	4.0	11.2	13.9	15.9	17.4	18.9
Collaboration & Milestones	3.1	(0.0)	0.0	(0.2)	-	(0.2)	-	-	-	-	-	-	-	-	-
Other															
Net revenues	**9.9**	**1.7**	**2.1**	**2.0**	**2.8**	**8.6**	**2.2**	**2.4**	**2.6**	**4.0**	**11.2**	**13.9**	**15.9**	**17.4**	**18.9**
Costs and expenses:															
Royalty expense	0.3	0.1	0.1	0.1	0.1	0.4	0.0	0.0	0.1	0.2	0.3	0.7	0.8	0.9	0.9
Research and development	13.7	29.1	5.9	4.0	15.3	30.0	7.5	10.0	14.0	18.5	50.0	55.0	60.0	65.0	70.0
General and administrative	11.7	3.5	3.4	2.8	3.3	13.0	3.7	3.8	3.9	4.1	15.5	17.5	20.0	22.5	25.0
IPRD / Amortization of intangible assets															
Total costs and expenses	**25.7**	**32.7**	**9.5**	**6.9**	**18.8**	**67.8**	**11.2**	**13.8**	**18.0**	**22.8**	**65.8**	**73.2**	**80.8**	**88.4**	**95.9**
Loss from operations	**(15.9)**	**(31.0)**	**(7.4)**	**(4.8)**	**(15.9)**	**(59.2)**	**(9.0)**	**(11.4)**	**(15.4)**	**(18.7)**	**(54.6)**	**(59.3)**	**(64.9)**	**(71.0)**	**(77.0)**
Other income (expense):															
Interest and other income (expense)	(0.1)		0.1	0.1	0.1	0.4	0.1	0.1	0.1	0.1	0.3	0.3	0.3	0.3	0.4
Interest expense	(2.7)	(0.8)	(0.8)	(0.8)	(1.1)	(3.6)	(1.0)	(1.0)	(1.0)	(9.0)	(12.0)	(10.2)			
Total other income	(2.9)	(0.8)	(0.8)	(0.7)	(1.0)	(3.3)	(1.0)	(1.0)	(1.0)	(8.9)	(11.8)	(9.9)	0.3	0.3	0.4
Net loss	**(18.7)**	**(31.8)**	**(8.1)**	**(5.5)**	**(16.9)**	**(62.4)**	**(10.0)**	**(12.4)**	**(16.4)**	**(27.6)**	**(66.4)**	**(69.2)**	**(64.6)**	**(70.7)**	**(76.6)**
EPS (basic)	($0.22)	($0.30)	($0.06)	($0.04)	($0.13)	($0.51)	($0.08)	($0.10)	($0.13)	($0.20)	($0.50)	($0.45)	($0.39)	($0.41)	($0.42)
EPS (diluted)*	($0.22)	($0.30)	($0.06)	($0.04)	($0.13)	($0.51)	($0.08)	($0.10)	($0.13)	($0.20)	($0.50)	($0.45)	($0.39)	($0.41)	($0.42)
Shares outstanding (basic)	85.97	107.93	128.35	128.39	129.03	123.43	129.68	130.33	130.98	141.63	133.16	154.47	167.56	170.91	184.33
Shares outstanding (diluted)	94.45	116.59	137.08	137.20	137.91	132.20	138.63	139.36	140.09	150.82	142.22	161.97	175.14	178.56	192.06

Source: Company reports and RBC Capital Markets estimates

Valuation

We arrive at our $7 price target using a DCF/ sum of the parts analysis probability adjusted for the pipeline. For Erivedge in basal cell carcinoma, we value the royalties at ~$2/share. We also include ~$5 in value from the proprietary pipeline using a probability adjusted DCF based analysis and cash. We do not include the earlier-stage pre-clinical pipeline.

Price target impediments

Main risks that could cause CRIS shares to fall short of our price target:

- **Commercial and clinical risk for Erivedge:** Any commercial or clinical setback or slip in the timeline for this program would adversely affect CRIS shares.
- **Clinical risk for proprietary and partnered pipeline:** Progress in Phase I and II studies for proprietary drugs including CUDC-907 and CUDC-427 as well as partnered product candidate Debio 0932 is essential to achieving our price target. Any clinical, regulatory, or commercial setbacks would be a negative for CRIS shares.

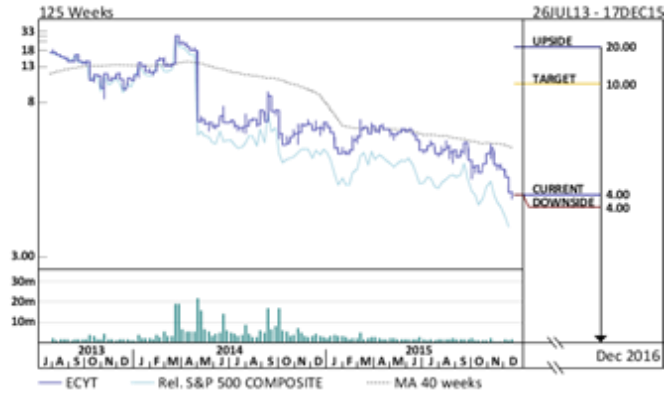
Endocyte, Inc. (ECYT)

Outperform, Speculative Risk

Price Target USD $10.00

Target/Upside/Downside Scenarios

Exhibit 208: Endocyte, Inc.



Source: RBC Capital Markets estimates

Target price/base case

We value ECYT at $10 per share, valuing the Phase I EC1456 and other proprietary programs at ~$6 share, assigning a probability of success of 10–20%. Net cash and NOLs total ~$4 per share.

Upside scenario

Our $20 per share upside scenario assumes EC1456 and EC1169 and other proprietary programs at ~$16 per share, with probabilities of success varying from 10% to 20%. Net cash and NOLs total ~$4/ share.

Downside scenario

Our $4 downside scenario assumes that vintafolide fails and excludes all other pipeline candidates from our valuation as well, leaving current cash and NOLs of ~$4 share.

Investment summary

Endocyte's small-molecule drug conjugate technology has generated several drug candidates. The lead candidate, vintafolide in combination with docetaxel in Phase II study in NSCLC (non-small cell lung cancer), showed statistically significant PFS (progression-free survival) benefit compared to docetaxel alone and an OS benefit in adenocarcinoma. The ability to select patients with folate receptor expression allows targeted therapy and likely better efficacy. Positive data from pipeline candidates including EC1456, a more potent form of vintafolide, and ECYT's small-molecule drug conjugate (SMDC) technology platform could provide a greater valuation and significant upside to shares.

Potential catalysts for the stock

Our investment view is driven by:

- **EC1456 data Phase I data** in 2016.
- **EC1169 Phase I data** in 2016
- **Proprietary pipeline data** and progress in 2015/ 2016.

Risks to our investment thesis:

- **FDA or EMA could require additional data** prior to approving vintafolide.
- **Pivotal and late-stage studies could fail,** including vintafolide for PROC and for NSCLC.
- **Partnerships even though not needed could fail to materialize.**
- **Sales ramp could lag expectations.**

Key questions and debates for ECYT

1. Is the folate receptor a good therapeutic target?	Both Endocyte and ImmunoGen are developing drugs targeting the folate receptor albeit the former with a small molecule drug conjugate and the latter with an antibody drug conjugate. While ECYT's Phase III study in PROC showed futility, a Phase II study in lung cancer demonstrated activity with a PFS benefit and earlier stage studies also showed targeting the folate receptor offered a therapeutic benefit. IMGN's clinical program is also advancing. Phase I data expected from EC1456 could add to the evidence of folate receptor being a validated and acceptable target.
2. Is vintafolide worth developing in NSCLC?	Phase IIb TARGET study showed vintafolide (EC145) plus docetaxel in FR+ NSCLC improved OS by 2.7m regardless of histology (median OS 11.5m vs. 8.8m; HR 0.86; 95% CI 0.58, 12.6) but in the predefined adenocarcinoma subset the benefit was 5.9m (12.5m vs. 6.6m; HR 0.72; 95% CI 0.44, 1.16). However, ECYT has begun developing EC1456, which has a more potent toxin attached to it than vintafolide does. Therefore, ECYT is likely to pursue the development of EC1456 over vintafolide, in our view.
3. Has EC1456 demonstrated activity in the ongoing Phase I study so far?	EC1456 could potentially be more potent than vintafolide since it uses tubulysin, with ~20x the potency. On a weekly schedule, EC1456 dose is now in the 8th cohort (10 mg/ m2) and far above vintafolide's exposure. The twice per week dose is 4.5 mg/m2. ECYT is also exploring a schedule with no rest. While the company continues to dose up since EC1456 still appears tolerable, we believe an activity update will be presented once a recommended Phase II dose is achieved possibly in 2016. Based on precedence EC1456 should have activity.
4. When can ECYT initiate expansion cohorts for EC1456?	We think this is most likely in 1H/mid-2016 and could include ovarian, endometrial, non-small cell, and triple negative breast cancers. The expansion cohorts will focus on both monotherapy and combination studies and could lead to a pivotal 'go/ no-go' decision in 2017.
5. Is the technology platform validated?	Since validation was initially built upon vintafolide, when that program failed in Phase III value for the platform technology left as well. Success for EC1456 is likely to lead to greater confidence and then should EC1169, a PSMA targeted SMDC, in a Phase I study in patients with castration-resistant prostate cancer also demonstrate activity, confidence in a small molecule drug conjugate platform could return quickly.

Exhibit 209: Expected news flow for ECYT

Timing	Expected News Flow	Program
2015/16	Potential IND	TBD
YE:15/ 1H:16	Initiate Phase I study in inflammatory disorders (osteoarthritis)	EC1669
YE:15/ 1H:16	Phase Ib data in FR+ tumors	EC1456
YE:15/ 1H:16	Phase I data in prostate cancer	EC1169 / EC0652
Mid-2016	Phase I/ II 'go/ no-go' decision for expansion cohorts (ovarian, endometrial, NSCLC, TNBC)	EC1456
Mid-2016	Phase II 'go/ no-go' decision in prostate cancer	EC1169 / EC0652
2H:16/ 1H:17	Phase I/ II expansion cohort update (ovarian, endometrial, NSCLC, TNBC)	EC1456
2H:16/ 1H:17	Phase I/ II expansion cohort update	EC1169 / EC0652
2016/ 2017	Update on regulatory pathways	EC1456
YE:16/ early 2017	Pivotal or Phase III 'go/ no-go' decision	EC1456

Source: Company reports and RBC Capital Markets estimates

Exhibit 210: ECYT pipeline

Product	Indication	Target	Payload	Status	Partner
Oncology					
Vintafolide (EC145)	Platinum resistant ovarian cancer (FR100%) (PROC)	FR	DAVLBH	Phase III trial halted for futility	Proprietary
	Non-small cell lung cancer (NSCLC)	FR	DAVLBH	Phase II (TARGET)	
	Triple-negative breast cancer (TNBC)	FR	DAVLBH	Phase II ready	
	Platinum sensitive ovarian cancer; NSCLC	FR	DAVLBH	Phase I combination with carboplatin / paclitaxel	
EC0489	Solid tumors	FR	DAVLBH	Phase I	
EC0225	Solid tumors	FR	DAVLBH / Mitomycin-C	Phase I	
EC1456 (Folate-Tubulysin)	Solid tumors	FR	Tubulysin-B	Phase I	Proprietary
EC1169 (PSMA-Tubulysin)	Prostate cancer		Tubulysin-B	Phase I	Proprietary
EC1788 (Folate-DNA alkylator)	Solid tumors	FR	DNA alkylator	Pre-clinical	Proprietary
Inflammation					
EC1669 (Folate-Aminopterin)	Inflammation	FR	Aminopterin	Pre-clinical	Proprietary
Kidney Disease					
EC0371	Polycystic kidney disease (PKD)	FR	mTor inhibitor	Preclinical	Proprietary
Companion Imaging Diagnostics					
Etarfolatide (EC20)	Diagnostic (folate receptor)	FR	Tc-99m	Phase III	Proprietary
EC0652	Diagnostic (prostate)	PSMA	Tc-99m	Phase I	Proprietary

Source: Company reports and RBC Capital Markets estimates

Exhibit 211: Income statement for ECYT

($ in MM; except per share)	2014A	Q1:15A	Q2:15A	Q3:15A	Q4:15E	2015E	Q1:16E	Q2:16E	Q3:16E	Q4:16E	2016E	2017E	2018E	2019E	2020E
EC1456 US NSCLC															
EC1456 EU Royalty NSCLC															
EC1169															
U.S. profit split - PROC															
EU Royalty - PROC															
EC20															
EC145 - NSCLC															
Total Product Revenues															
Collaboration revenue	70.4	0.0	0.0	0.0	-	0.1	-	-	-	-	-	-	-	-	-
Total Revenues	70.4	0.0	0.0	0.0	-	0.1	-	-	-	-	-	-	-	-	-
COGS															
Research and Development Expenses	41.7	6.6	6.7	6.6	6.6	26.5	6.7	6.8	6.9	7.0	27.4	42.5	55.0	60.0	65.0
Sales, General and Administrative Expenses	23.7	4.4	4.1	3.8	3.8	16.0	3.9	3.9	4.0	4.0	15.7	16.5	17.5	22.5	27.5
Total Costs and Expenses	65.3	11.0	10.8	10.4	10.4	42.5	10.6	10.7	10.9	11.0	43.1	59.0	72.5	82.5	92.5
Operating Income (Loss)	5.0	(11.0)	(10.8)	(10.3)	(10.4)	(42.4)	(10.6)	(10.7)	(10.9)	(11.0)	(43.1)	(59.0)	(72.5)	(82.5)	(92.5)
Other Income/(Expense), Net	0.4	0.1	0.2	0.3	(0.3)	0.3	0.1	0.1	0.1	0.1	0.4	0.3	0.3	0.4	0.4
Income (Loss) before Tax	5.5	(10.9)	(10.6)	(10.0)	(10.7)	(42.1)	(10.7)	(10.8)	(11.0)	(11.1)	(43.5)	(58.7)	(72.3)	(82.2)	(92.2)
Provision for Income Tax															
Net Income (Loss) - GAAP	**5.5**	**(10.9)**	**(10.6)**	**(10.0)**	**(10.7)**	**(42.1)**	**(10.7)**	**(10.8)**	**(11.0)**	**(11.1)**	**(43.5)**	**(58.7)**	**(72.3)**	**(82.2)**	**(92.2)**
EPS, Basic (GAAP)	$0.14	($0.26)	($0.25)	($0.24)	($0.25)	($1.00)	($0.25)	($0.25)	($0.25)	($0.25)	($1.01)	($1.33)	($1.21)	($1.36)	($1.21)
EPS, Diluted (GAAP)	$0.13	($0.26)	($0.25)	($0.24)	($0.25)	($1.00)	($0.25)	($0.25)	($0.25)	($0.25)	($1.01)	($1.33)	($1.21)	($1.21)	($1.11)
Shares Outstanding, Basic	40.2	41.9	41.9	42.0	42.1	42.0	42.5	42.9	43.4	43.8	43.1	44.2	59.7	60.3	75.9
Shares Outstanding, Diluted	41.8	47.5	47.7	47.7	47.9	48.7	49.0	49.5	50.0	50.5	50.1	51.5	67.2	68.1	82.9

Source: Company reports and RBC Capital Markets estimates

Valuation

We value ECYT at $10 per share. We value the Phase I EC1456 and other proprietary programs at ~$6 share (previously ~$7/share, assuming probabilities of success of 10–20% and peak sales opportunities in the $500M to $1B+ range). Current net cash and NOLs total ~$4 share (previously ~$5/share).

Price target impediments

Our price target is dependent primarily on the clinical success of vintafolide (EC145), EC1456 in non-small cell lung cancer, and/or other proprietary programs. Any setbacks in clinical development, delay in launch, increased competition, or other limitations to the market potential of EC145 could negatively affect our valuation. Upside could come from new partnerships, clinical success of earlier-stage programs that are not included in our valuation, and/or setbacks for potential competitors.

Intra-Cellular Therapies Inc. (ITCI)

Outperform, Speculative Risk

Price Target USD $74.00

Target/Upside/Downside Scenarios

Exhibit 212: Intra-Cellular Therapies.

Source: RBC Capital Markets estimates

Target price/base case

We value ITCI at $74 per share, which includes US and EU sales of ITI-007 with a probability of success of 75% for US schizophrenia (~$31), 75% for EU schizophrenia (~$5), 60% for US bipolar depression (~$21), and 60% for EU bipolar depression (~$5). Currently, we assume that ITCI will sell ITI-007 in the US and assume a partnership for ex-US sales and forecast peak sales of $2–4B+ worldwide with a 20% royalty on ex-US sales.

Upside scenario

Our upside scenario of $131 per share includes ITI-007 sales in schizophrenia for ~$61 per share, bipolar depression for ~$46 share, and dementia for ~$17 per share. We forecast peak ITI-007 sales of ~$2.1B+ and ~$2B for US and ex-US, respectively. We also include PDE1 and others for ~$7 per share with peak sales of $4.0–4.5B and $3.2–3.7B for US and ex-US, respectively.

Downside scenario

Under this scenario, we only include ITI-007 US schizophrenia sales and exclude all ex-US sales. We assume ITI-007 schizophrenia US market peak sales of $550–600M and would be valued at ~$5 per share.

Investment summary

We believe ITCI shares offer the potential for strong upside as the lead product in development, ITI-007, has a unique mechanism of action for the treatment of schizophrenia, a blockbuster potential market, and likely other neuropsychiatric indications as well. ITI-007 is already in Phase III trials with positive, differentiated Phase III and Phase II data reported, and could enter further label expansion studies targeting bipolar disorder and/or behavioral disturbances associated with dementia in 2015/2016. We expect results from these and additional studies in 2016-2017 and beyond. Millions of patients worldwide suffer from schizophrenia, bipolar disorder, dementia, and other neuropsychiatric disorders, and we forecast ITI-007 becomes a blockbuster drug. ITCI owns 100% of the rights to ITI-007 and its pipeline worldwide. Patent protection extends into 2030 and potentially longer, freeing the company to partner or be acquired.

Potential catalysts for the stock

- ITI-007 Phase III data in schizophrenia by 2H:16. This is the second Phase III study with the primary efficacy endpoint at four weeks.
- ITI-007 Phase III data in bipolar depression in 2H:16/ 2017. This would be the first Phase III study, with the primary efficacy endpoint at six weeks.
- ITI-007 clinical trial initiation in 2015. ITCI plans to evaluate ITI-007 in behavioral disturbances in dementia.

Risks to our investment thesis

- EMA or FDA could require additional trials.
- EMA or FDA could fail to approve inhaled AAT in the EU and/ or US, respectively.
- KMDA could fail to find a partner for inhaled AAT in the US or KMDA could opt for a different selling model.
- Addition studies ongoing could fail.

Key questions and debates for ITCI

1. Does ITI-007 have a new mechanism of action?

ITI-007's activity and safety profile is unique and unlike that of currently approved antipsychotics drugs. ITI-007 is a potent 5-HT2A receptor antagonist that also has strong affinity for dopamine D2 receptors, the serotonin transporter, and is a glutamatergic modulator, all of which confer therapeutic effects. It also appears to have negligible binding affinities at two receptors that are implicated in side effects, the H1 receptor and the serotonin 5-HT2C receptor. Differential receptor binding allows for the potential for activity across various indications at different doses. Most importantly, ITCI has generated data that shows differential binding affinity for ITI-007 vs. other antipsychotic drugs that appears to prove ITI-007 works different than any other 5-HT2A receptor antagonist.

2. Is the recent Phase III ITI-007 data in Schizophrenia differentiated?

The primary endpoint of total PANSS was met in patients with schizophrenia with the 60 mg dose showing statistical significance compared to placebo at week 4 (p=0.022). While the 40 mg dose showed a benefit, it did not achieve statistical significance (p=0.164). However, both doses reached stat sig for the secondary endpoint of clinical global impression scale of severity of illness and improved the PANSS Negative Symptom Subscale score more than placebo (not stat sig). Most importantly, safety appears largely clean and differentiated with ITI-007 leading to little to no metabolic and movement disorders, which are an important cause of discontinuation. Details are yet to be presented and somnolence stood out as being higher than placebo (17% vs. 4%). KOLs have always stated that a drug with clean metabolic and movement adverse events would be successful.

3. Will the second Phase III study in schizophrenia be successful?

The first Phase III study that compared ITI-007 to placebo was successful. The second Phase III study, where data are expected mid/2H:16 again compares the 60 mg dose to placebo but also has Risperdal as a positive control with the primary endpoint reading out at week 6. This design to nearly identical to the successfully completed Phase II study that also met the primary endpoint, showed superiority to placebo, efficacy similar to and differentiated vs. Risperdal, and a much better safety profile, except in the Phase II the primary endpoint was measured at week 4. Based on the success of Phase II and first Phase III, chances of the second Phase III trial working are high.

4. Can ITI-007's label be expanded to include additional indications?

The fact that the safety profile is clean and that efficacy is seen even at lower receptor occupancy broadens the therapeutic window further, especially for those indications where lower doses are needed, such as bipolar disorder and/or behavioural disturbances associated with schizophrenia. The latter indication could be the first of its kind granted by the FDA. In fact, ITCI has started Phase III trials in bipolar depression and a Phase II/III behavioral disturbances in dementia study is also expected. Further label expansion studies could target major depressive disorder (MDD). A number of antipsychotic drugs have been approved for more than one indication.

5. Is ITCI a take out candidate?

Though a differentiated antipsychotic drug could be marketed by ITCI, most companies marketing antipsychotic drugs targeting indications like schizophrenia, bipolar depression, and other neuropsychiatric indications, are much larger biopharma companies. Hence, chances of a takeout are high, in our view, especially if the second Phase III study is successful.

Exhibit 213: Expected news flow for ITCI

Timing	Description	Product
YE:15/ 1H:16	Behavioral disturbances in dementia potential Phase II/ III initiation	ITI-007
2015/ 2016	PDE1 Program - Initiate clinical trials	PDE1
2H:16	Schizophrenia - Second Phase III trial data	ITI-007
2016	Initiate additional studies (major depressive disorder, etc.)	ITI-007
2016	First Phase III and PET study publication	ITI-007
2H:16/1H:17	Schizophrenia - File NDA	ITI-007
2016/ 2017	Bipolar depression Phase III results	ITI-007
2016/ 2017	Behavioral disturbances Phase II/ III results	ITI-007
2016/ 2017	Behavioral disturbances pivotal go/no-go decision	ITI-007
2016/ 2017	Partner ex-US	ITI-007
2H:17/ 1H:18	Approval in schizophrenia	ITI-007

Source: Company reports and RBC Capital Markets estimates

Exhibit 214: ITCI pipeline

Product	Indication	Stage
ITI-007	Schizophrenia	Phase III
	Bipolar Depression	Phase III
	Behavioral disturbances assoc. w/ Dementia, including AD	Phase II/III
	Sleep maint. Insomnia & sleep disturb. assoc. w/ Neuropsychiatric disorders	Phase II
	Other Neuro-psychiatric conditions including MDD and Autism	Phase I
	LAI program	Pre-clinical
	IC200131 Program: Mood + other disorders	Pre-clinical
ITI-214	CNS, cardiovascular, peripheral neurodegenerative diseases	Phase I
PDE2	Alzheimer's disease, disorders of cognitive function	Pre-clinical
PDE9	Alzheimer's disease, schizophrenia	Pre-clinical

Source: Company reports and RBC Capital Markets estimates

Exhibit 215: Income statement for ITCI

($ in MM; except per share)	2014A	1Q:15A	2Q:15A	3Q:15A	4Q:15E	2015E	2016E	2017E	2018E	2019E	2020E	2021E
Revenue												
License and collaboration	0.6	0.0	0.1	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0
ITI-007 US Sales - Schizophrenia	0.0	0.0	0.0	0.0	0.0	0.0	0.0	72.8	149.3	306.0	470.6	723.6
ITI-007 US Sales - Bipolar disorder	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	122.7	251.6	515.9
ITI-007 Ex-US Royalties - Schizophrenia	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	15.3	30.6	61.4
ITI-007 Ex-US Royalties - Bipolar	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	49.2
Grant revenue	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Other	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total Revenue	**0.6**	**0.0**	**0.1**	**0.0**	**0.0**	**0.1**	**0.0**	**72.8**	**149.3**	**444.1**	**752.9**	**1,350.1**
Operating expenses												
R&D	21.2	18.6	17.8	28.5	33.1	98.0	125.5	130.0	114.0	60.0	60.0	65.0
SG&A	10.3	3.8	4.0	3.9	5.4	17.0	25.0	40.0	57.5	80.0	105.0	171.5
COGS	0.0	0.0	0.0	0.0	0.0	0.0	0.0	10.9	22.4	64.3	108.3	185.9
Royalty expense	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.2	4.5	12.9	21.7	37.2
Other	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total operating expenses	**31.6**	**22.4**	**21.7**	**32.3**	**38.5**	**115.0**	**150.5**	**172.2**	**176.0**	**152.9**	**186.7**	**273.7**
Operating Income (Loss)	**(31.0)**	**(22.4)**	**(21.7)**	**(32.3)**	**(38.5)**	**(114.9)**	**(150.5)**	**(99.4)**	**(26.7)**	**291.2**	**566.2**	**1,076.4**
Other income (expenses)												
Interest expense	(0.0)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Interest income	0.3	0.1	0.2	0.2	0.2	0.7	0.8	0.8	0.8	0.8	0.8	0.8
Other	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total other income (expense)	**0.3**	**0.1**	**0.2**	**0.2**	**0.2**	**0.7**	**0.8**	**0.8**	**0.8**	**0.8**	**0.8**	**0.8**
Pretax Income	(30.7)	(22.3)	(21.5)	(32.2)	(38.3)	(114.3)	(149.7)	(98.6)	(25.9)	292.0	567.0	1,077.1
Income tax expense	(0.0)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	(102.2)	(198.4)	(377.0)
Net income (loss)	**(30.7)**	**(22.3)**	**(21.5)**	**(32.2)**	**(38.3)**	**(114.3)**	**(149.7)**	**(98.6)**	**(25.9)**	**189.8**	**368.5**	**700.1**
Dividend on convertible pref. stock	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net income (loss)	**(30.7)**	**(22.3)**	**(21.5)**	**(32.2)**	**(38.3)**	**(114.3)**	**(149.7)**	**(98.6)**	**(25.9)**	**189.8**	**368.5**	**700.1**
EPS - Basic (GAAP)	**($1.07)**	**($0.72)**	**($0.61)**	**($0.91)**	**($0.89)**	**($3.17)**	**($3.40)**	**($1.96)**	**($0.50)**	**$3.55**	**$6.70**	**$12.36**
EPS - Diluted (GAAP)	**($1.07)**	**($0.72)**	**($0.61)**	**($0.91)**	**($0.89)**	**($3.17)**	**($3.40)**	**($1.96)**	**($0.50)**	**$3.47**	**$6.55**	**$12.08**
Shares (basic)	28.6	30.8	35.0	35.3	43.2	36.1	44.0	50.3	51.8	53.4	55.0	56.7
Shares (diluted)	29.7	31.8	36.1	36.4	44.3	37.1	45.1	51.5	53.0	54.6	56.3	57.9

Source: Company reports and RBC Capital Markets estimates

Valuation

We arrive at our $74 (from $62) per share price target using a sum-of-the parts discounted cash flow analysis for ITCI shares. The primary driver of our valuation includes ITI-007 for schizophrenia and bipolar depression sales in the US and royalties ex-US. Our base, upside, and downside scenarios use a discount rate of 15% to reflect potential clinical and regulatory risk. In our base case, we assign 75% and 60% probability of success of regulatory approval to ITI-007 in schizophrenia (from 75% and 50%) and in bipolar disease (from 65% and 40%), respectively, in the US and ex-US.

Price target impediments

Our price target is dependent on the clinical, regulatory, and commercial success of ITI-007 in schizophrenia and bipolar depression. Two Phase III studies for ITI-007 in schizophrenia are planned and data for the first Phase III study is expected YE:15 and the second in 2H:16. Failure to demonstrate efficacy or safety in any of these studies would be a significant

setback. Furthermore, any setbacks in regulatory approvals in the US or EU, delay in launch, failure to secure a partnership outside the US, increased competition or other limitations to the market potential of these products either due to better efficacy and/or safety outcomes or pricing pressure due to the availability of generic drugs could negatively affect our valuation.

The Medicines Company (MDCO)

Outperform

Price Target USD $48.00

Target/Upside/Downside Scenarios

Exhibit 216: The Medicines Company.

Source: RBC Capital Markets estimates

Target price/base case

Base case: $48. Our price target is based on $12/share for Ionsys (80% probability adjusted), ~$4 for oritavancin and Minocin (80% and 65% probability adjusted), ~$2/share for Raplixa (65% probability), $8/share for Carbavance (55% probability), ~$2/share for PreveLeak (80% probability), ~$3/share for cangrelor (80% probability), $10/ share for ALN-PCSsc and $3/ share for MDCO-216. We include $4/share for other marketed products, including $2/share for Angiomax and $1/ share for Cleviprex and other products, and ~$2/share for Recothrom.

Upside scenario

Upside case: $67. We also increase Carbavance to $24/share, cangrelor to $6, and angiomax to $4. The earlier-stage cardiovascular programs could be upside drivers especially if longer duration of activity for ALN-PCSsc holds out.

Downside scenario

Downside case: $18. We reduce peak sales forecast for cangrelor and carbavance and the probabilities of success for Ionsys and exclude the earlier-stage cardiovascular programs from our valuation.

Investment summary

Our Outperform rating is based on significant upcoming news flow, which could potentially include several product launches and early and late stage data from additional products, some of which are now key drivers for MDCO, including ALN-PCSsc for LDL-C entering Phase II studies and Carbavance for gram negative infections in Phase III trials. We believe MDCO shares offer an attractive risk-reward with base support from upcoming launches and potential for upside from the pipeline, where investor expectations are still in check, especially with regard to the cardiovascular and antibiotics franchises.

Potential catalysts for the stock

- **ALN-PCSsc Phase II start in 2016.** Candidate could be differentiated on duration (longer than 3-6 months).
- **MDCO-216 Phase II data in 2016.**
- **Carbavance Phase III data in 2016/2017.**
- **Other clinical and business development news flow.** News flow from earlier-stage programs is also anticipated.

Risks to our investment thesis

- **Cardiovascular products could fail to differentiate.** We expect ALN-PCSsc Cangrelor to be filed for approval but regulatory agencies could require more data or fail to approve these drug candidates.
- **Pivotal studies could fail.** Carbavance pivotal studies could fail to demonstrate efficacy or lead to approval.
- **Sales ramp could lag expectations.** Angiomax and other marketed products as well as those in development could lose market share or fail to gain traction as rapidly as forecast.

Key questions and debates for MDCO

1. What are the chances that MDCO could be acquired?

With or without angiomax, MDCO's fundamentals are attractive with an acute care and hospital focus, several marketed and in development franchises, such as cardiovascular, antibiotic, pain, anesthesia, etc., that could be attractive as whole or in parts to other biopharma companies. The cardiovascular and antibiotics franchises together or separately could be of special interest as potential partnering or take out opportunities. There could be two groups of acquirers, those with a focus on the hospital and antibiotics and the other with an interest in picking up a high value and differentiated, albeit earlier-stage, cardiovascular portfolio.

2. Should MDCO be broken up? Are pieces worth more than the whole?

The main arguments for divesting one or more MDCO assets are to raise non-dilutive capital, tighten expenses, and enhance the focus on pipeline candidates deemed to be of highest value, thereby unlocking value for investors.

3. Are the gram negative assets differentiated and attractive?

There are several drugs in development for the treatment of gram negative infections; however, our conversations with KOLs in the antibiotics arena show the gram negative franchise could be differentiated, especially since they could target resistant organisms. There are several tailwinds for those participating in antibiotics development, including regulatory and national focus given the increase in resistance. There has also been consolidation in the industry with a number of companies being acquired such as Cubist Pharmaceuticals, Forest Laboratories, Actavis, Durata Therapeutics, Optimer and Trius, among other.

4. How should the earlier stage Phase II cardiovascular assets be viewed?

ALN-PCSsc is in Phase II but as an anti-PCSK9 it treads a well-validated route with peak sales of at least $1B+ and potentially much higher with the primary hurdle being clinical risk. Most importantly, Phase I ALC-PCSsc also has the potential to be differentiated since it can be dosed every 3 to 6 months vs. currently approved anti-PCSK9s that must be dosed every 2 or every 4 weeks. MDCO-216 is in Phase II studies but it could also be a blockbuster-potential product. In our view, these two programs, which would have data in 2016, respectively, could be important catalysts and get the stock moving quickly even with early-stage data. They are also meaningful enough to generate partnering or takeout interests, especially for companies that need to catch up quickly in the anti-PCSK9 arena.

5. What's the status on paragraph IV angiomax litigation with HSP?

A recent court decision vacating the patent invalidity decision and granting a hearing was an unexpected surprise. MDCO and Hospira have been engaged in paragraph 4 litigation over angiomax since July 2010. MDCO has claimed infringement of patents '727 and '343 while HSP has argued non-infringement and patent invalidity. Next steps involve briefings concerning the commercial on-sale bar issue, including US Department of Justice views with the entire Appeals Court reviewing the appeal from the start. Further development and next steps are likely due in 2016, but at this stage it is an upside option.

Exhibit 217: Expected news flow for MDCO

Timing	Expected News Flow	Program
2015	Quarterly financials	Angiomax, guidance, expenses
Nov. 12th, 2015	ORION program and Phase I data update	ALN-PCSsc
YE:15	Initiate Phase II program	ALN-PCSsc
YE:15	PreveLeak (ArterX) product re-launch in the US and EU	PreveLeak (ArterX)
YE:15/ 1Q:16	Expect EU approval	Ionsys
1Q/2Q:16	Potentially out-license/ sell assets	Recothrom, PreveLeak, Raplixa
1Q:16	Pilot/Phase II data	MDCO-216
Mid-2016	Phase II 'go/no-go' decision	MDCO-216
2H/YE:16	Phase II data	ALN-PCSsc
2H/YE:16	Phase II data	ABP-700
YE:16	Phase III data in CRE (carbapenem resistant enterobacteriaceae)	Carbavance
YE:16	Phase III data in cUTI	Carbavance
2016	Potential partnership(s) in EU	Orbactiv, Raplixa, Kangrexal, Ionsys, etc.
2017	Initiate Phase III program	ALN-PCSsc
2017	Initiate Phase III program	ABP-700
Mid-2017	File NDA and MAA	Carbavance
YE:17/ 1Q:18	Expect US approval	Carbavance
1H:18	Expect EU approval	Carbavance

Source: Company reports and RBC Capital Markets estimates

Exhibit 218: MDCO pipeline

Product	Stage	Indication	Partner(s)
Angiomax	Generics	Percutaneous coronary intervention (PCI)	Sandoz for authorized generic
Cleviprex	Marketed	Acute treatment of peri-procedural hypertension	Licensed from AstraZeneca
Argatroban	Marketed	Heparin induced thrombocytopenia	Licensed from Eagle Pharma.
Brilinta	Marketed	Anti-thrombotic for ACS	Co-marketed with AstraZeneca
Recothrom	Marketed	Recombinant thrombin for bleeding control during surgery	Bristol-Myers Squibb
PreveLeak (ArterX)	Marketed	Sealant for bleeding control during surgery	Tenaxis (acquired)
Orbactiv (Oritavancin)	Marketed	ABSSSI	
Minocin	Marketed	Gram-negative and gram-positive infections	
Ionsys	Approved	Transdermal fentanyl for post-surgical severe pain	Incline Therapeutics (acquired)
Raplixa (Fibrocaps)	Approved	Bleeding during surgery	
Cangrelor	AdCom recommended approval on 4/15/15	Percutaneous coronary intervention (PCI)	Licensed from AstraZeneca
RPX602	Approved/ Filed	Gram-negative and gram-positive infections (better formulation of Minocin)	
Carbavance (RPX2014/ RPX7009)	Phase III	Gram negative infections	
ALN-PCS (02 / sc)	Phase II planned	LDL-cholesterol lowering	Licensed from Alnylam
MDCO-216 (ApoA-I Milano)	Phase II	Acute Coronary Syndrome (plaque reduction)	Licensed from Pfizer
ABP-700	Phase I complete	Novel anesthetic	Acquired Annovation Biopharma

Source: Company reports and RBC Capital Markets estimates

Exhibit 219: Income statement for MDCO

($ in millions, except per share)	FYA	1QA	2QA	3QE	4QE	FYE	1QE	2QE	3QE	4QE	FYE	FYE	FYE	FYE	FYE
Fiscan Year Ends December	2014	Mar-15	Jun-15	Sep-15	Dec-15	2015	Mar-16	Jun-16	Sep-16	Dec-16	2016	2017	2018	2019	2020
US Angiomax sales	599.5	95.1	60.5	18.8	5.6	180.0	10.0	8.0	6.0	3.0	27.0	4.1	0.6	0.1	0.0
Ex-US Angiomax revenue	36.2	5.6	5.1	3.7	4.1	18.5	-	-	-	-	-	-	-	-	-
Royalty revenues	-	-	-	24.5	12.3	36.8	8.2	5.4	3.6	2.4	19.7	9.8	4.9	2.5	1.2
Recothrom	64.5	16.3	15.9	15.4	17.6	65.1	15.0	16.5	17.5	18.1	67.1	68.4	69.8	71.2	72.6
Raplixa (Fibrocaps)	-	-	-	0.2	1.8	2.0	2.5	4.5	6.5	8.4	21.9	32.8	41.0	46.1	51.9
Ionsys	-	-	-	0.7	1.3	2.0	2.0	5.0	10.0	18.3	35.3	91.9	177.2	270.2	367.8
Cangrelor	-	-	-	0.3	0.8	1.0	1.0	2.0	4.5	7.6	15.1	32.1	46.2	64.7	93.8
Carbavance	-	-	-	-	-	-	-	-	-	-	-	4.1	95.7	185.0	319.4
Other products	21.6	9.6	9.0	9.1	10.6	38.4	10.5	16.5	20.6	27.5	75.0	133.4	184.3	228.5	270.9
Licensing fees, royalties and milestones	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Total Revenues	**721.8**	**126.5**	**90.5**	**72.7**	**54.0**	**343.7**	**49.2**	**57.9**	**68.7**	**85.2**	**261.0**	**376.5**	**619.7**	**868.1**	**1,177.8**
Cost of sales	287.6	33.7	37.0	87.0	36.3	194.0	21.3	23.2	25.3	28.4	38.2	79.2	95.8	132.9	177.3
% Sales	40%	25%	37%	107%	57%	51%	35%	31%	28%	25%	11%	16%	12%	12%	12%
Research and development	159.2	23.9	36.2	30.1	64.7	155.0	40.0	42.5	45.0	47.5	175.0	185.0	190.0	195.0	200.0
Selling, general and administrative	342.2	80.5	96.2	82.5	108.2	367.5	90.0	80.0	75.0	70.0	315.0	320.0	325.0	330.0	335.0
Total Operating Expenses	**789.0**	**138.2**	**169.5**	**199.6**	**209.2**	**716.5**	**151.3**	**145.7**	**145.3**	**145.9**	**528.2**	**584.2**	**610.8**	**657.9**	**712.3**
Operating Income (Loss)	**(67.2)**	**(11.7)**	**(78.9)**	**(126.9)**	**(155.2)**	**(372.8)**	**(102.1)**	**(87.8)**	**(76.6)**	**(60.7)**	**(267.2)**	**(207.7)**	**8.9**	**210.2**	**465.5**
Total Other Income (Expense)	25.38	22.49	11.16	(3.70)	(7.56)	22.38	(9.40)	(9.30)	(9.25)	(9.15)	(37.09)	(18.00)	1.20	1.30	1.40
Income before Tax	(39.2)	10.8	(67.8)	(130.6)	(162.8)	(350.4)	(111.5)	(97.1)	(85.9)	(69.8)	(304.3)	(225.7)	10.1	211.5	466.9
Provision for taxes	(6.8)	5.8	(21.3)	(25.4)	(20.0)	(61.0)	-	-	-	-	-	-	3.5	74.0	163.4
Net Income (Loss)	**(32.3)**	**5.0**	**(46.5)**	**(105.1)**	**(142.8)**	**(289.4)**	**(111.5)**	**(97.1)**	**(85.9)**	**(69.8)**	**(304.3)**	**(225.7)**	**6.6**	**137.5**	**303.5**
EPS - Basic (GAAP)	($0.50)	$0.08	($0.71)	($1.57)	($2.12)	($4.36)	($1.64)	($1.43)	($1.26)	($0.95)	($4.38)	($3.06)	$0.09	$1.86	$4.09
EPS - Diluted (GAAP)	**($0.48)**	**$0.08**	**($0.67)**	**($1.48)**	**($2.00)**	**($4.15)**	**($1.55)**	**($1.35)**	**($1.19)**	**($0.90)**	**($4.14)**	**($2.91)**	**$0.08**	**$1.76**	**$3.88**
Shares Outstanding - Basic (MM)	64.5	65.2	65.9	67.1	67.3	66.4	68.0	68.1	68.3	73.5	69.5	73.7	73.9	74.0	74.2
Shares Outstanding - Diluted (MM)	68.1	66.9	69.9	71.1	71.3	69.8	72.0	72.1	72.3	77.5	73.5	77.7	77.9	78.0	78.2
EPS - Basic, Non-GAAP	$1.05	$0.09	($0.65)	($0.82)	($2.00)	($3.41)	($1.52)	($1.30)	($1.13)	($0.84)	($3.90)	($2.61)	$0.54	$2.31	$4.54
EPS - Diluted, Non-GAAP	**$1.02**	**$0.08**	**($0.50)**	**($0.64)**	**($1.55)**	**($2.78)**	**($1.54)**	**($1.01)**	**($0.88)**	**($0.66)**	**($3.04)**	**($2.06)**	**$0.47**	**$1.99**	**$3.91**
Shares Outstanding - Basic (MM)	64.5	65.2	65.9	67.1	67.3	66.4	68.0	68.1	68.3	73.5	69.5	73.7	73.9	74.0	74.2
Shares Outstanding - Diluted (MM)	66.3	66.9	85.5	86.8	86.9	81.5	66.9	87.8	88.0	93.1	89.1	93.3	85.8	86.0	86.2

Source: Company reports and RBC Capital Markets estimates

Valuation

Our $48 per share price target for our base case scenario includes $12/share for Ionsys (80% probability adjusted), ~$4 for oritavancin and Minocin (80% and 65% probability adjusted), ~$2/share for Raplixa (65% probability), $8/share for Carbavance (55% probability), ~$2/share for PreveLeak (80% probability), ~$2/share for cangrelor (80% probability), $10/ share for ALN-PCSsc and $3/ share for MDCO-216. We include $4/share for other marketed products, including $2/share for Angiomax and $1/ share for Cleviprex and other products, and ~$2/share for Recothrom.

Price target impediments

Risks to our price target include lower-than-forecast sales of marketed products, ongoing or future litigation vs. paragraph IV challengers, and pipeline setbacks, including negative data as well as potential regulatory and commercial risk.

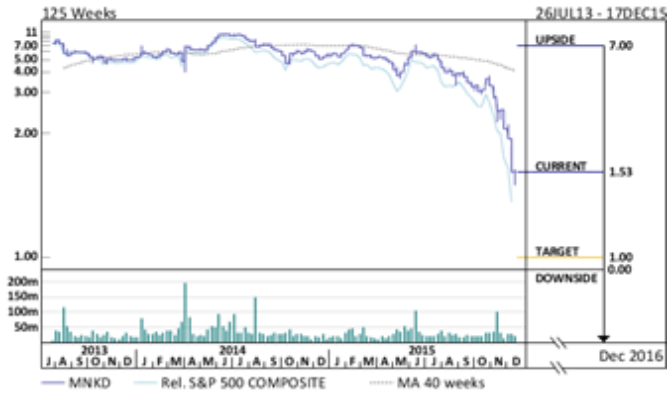
MannKind Corporation (MNKD)

Underperform, Speculative Risk

Price Target USD $1.00

Target/Upside/Downside Scenarios

Exhibit 220: MannKind Corporation.



Source: RBC Capital Markets estimates

Target price/base case

We value MNKD at $1 per share, which includes US and EU profit/expense splits for Afrezza with Sanofi. We assume a US launch in 2015 and EU in 2017. MNKD will retain manufacturing responsibilities while Sanofi is responsible for commercial efforts. We forecast peak Afrezza sales of more than $1B WW; however, it takes several years to reach that peak.

Upside scenario

Our upside scenario includes $7 in value for the US and EU opportunity. We assume peak Afrezza sales of ~$6B in the US and peak Afrezza sales of ~$3B ex-US. This results in profit split revenue of over $2B. We also assume a faster ramp and higher peak sales potential for Afrezza.

Downside scenario

Our $0 per share downside scenario assumes that Afrezza fails due to either a perceived lack of equivalent efficacy to an injected insulin, safety overhang from the prior Exubera (Pfizer) experience, or dosing complexity.

Investment summary

Mannkind (MNKD) is leveraging its inhaled drug delivery platform to create better ways to deliver existing drugs. Afrezza, the lead drug candidate, is an inhaled insulin designed for meal-time use. The diabetes market is large and growing, and upon approval Afrezza could be the most convenient and fastest-acting alternative to injected prandial insulin. The device is small, discrete, and easy to use and maintain. However, launch has been slow and turn-around could require more investment and time by partner SNY.

Potential catalysts for the stock

Our investment view is driven by:

- **EU filing plans in 2015/2016:** MNKD will count on Sanofi for an MAA filing where visibility on approval would be a positive.
- **Afrezza post-approval study details,** timelines have implications for label expansion.
- **Launch trajectory over the next 12-18 months**.

Risks to our investment thesis

- **Sales ramp could beat expectations.** Physicians and patients could be quicker to adopt Afrezza than expected.
- **SNY could remain committed and invest more into Afrezza clinical and commercial development.**

Key questions and debates for MNKD

1. Is demand for Afrezza, as reflected by weekly and monthly prescriptions, going to grow?

In the proprietary survey we conducted five things stood out: 1) doctors prescribed Afrezza when patients asked for it; 2) not many patients were asking for Afrezza; 3) when Afrezza was prescribed payers tended to reject a majority of prescriptions; 4) more prescriptions were lost when doctors did not always follow up; and 5) potential theoretical market opportunity remained large. Therefore, without ironing out reimbursement or contracting with payers and making patients more aware of Afrezza, demand is unlikely to pick up.

2. Is SNY really committed to Afrezza marketing and development?

Sales so far have been sluggish at best, so SNY's commitment to the company is of great importance. SNY also needs to conduct post-approval studies, including a large and long safety study for Afrezza. Furthermore, as part of its partnership with MNKD, it has put several hundred million dollars in capital at risk near term and even more longer term for launching and developing Afrezza. However, SNY has neither announced the start of the long-term safety study nor emphasized its commitment to Afrezza and unless sales grow, the Street is likely to become more skeptical as to SNY's outlook and commitment for Afrezza.

3. Will doctors and patients accept Afrezza, an inhaled insulin?

As part of launch prep, SNY conducted patient-preference studies that showed 60% of those starting insulin and 57% of those who need more insulin preferred Afrezza's profile. We believe doctors may be more hesitant in their acceptance of Afrezza given that it requires more work for them to train and change their own practices but given the option to put patients on drug sooner and manage their disease at an earlier stage they too could become more enthusiastic, especially as the planned safety study shows clean outcomes. However, this has not yet transpired and our survey at least seemed to indicate that doctors are not putting a majority of their patients on Afrezza.

4. Are Afrezza and Exubera differentiated or is Afrezza going to meet the same fate as Exubera?

Afrezza and Exubera are clearly different drugs with the simplicity, size and ease of use of the Afrezza device superior to Exubera. However, commercially the ramp for Afrezza has lagged even that of Exubera's which is challenging.

Exhibit 221: Expected news flow for MNKD

Timing	Expected News Flow	Program
2015/ 2016	Details on post marketing, label expansion and ex-US regulatory timelines	Afrezza
2015/ 2016	Plans on potential ex-US/ MAA filing	Afrezza
3Q:15	Launch 12U dose	Afrezza
2015	Initiate pipeline development in pulmonary disease, pain, and oncology support	Technosphere platform
2015	Initiate pediatric studies	Afrezza
2015/ 2016	Development plans for 2U dose	Afrezza
2015/ 2016	Afrezza 16U dose sBLA	Afrezza
2015/ 2016	Complete post-approval PK/ PD studies	Afrezza
2015/ 2016	Label update with PK/ PD data	Afrezza
1Q/ 1H:16	Initiate Phase IV safety study	Afrezza
1H:16	Data form dose ranging study	Afrezza

Source: Company reports and RBC Capital Markets estimates

Exhibit 222: MNKD pipeline

Product	Mechanism	Stage	Indication	Partner
Afrezza	Ultra rapid-acting inhaled insulin	Approved	Type 1 and type 2 diabetes	Sanofi
MKC253	Inhaled GLP-1	Phase I completed	Type 2 diabetes	
TBD		Pre-clinical	Pulmonary arterial hypertension	
TBD		Pre-clinical	Pain	

Source: Company reports and RBC Capital Markets estimates

Exhibit 223: Income statement for MNKD

($ in millions, except per share) *Fiscal Year Ends December*	2014A	1Q:15A	2Q:15A	3Q:15A	4Q:15E	2015E	1Q:16E	2Q:16E	3Q:16E	4Q:16E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E
Revenue																		
Milestone	-	-	-	-	-	-	-	-	-	-	-	-	-	-	78.8	78.8	53.8	15.0
Collaboration profit split	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	28.2	42.2	67.8
Other revenue	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Total Revenue	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**78.8**	**106.9**	**95.9**	**82.8**
Operating expenses																		
COGS	-	1.9	5.7	8.1	4.3	20.0	2.8	1.9	1.3	3.1	9.1	13.4	19.7	25.0	30.4	51.8	62.8	81.5
R&D	100.2	9.4	7.7	6.3	8.5	32.0	7.0	6.5	6.0	5.5	25.0	20.0	20.0	21.0	22.0	23.0	24.0	25.0
SG&A	79.4	10.5	10.6	11.5	7.4	40.0	7.4	7.5	7.6	7.6	30.0	29.4	33.0	33.5	34.0	34.5	35.0	35.5
In-process R&D costs	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Goodwill	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Total operating expenses	**179.6**	**21.7**	**24.1**	**26.0**	**20.2**	**92.0**	**17.1**	**15.9**	**14.9**	**16.2**	**64.1**	**62.8**	**72.7**	**79.5**	**86.4**	**109.3**	**121.8**	**142.0**
Operating Income (Loss)	**(179.6)**	**(21.7)**	**(24.1)**	**(26.0)**	**(20.2)**	**(92.0)**	**(17.1)**	**(15.9)**	**(14.9)**	**(16.2)**	**(64.1)**	**(62.8)**	**(72.7)**	**(79.5)**	**(7.6)**	**(2.4)**	**(25.8)**	**(59.2)**
Other income (expense)	1.7	1.4	(0.0)	0.1	-	1.5	-	-	-	-	-	-	-	-	-	-	-	-
Interest income (expense)	(20.4)	(10.3)	(4.8)	(5.9)	(4.9)	(26.0)	(4.9)	(4.9)	(4.9)	(4.9)	(19.5)	(19.5)	(19.5)	(19.5)	(19.5)	(19.5)	(19.5)	(19.5)
Total other income	**(18.8)**	**(8.9)**	**(4.9)**	**(5.9)**	**(4.9)**	**(24.5)**	**(4.9)**	**(4.9)**	**(4.9)**	**(4.9)**	**(19.5)**	**(19.5)**	**(19.5)**	**(19.5)**	**(19.5)**	**(19.5)**	**(19.5)**	**(19.5)**
Pretax Income	**(198.4)**	**(30.7)**	**(28.9)**	**(31.9)**	**(25.0)**	**(116.5)**	**(22.0)**	**(20.8)**	**(19.8)**	**(21.0)**	**(83.6)**	**(82.3)**	**(92.2)**	**(99.0)**	**(27.1)**	**(21.9)**	**(45.3)**	**(78.7)**
Income tax expense	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Net income (loss)	**(198.4)**	**(30.7)**	**(28.9)**	**(31.9)**	**(25.0)**	**(116.5)**	**(22.0)**	**(20.8)**	**(19.8)**	**(21.0)**	**(83.6)**	**(82.3)**	**(92.2)**	**(99.0)**	**(27.1)**	**(21.9)**	**(45.3)**	**(78.7)**
EPS - Basic (GAAP)	**($0.51)**	**($0.08)**	**($0.07)**	**($0.08)**	**($0.06)**	**($0.28)**	**($0.05)**	**($0.04)**	**($0.04)**	**($0.04)**	**($0.18)**	**($0.15)**	**($0.16)**	**($0.15)**	**($0.04)**	**($0.03)**	**($0.07)**	**($0.12)**
EPS - Diluted (GAAP)	**($0.51)**	**($0.08)**	**($0.07)**	**($0.08)**	**($0.06)**	**($0.28)**	**($0.05)**	**($0.04)**	**($0.04)**	**($0.04)**	**($0.18)**	**($0.15)**	**($0.16)**	**($0.15)**	**($0.04)**	**($0.03)**	**($0.07)**	**($0.12)**
Shares (basic)	385.2	398.9	401.0	405.2	444.3	412.4	459.2	470.3	471.5	472.7	468.4	532.1	571.3	644.3	650.7	657.2	663.8	670.5
Shares (diluted)	438.6	443.6	445.7	447.3	479.4	454.0	480.6	491.8	493.0	494.2	489.9	553.8	594.3	670.7	677.4	684.2	691.0	697.9

Source: Company reports and RBC Capital Markets estimates

Valuation

We value MNKD at $1 per share, which includes US and EU profit/expense splits for Afrezza with Sanofi. We assume a US launch in 2015 and EU in 2017. MNKD will retain manufacturing responsibilities while Sanofi is responsible for commercial efforts. We forecast peak Afrezza sales of more than $1B+ WW with peak profit split ~$400M+ for sales in the US and outside the US for MNKD. However, initial ramp costs are high and revenues take time to grow to our peak forecast in this scenario.

Price target impediments

Our price target is dependent solely on the regulatory and commercial success of Afrezza. Given the prior clinical safety and commercial overhangs seen with Pfizer's Exubera, long-term safety is also going to be scrutinized and a worsening of lung function or the emergence of lung cancer would likely impede commercialization. Furthermore, any setbacks in regulatory approvals inside or outside the US or a change in competitive dynamics could all negatively impact our valuation. MNKD's success requires commitment by partner SNY to develop and commercialize Afrezza further so any setbacks could further impact valuation.

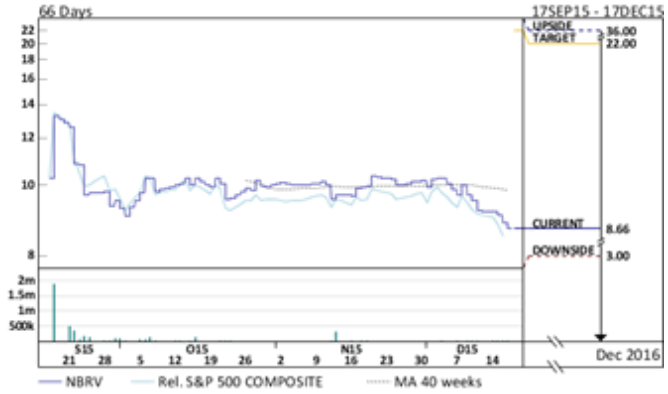
Nabriva Therapeutics AG (NBRV)

Outperform, Speculative Risk

Price Target USD $22.00

Target/Upside/Downside Scenarios

Exhibit 224: Nabriva Therapeutics.



Source: RBC Capital Markets estimates

Target price/base case

We value NBRV at $22 per share, which includes US and ROW royalties on lefamulin. We assign a probability of success of 60% and 50% to CAP and HAP, respectively. We assign a value of ~$15 per share to the CAP and $7 per share to the HAP opportunity. We forecast peak lefamulin sales of $1.5B+ in the US and $675M in the ROW. We currently assign no additional value to the earlier-stage pipeline. Finally, we assume product sales extend into 2033 and include a terminal value based on a terminal growth rate of -50% and a discount rate of 15%.

Upside scenario

Our upside scenario of $36 per share, includes ~$22 per share in value for the CAP opportunity, ~$9 per share in value for the HAP opportunity, and ~$9 for the ABSSSI opportunity. We forecast peak lefamulin sales of ~$2.85B in the US and ~$1.03B in the ROW. We assign a discount rate of 15%, and use a terminal growth rate of -50%.

Downside scenario

Our downside scenario values NBRV at $3 per share, and assumes that NBRV will only be successful in CABP and will achieve less market penetration.

Investment summary

We believe NBRV shares offer potential for significant upside, as the lead product candidate, lefamulin, has a unique mechanism of action and belongs to a new class of antibiotics called pleuromutilins. Lefamulin could be a blockbuster drug in CAP and other bacterial infections, such as HAP/ VAP and ABSSSI. NBRV has secured an SPA for the Phase III study in CAP, reported positive Phase II data in ABSSSI, and shown pre-clinical data that demonstrates lefamulin is active in treatment resistant bacteria. While CAP is the initial focus, the label could expand with HAP/ VAP and other indications. Results from these and additional studies are expected in 2016 and 2017 and beyond.

Millions of patients worldwide are treated for CAP, HAP/ VAP, ABSSSI, and other life-threatening bacterial infections, including a significant proportion who are infected by resistant organisms. We forecast peak sales of lefamulin at ~$1B+ in CAP alone. NBRV owns 100% of the rights to lefamulin and its pipeline worldwide with composition of matter protection for lefamulin into 2028 and likely into 2033 with extensions. Given that antibiotic resistant infections are an unmet need and a focus for clinicians, regulators and national governments, and NBRV's product candidates represent an entirely new class of antibiotic drugs, progress through clinical and regulatory milestones, as well as a partnership, could all be upside catalysts.

Potential catalysts for the stock

- **Lefamulin Phase III interim analysis in CAP in 2016.** This is the first look into the Phase III study, which could show how the trial is tracking vs. assumptions.
- **Lefamulin Phase I data in HAP/VAP in 2016.** This would be the first indication outside of CAP that NBRV could pursue.
- **Lefamulin Phase III data in CAP by YE:17.** Both lefamulin Phase III studies are expected to report top-line data.

Risks to our investment thesis

- **Phase III studies for lefamulin in CAP could fail.** Lefamulin must demonstrate non-inferiority to an active drug.
- **Pipeline and label expansion could suffer setbacks.** We assume successful development in HAP/VAP
- **NBRV could fail to find a partner for lefamulin.**
- **Sales of lefamulin could lag expectations.** Without differentiation and pharmacoeconomics data clinicians and patients could be slow to use lefamulin putting its assumed blockbuster potential at risk.

Key questions and debates for NBRV

1. Is lefamulin differentiated especially in CAP?

Lefamulin belongs to the pleuromutilin class of antibiotics, an entirely new drug class. While many companies have developed antibiotics against severe skin infections, there is comparatively less drug development targeting CAP. Furthermore, since this is the first time a drug from the pleuromutilin class is being administered systemically to human patients, the chances of seeing or developing bacterial resistance are low.

2. Will the planned phase III trials in CAP work?

Our confidence in the efficacy of lefamulin in CAP rests in its in vitro and in vivo activity profile as well as safety and efficacy data from the completed Phase II study in ABSSSI patients that showed favorable efficacy and safety. To date, lefamulin has demonstrated broad-spectrum activity against gram-positive, atypical and even some gram-negative pathogens, and proven safe and effective in human patients treated with the intravenous and oral dosage forms.

3. Can lefamulin's label be expanded to include additional indications?

Most antibiotic drugs are approved for more than one indication. NBRV has already evaluated lefamulin in ABSSSI in a Phase II study and announced plans to study it in HAP/VAP in a Phase I study. Therefore, it seems likely that the label could expand to include additional patient types and infections.

4. What is the probability that timelines can slip?

Phase III studies in CAP conducted by other companies have taken less than two years from start to finish. NBRV announced in November 2015 that they initiated first Phase III and the second Phase III study in 2016 with both reading out by the end of 2017. In short, timelines appear reasonable, especially for the first Phase III study, which is being conducted under an SPA and is needed to file for approval along with data from the completed phase II.

The company appears fully funded through Phase III data in CAP in late 2017.

5. Will NBRV need to raise capital again?

However, prior to commercialization and likely additional late-stage studies in HAP/VAP or ABSSSI, NBRV could require additional funding. Future capital needs could be a function of the amount of non-dilutive financing NBRV secures from partners or governmental agencies such as BARDA; clinical success NBRV sees for lefamulin in CAP or other indications; progress in its earlier-stage pipeline; or to further improve its strategic position in any partnership or takeout negotiations.

Exhibit 225: Expected news flow for NBRV

News Flow

Timing	Description	Product
2H:15	Initiate first Phase III clinical trial in CABP	Lefamulin
2H:15	Initiate Phase I clinical trial in VABP	Lefamulin
1H:16	Initiate second Phase III clinical trial in CABP	Lefamulin
1H:17	Complete Phase I clinical trial in VABP	Lefamulin
2H:17	Initiate Phase II clinical trial in HABP	Lefamulin
Late 2017	Top-line data available for both Phase III trials in CABP	Lefamulin
2018	Submit NDA to FDA and MAA to EMA for CABP	Lefamulin

Source: Company reports and RBC Capital Markets estimates

Exhibit 226: NBRV pipeline

Pipeline

Product	Stage	Indication
Lefamulin (IV/ oral)	Phase III planned	Community-acquired bacteria pneumonia (CABP)
Lefamulin (IV/ oral)	Phase II completed	Acute bacterial skin structure infections (ABSSSI)
Lefamulin (IV)	Phase I planned	Hospital-acquired bacterial pneumonia (HABP)/Ventilator-associated bacterial pneumonia (VABP)
Lefamulin (IV/ oral)	Formulation development ongoing	Pediatric indications
Lefamulin (IV/ oral)	Pre-clinical	STIs, osteomyelitis, prosthetic joint infections
BC-7013	Phase I completed	Uncomplicated skin and skin structure infections (uSSSIs)
Extended Spectrum Pleuromutilins (ESPs)	Discovery	Complicated urinary tract infections (cUTIs)/ Complicated intra-abdominal infections (cIAI)

Source: Company reports and RBC Capital Markets estimates

Exhibit 227: Income statement for NBRV

(EUR in millions, except per share) Fiscal Year Ends December	3Q:15A	4Q:15E	2015E	1Q:16E	2Q:16E	3Q:16E	4Q:16E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E
Revenue															
Lefamulin	-	-	-	-	-	-	-	-	-	-	26.61	55.63	116.30	217.99	296.87
Ex-US Royalties															
Lefamulin - EU Royalties	-	-	-	-	-	-	-	-	-	-	-	3.53	7.06	14.15	25.41
Total Lefamulin Revenue (EUR MM)	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**26.61**	**59.16**	**123.36**	**232.14**	**322.28**
Other income															
Other income	1.17	1.17	3.69	0.70	0.73	0.75	0.83	3.00	4.00	4.00	4.00	4.00	4.00	4.00	4.00
Other gain/(loss), net	-	-	-	0.02	0.02	0.02	(0.06)	-	-	-	-	-	-	-	-
Total other income	**1.17**	**1.17**	**3.69**	**0.72**	**0.75**	**0.77**	**0.77**	**3.00**	**4.00**	**4.00**	**4.00**	**4.00**	**4.00**	**4.00**	**4.00**
Operating expenses															
R&D	7.09	9.38	23.27	6.50	7.50	8.50	11.95	34.45	40.27	44.75	40.27	45.00	47.50	50.00	52.50
SG&A	1.60	1.92	5.82	1.60	1.70	1.80	2.06	7.16	10.29	34.68	35.13	45.87	48.55	52.35	52.80
Acquired in-process R&D	(0.15)	(0.15)	(0.31)	-	-	-	-	(0.31)	(0.31)	(0.31)	(0.31)	(0.31)	(0.31)	(0.31)	(0.31)
COGS	-	-	-	-	-	-	-	-	-	-	2.66	5.56	11.63	21.80	29.69
Total operating expenses	**8.53**	**11.14**	**28.78**	**8.10**	**9.20**	**10.30**	**14.01**	**41.31**	**50.26**	**79.12**	**77.75**	**96.12**	**107.37**	**123.85**	**134.68**
Operating Income (Loss)	**(7.36)**	**(9.98)**	**(25.09)**	**(7.38)**	**(8.46)**	**(9.53)**	**(13.25)**	**(38.31)**	**(46.26)**	**(75.12)**	**(47.14)**	**(32.96)**	**19.99**	**112.29**	**191.60**
Finance income (expenses)															
Finance income	0.00	0.00	6.16	0.30	0.31	0.32	0.33	1.26	1.29	1.31	1.34	1.36	1.39	1.42	1.45
Finance expenses	(0.27)	(0.71)	(13.45)	(0.71)	(0.71)	(0.71)	(0.71)	(2.86)	2.83	-	-	-	-	-	-
Total finance income (expense), net	**(0.26)**	**(0.71)**	**(7.29)**	**(0.41)**	**(0.40)**	**(0.39)**	**(0.38)**	**(1.60)**	**4.11**	**1.31**	**1.34**	**1.36**	**1.39**	**1.42**	**1.45**
Pretax Income	**(7.63)**	**(10.69)**	**(32.39)**	**(7.79)**	**(8.86)**	**(9.92)**	**(13.63)**	**(39.90)**	**(42.14)**	**(73.81)**	**(45.80)**	**(31.60)**	**21.38**	**113.71**	**193.05**
Income tax expense	0.23	-	0.22	-	-	-	-	-	-	-	-	-	(7.48)	(39.80)	(67.57)
Net income (loss)	**(7.40)**	**(10.69)**	**(32.17)**	**(7.79)**	**(8.86)**	**(9.92)**	**(13.63)**	**(39.90)**	**(42.14)**	**(73.81)**	**(45.80)**	**(31.60)**	**13.90**	**73.91**	**125.48**
EPS - Basic (GAAP)	(€ 6.55)	(€ 0.50)	**(€ 5.42)**	(€ 0.37)	(€ 0.41)	(€ 0.46)	(€ 0.63)	**(€ 1.85)**	**(€ 1.32)**	**(€ 2.26)**	**(€ 1.20)**	**(€ 0.81)**	**€ 0.35**	**€ 1.82**	**€ 3.03**
EPS - Diluted (GAAP)	(€ 6.55)	(€ 0.50)	**(€ 5.42)**	(€ 0.37)	(€ 0.41)	(€ 0.46)	(€ 0.63)	**(€ 1.85)**	**(€ 1.32)**	**(€ 2.26)**	**(€ 1.20)**	**(€ 0.81)**	**€ 0.33**	**€ 1.73**	**€ 2.88**
Shares (basic)	1.13	21.16	5.94	21.27	21.37	21.48	21.59	21.58	32.02	32.66	38.31	39.08	39.86	40.66	41.47
Shares (diluted)	1.1	23.3	6.49	23.39	23.5	23.6	23.7	23.70	34.14	34.78	40.43	41.20	41.98	42.77	43.59

Source: Company reports and RBC Capital Markets estimates

Valuation

We value NBRV at $22 per share, which includes US and ROW sales of lefamulin. We assign a probability of success of 60% and 50% to CABP and HAP indications, respectively. We assign a value of ~$15 per share to the CABP and $7 per share to the HAP opportunity. We assume a US launch in 2019 and an ROW launch in 2020. Currently, we assume that NBRV will sell lefamulin in the US and a partner will commercialize these compounds outside the US. We

forecast peak lefamulin sales of ~$1.5B in the US and $675M in the ROW. We currently assign no additional value to the earlier-stage pipeline. Finally, we assume product sales extend into 2033 and include a terminal value based on a terminal growth rate of -50% and a discount rate of 15%.

Price target impediments

Our price target is dependent on the clinical, regulatory, and commercial success of lefamulin, largely in CAP but also in HAP/VAP. Data from the Phase III study for lefamulin is expected in 2017. Failure to demonstrate efficacy or safety in these studies would be a significant setback as would failure to advance to the next stage of clinical trials. Furthermore, any setbacks in regulatory approvals in the US or EU, delay in launch, failure to secure a partnership outside the US, increased competition or other limitations to the market potential of lefamulin could negatively impact our valuation.

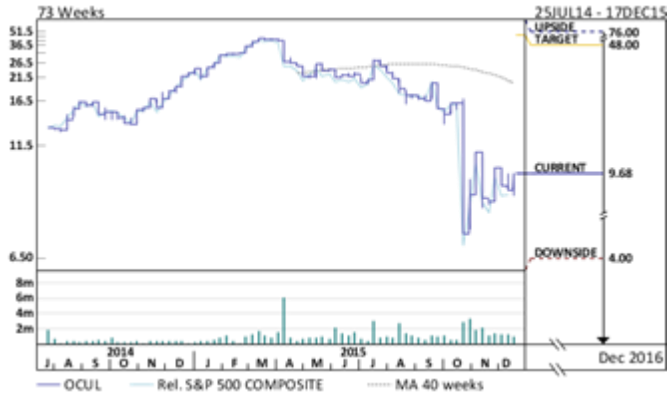
Ocular Therapeutix (OCUL)

Outperform, Speculative Risk

Price Target USD $48.00

Target/Upside/Downside Scenarios

Exhibit 228: Ocular Therapeutix.



Source: RBC Capital Markets estimates

Target price/base case

We value OCUL at $48, which includes US and EU sales with a probability of success of 85% to ReSure (~$3/share), 75% to OTX-DP inflammation (~$3/share), 60% to OTX-DP allergy (~$4/share), 55% to OTX-DP dry eye (~$8/share), 60% to OTX-TP glaucoma for (~$15/share), and 25% (prev. 20%) to Anti-VEGF hydrogel (~$16/share). We forecast US and ex-US combined peak sales of ReSure, OTX-DP inflammation, OTX-DP allergic conjunctivitis, OTX-DP dry eye, OTX-TP glaucoma, and anti-VEGF hydrogel at ~$8B and ~$10B, respectively.

Upside scenario

Our upside scenario at $76 includes US and EU sales with a probability of regulatory and commercial success of 70% to ReSure (~$4/share), 60% to OTX-DP inflammation (~$5/share), 55% to OTX-DP allergy (~$5/share), 30% to OTX-DP dry eye (~9/share), 45% to OTX-TP glaucoma for (~$19/share), and 50% to anti-VEGF hydrogel (~$32/share). We forecast US and ex-US combined peak sales of ReSure, OTX-DP inflammation, OTX-DP allergic conjunctivitis, OTX-DP dry eye, OTX-TP glaucoma, and anti-VEGF hydrogel at ~$9B+ and ~$11B+, respectively.

Downside scenario

Our downside scenario is $4 and ascribes no value to OTX-TP and anti-VEGF programs.

Investment summary

We believe OCUL shares offer the potential for upside as the hydrogel, sustained technology platform lowers clinical and development risk, allows multiple shots at success and the pipeline to be diversified, and increases the chances of a candidate making it through the clinic and onto the market. OTX-DP is in Phase III studies for inflammation and pain, and in Phase II studies for allergic conjunctivitis. OTX-TP is in a Phase IIb study for glaucoma, having posted promising Phase IIa, and earlier-stage compounds represent upside optionality. Results from these studies are expected in 2014 and 2015, assuming progress going forward through 2017. Target markets represent millions of patients worldwide, and we forecast peak sales of OCUL's products totaling ~$1.7B.

OCUL owns 100% of the rights to its pipeline, and patent protection extends into 2030, meaning the company is free to commercialize itself, partner, or to be acquired. Because ophthalmology remains an attractive therapeutic area and OCUL's product candidates have potential for improved dosing, convenience as well as safety advantages, progress through clinical and regulatory milestones, and any partnerships could be value-enhancing.

Potential catalysts for the stock

- **Phase IIb data for OTX-TP in 3Q/4Q:15:** Potential to show efficacy and three-month plug retention for glaucoma.
- **Phase III data for OTX-DP by YE:15/ 1Q:16:** Prior phase II data in allergic conjunctivitis mixed.
- **Potential OTX-DP approvals and launches in 2016/ 2017 in the US and EU.**
- **ReSure sales** could be higher than expected.

Risks to our investment thesis

- **Pivotal Phase III and earlier-stage studies could fail:** Phase II and Phase III data for OTX-DP are expected in 2014-2017 and one or more products could fail.
- **Sales ramp of punctum plug technology could be slow** as clinicians fail to adopt, payers put up hurdles for reimbursing branded drugs, and cheaper generics hamper market penetration.
- Sales of ReSure Sealant could lag sales expectations as surgeons maintain current practices.
- **OCUL could fail to find a partner** for product commercialization outside the US.
- Other sustained-release technologies could preempt OCUL's platform, thereby leading to a move away from hydrogel-based products.

Key questions and debates for OCUL

1. What are the chances of the third Phase III Dextenza (OTX-DP) post-cataract ocular inflammation and pain trials working

Generally, the trial should work because steroid eye drops are known to reduce pain and inflammation post eye surgery. More specifically, of the first two Phase III studies completed one showed a stat sig benefit in both pain and inflammation while the second showed a stat sig benefit in pain only. So the third Phase III study, which is designed with the shortcomings of the second Phase III in mind, has a high chance of being successful. Dextenza (OTX-TP) has also succeeded in a Phase III study in allergic conjunctivitis (second Phase III ongoing) that also validates its activity.

2. Is OTX-TP still a viable candidate?

Phase II data for OTX-TP in glaucoma showed good retention and predictable efficacy for OTX-TP, but a better than expected response for the timolol+placebo plug arm. The complicating factor here is that a Phase III trial should look similar in design to the complete Phase II and based on data seen so far, the bar for success is now much higher than previously. However, OCUL has yet to hold an end of Phase II meeting with the FDA to think of ways it would address this better than expected timolol response, such as not using a placebo plug for the timolol arm and reflecting more a real world situation.

3. Is the competitive landscape for anti-glaucoma drugs becoming crowded?

There appear to be many more companies with long acting prostaglandins in development, with the lead belonging to Allergan that has a 3-4 month+ insert for bimatoprost in Phase III studies. OCUL still appears to be second and while the duration of effect of 2.5-3 months does not appear as long as what some of the other companies are claiming, competitors also have reported mostly only short term results. Furthermore, OCUL has opted for a non-invasive procedure, i.e., placement into the punctum. It is just as capable of developing an insert that goes into the eye and lasts longer, in our view.

4. Is a sustained release anti-VEGF viable and does it lead to upside for OCUL?

The anti-VEGF hydrogel depot program is where OCUL is collaborating with companies in the wet AMD space and advancing plans for its own small molecule depot program. Timing of a partnership is unpredictable – Roche's plans to advance RG3635 into Phase II could have dampened expectations somewhat too - but OCUL's proprietary plans could start panning out in 2017 and a partnership is not out of the question as here the main decision appears to be over terms and control. Either development should mean upside for OCUL.

5. Does OCUL need more cash prior to launching Dextenza (OTX-DP)?

Since the Dextenza NDA is filed and accepted for review by the FDA for the treatment of post-ocular surgical pain, there is more than sufficient capital through that event. OCUL could begin building its sales force ahead of a full launch in 2017 when the sNDAs for inflammation and possibly allergic conjunctivitis could be filed and reviewed so we think more capital is not required for the initial launch but it will be likely for a full launch and to advance other programs.

Exhibit 229: Expected news flow for OCUL

Timing	Expected News Flow	Program
4Q:15	File NDA in post-cataract pain	Dextenza (OTX-DP)
4Q:15	Initiate 3rd Phase III in cataract pain/ inflamm.	Dextenza (OTX-DP)
4Q:15	Potential Phase II data in inflammatory dry eye	Dextenza (OTX-DP)
YE:15	Initiate second Phase III study in allergic conjunctivitis	Dextenza (OTX-DP)
2015/ 2016	Update on clinical program or partnership(s)	IHD-VEGF
YE:15/ 1H:16	Initiate 2nd Phase III trial in allergic conjunctivitis	Dextenza (OTX-DP)
1Q:16	End of Phase II meeting for glaucoma	OTX-TP
2H:16	Initiate Phase III study in glaucoma	OTX-TP
1H:16	Phase III 'go/ no-go' decision in dry eye	Dextenza (OTX-DP)
Mid-2016	Second Phase III results in allergic conjunctivitis	Dextenza (OTX-DP)
Mid-/ 3Q:16	Phase III data in cataract pain/ inflamm. (3rd Phase III)	Dextenza (OTX-DP)
YE:16	File sNDA/ MAA in allergic conjunctivitis	Dextenza (OTX-DP)
3Q/ 4Q:16	FDA decision on NDA in cataract pain	Dextenza (OTX-DP)
YE:16/ 1Q:17	US launch in post-cataract/ surgical pain	Dextenza (OTX-DP)
2016	Update on pre-clinical back-of-the-eye program	Anti-VEGF/ TKI
2016/ 2017	Potential anti-VEGF plans	Anti-VEGF/ TKI
1H/ Mid-2017	Potential sNDA approval for cataract pain/ inflammation and conjunctivitis	Dextenza (OTX-DP)
1H:17	Phase III results in glaucoma	OTX-TP
2H:17/ 1Q:18	File NDA/ MAA in glaucoma	OTX-TP
2017/ 2018	Potential Phase I data in wAMD	Anti-VEGF/ TKI
2017/ 2018	Update on clinical program or partnership(s)	IHD-VEGF
2H:18/ 1Q:19	Potential NDA approval for glaucoma	OTX-TP

Source: Company reports and RBC Capital Markets estimates

Exhibit 230: OCUL pipeline

Product	Mechanism	Stage	Indication
ReSure	Ocular sealant	FDA approved	Sealant post cataract surgery
Dextenza (OTX-DP)	Dexamethasone plug	Pre-NDA (pain)	Post-cataract/ surgical inflammation and pain
		3rd Phase III planned	
		Phase III	Allergic conjunctivitis
		Phase II	Inflammatory dry eye
OTX-TP	Travoprost plug	Phase II	Glaucoma
OTX-MP	Moxifloxacin plug	Phase I	Bacterial conjunctivitis
Intravitreal Hydrogel Depot (anti-VEGF)	Sustained release anti-VEGF depot	Pre-clinical	Wet AMD/ RVO/ DME
Intravitreal Hydrogel Depot (TKI)	Sustained release TKI	Pre-clinical planned	Wet AMD/ RVO/ DME

Source: Company reports and RBC Capital Markets estimates

Exhibit 231: Income statement for OCUL

($ in millions, except per share) Fiscal Year Ends December	2014A	1Q:15A	2Q:15A	3Q:15A	4Q:15E	2015E	1Q:16E	2Q:16E	3Q:16E	4Q:16E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E
Revenue																		
ReSure	0.4	0.2	0.3	0.4	0.6	1.6	0.8	0.9	1.0	39.8	3.6	11.0	21.0	39.8	59.4	70.1	78.0	89.5
OTX-DP Inflammation	-	-	-	-	-	-	-	-	-	41.3	-	5.0	20.2	41.3	63.2	80.6	93.1	106.2
OTX-DP allergy	-	-	-	-	-	-	-	-	-	27.7	-	3.3	13.6	27.7	56.4	86.4	102.8	119.8
OTX-DP dry eye	-	-	-	-	-	-	-	-	-	-	-	-	-	-	23.4	71.7	121.9	174.1
OTX-TP glaucoma	-	-	-	-	-	-	-	-	-	14.4	-	-	-	14.4	45.9	97.1	205.7	326.8
ROW Royalties	-	-	-	-	-	-	-	-	-	4.5	-	0.1	1.2	4.5	12.6	25.5	42.6	66.8
Other	0.3	0.2	0.1	0.0	(0.0)	0.3	-	-	-	-	-	-	-	-	-	-	-	-
Total Revenue	**0.8**	**0.4**	**0.5**	**0.4**	**0.6**	**1.9**	**0.8**	**0.9**	**1.0**	**127.7**	**3.6**	**19.4**	**56.1**	**127.7**	**260.9**	**431.3**	**644.1**	**883.1**
Operating expenses																		
Royalty expense	-	-	-	-	0.0	0.0	0.0	0.0	0.0	4.9	0.1	0.8	2.2	4.9	9.0	13.4	19.2	25.7
COGS	0.1	0.1	0.1	0.1	0.1	0.3	0.1	0.1	0.2	18.5	0.5	2.9	8.2	18.5	37.2	60.9	90.2	122.5
R&D	18.9	4.7	6.7	8.3	6.8	26.5	7.5	8.3	9.0	52.5	34.3	40.0	50.0	52.5	55.0	57.5	60.0	62.5
SG&A	8.9	2.8	3.3	3.2	3.9	13.2	5.0	5.5	10.0	70.0	38.0	52.5	65.0	70.0	75.0	80.0	128.8	176.6
Total operating expenses	**27.9**	**7.5**	**10.1**	**11.6**	**10.8**	**40.0**	**12.6**	**13.9**	**19.2**	**145.9**	**72.9**	**96.2**	**125.4**	**145.9**	**176.2**	**211.7**	**298.2**	**387.3**
Operating Income (Loss)	**(27.1)**	**(7.1)**	**(9.6)**	**(11.2)**	**(10.3)**	**(38.2)**	**(11.9)**	**(13.0)**	**(18.2)**	**(18.2)**	**(69.3)**	**(76.8)**	**(69.4)**	**(18.2)**	**84.6**	**219.6**	**345.9**	**495.9**
Interest income	0.0	0.0	0.0	0.1	0.0	0.1	0.0	0.0	0.0	0.1	0.1	0.1	0.1	0.1	0.2	0.2	0.2	0.2
Interest expense	(1.1)	(0.5)	(0.4)	(0.4)	(0.1)	(1.4)	(0.1)	(0.1)	(0.1)	(0.5)	(0.2)	(0.5)	(0.5)	(0.5)	(0.5)	(0.5)	(0.5)	(0.5)
Other income (expense)	(0.4)	-	0.0	0.0	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.4)	(0.4)	(0.4)	(0.4)	(0.4)	(0.4)	(0.4)	(0.4)	(0.4)
Total other income	**(1.6)**	**(0.5)**	**(0.4)**	**(0.4)**	**(0.1)**	**(1.3)**	**(0.1)**	**(0.1)**	**(0.1)**	**(0.8)**	**(0.5)**	**(0.8)**	**(0.8)**	**(0.8)**	**(0.8)**	**(0.7)**	**(0.7)**	**(0.7)**
Pretax Income	**(28.7)**	**(7.6)**	**(10.0)**	**(11.5)**	**(10.4)**	**(39.5)**	**(12.0)**	**(13.2)**	**(18.3)**	**(19.0)**	**(69.8)**	**(77.6)**	**(70.2)**	**(19.0)**	**83.9**	**218.9**	**345.2**	**495.2**
Income tax expense	-	-	-	-	-	-	-	-	-	-	-	-	-	-	29.4	76.6	120.8	173.3
Net income (loss)	**(28.7)**	**(7.6)**	**(10.0)**	**(11.5)**	**(10.4)**	**(39.5)**	**(12.0)**	**(13.2)**	**(18.3)**	**(19.0)**	**(69.8)**	**(77.6)**	**(70.2)**	**(19.0)**	**54.5**	**142.3**	**224.4**	**321.9**
EPS - Basic (GAAP)	**($2.69)**	**($0.35)**	**($0.45)**	**($0.47)**	**($0.42)**	**($1.70)**	**($0.48)**	**($0.52)**	**($0.71)**	**($0.54)**	**($2.73)**	**($2.50)**	**($2.24)**	**($0.54)**	**$1.55**	**$4.00**	**$6.25**	**$8.87**
EPS - Diluted (GAAP)	**($2.69)**	**($0.35)**	**($0.45)**	**($0.47)**	**($0.42)**	**($1.70)**	**($0.48)**	**($0.52)**	**($0.71)**	**($0.54)**	**($2.73)**	**($2.50)**	**($2.24)**	**($0.54)**	**$1.42**	**$3.65**	**$5.66**	**$7.98**
Shares (basic)	10.7	21.4	22.2	24.7	25.0	23.3	25.2	25.5	25.7	34.9	25.6	31.0	31.3	34.9	35.2	35.6	35.9	36.3
Shares (diluted)	12.5	23.2	24.1	26.6	26.9	25.3	27.2	27.5	27.8	37.7	27.8	33.4	33.9	37.7	38.3	39.0	39.6	40.4

Source: Company reports and RBC Capital Markets estimates

Valuation

We arrive at our $48 price target using a sum-of-the parts analysis for OCUL shares. The primary components of our valuation include OCUL's ReSure sealant, OTX-DP for inflammation, OTX-DP for allergy, OTX-DP for dry eye, anti-VEGF hydrogel, and OTX-TP for glaucoma product sales in the US and royalty revenues from sales in ROW. Our base case, upside, and downside scenarios use a discount rate of 15% to reflect potential clinical and commercial risk and assign a probability of success of the clinical and commercial rollout of ReSure, OTX-DP for inflammation, OTX-DP for allergic conjunctivitis, and OTX-TP for glaucoma.

Price target impediments

Our price target is dependent on the clinical, regulatory, and commercial success of the ReSure sealant, OTX-DP inflammation, OTX-DP allergy, OTX-DP dry eye, anti-VEGF hydrogel, and OTX-TP glaucoma. The phase IIa clinical trial for OTX-TP has been completed and a Phase IIb clinical trial in OTX-TP is expected in 4Q:15. Failure to demonstrate efficacy or safety in any of these studies would be a significant setback. Furthermore, any setbacks in regulatory approvals in the US or EU, delay in launch, failure to secure a partnership outside the US, increased competition, or other limitations to the market potential of these products due to better efficacy and/or safety outcomes or pricing pressure due to the availability of generic drugs for glaucoma could negatively affect our valuation.

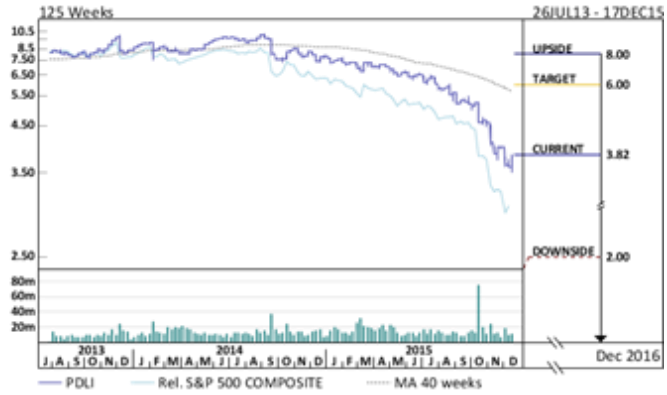
PDL BioPharma Inc. (PDLI)

Sector Perform

Price Target USD $6.00

Target/Upside/Downside Scenarios

Exhibit 232: PDL BioPharma Inc.



Source: RBC Capital Markets estimates

Target price/base case

Price target/base case: $6. We arrive at our price target using a product level DCF valuation. Our product level NPV assigns a value of ~$2/share to the Direct Flow Medical, Paradigm Spine, Kaleo, Careview, and Visc. Bros deal while assigning ~$2/share to the Ariad, Depomed, and Cerdelga royalty. We also include ~$2 for the Queens patent royalty and future deals.

Upside scenario

Our $8 upside includes solanezumab for Alzheimer's and future deals for an additional ~$1/ share.

Downside scenario

Our $2 downside scenario assumes cash per share.

Investment summary

PDLI is a unique asset in biotech, collecting royalties on several of the industry's biggest blockbusters, maintaining an extremely low-cost structure, and distributing the cash flow to investors. PDLI is committed to paying a $0.60/year dividend for the foreseeable future and to using any excess cash to procure more revenue streams to continue paying dividends. The company has closed several transactions and is expected to continue doing so. The primary risk to PDLI comes from lower-than-forecast sales and deals not generating expected returns.

Potential catalysts for the stock

Our investment view is driven by:

- Quarterly financial results.
- Favorable deals with good economics.
- Positive solanezumab Phase III data.

Risks to our investment thesis

- Failure of partnered compounds to gain clinical or regulatory success.
- Lower-than-forecast sales and associated royalties.

Key questions and debates for PDLI

1. How safe is PDLI's ability to pay dividends going forward?

While total revenues could decline once the Queens et al-related royalties go away in 2016, current cash, future revenues, and visibility on ongoing deals gives us confidence that the ability to pay dividends of $0.60 per year extends beyond 2018+. PDLI typically announces its dividend payout decision in the first quarter. There is at least a theoretical chance that the dividend could be reduced but a payout ratio of 5%-10% would still be higher than that of many dividend-paying companies.

2. What's PDLI's business development track record to date?

The track record is favorable, with a low rate of attrition. The company has completed 15 deals so far, with potentially two at risk. The Lensar deal seems back on track, with Lensar recently acquired by Alphaeon, and Wellstat and Kaleo still need resolution. Arguably, at times these road bumps are the result of unexpected developments such as for Glumetza and Kaleo.

3. Can PDLI keep finding high-quality deals?

Drug and device development is a capital-intensive business that requires upfront cash either to conduct clinical trials or to launch products. As such, given the dynamics of the healthcare sector, specifically biotech medical device companies, we believe PDLI will be able to find opportunities where its prior expertise in biotech is likely to generate a positive return.

4. What types of returns does PDLI seek and do current deal structuers allow room for upside?

PDLI has disclosed the pre-tax IRR for Merus at 15%, Axogen at 24%, Durata at 21% and Avinger at 13% for an average of 18%, which are all completed transactions. Though the economics of the loan deals are fixed, PDLI has also undertaken royalty deals, which could lead to upside. The Glumetza-related Depomed deal is one example as is the Cerdelga deal with the University of Michigan. Should sales of these products exceed Street expectations, PDLI stands to reap the rewards of the upside. PDLI could also receive royalties on future sales of solanezumab, which is in Phase III trials by LLY for Alzheimer's disease and is a high risk/high reward opportunity.

5. Is the company sufficiently funded or does it need further capital to do more deals?

PDLI may be opportunistic about raising more capital, especially if their transactions are successful and if it were to compete against other companies to secure larger transactions. However, it could also partner with others to close larger-sized deals.

Exhibit 233: Expected news flow for PDLI

Timing	Expected News Flow	Program
2015	Quarterly execution	
2015/ 2016	More revenue generating transactions	
YE:15/ 1H:16	WellStat and Lensar resolution update	
1Q:16	Annual dividend announcement	
YE:16/early 2017	Potential Phase III data in Alzheimer's disease	Solanezumab

Source: Company reports and RBC Capital Markets estimates

Exhibit 234: PDLI pipeline

Product	Indication	Status	Partner
Proprietary Royalty/Revenue Generating Assets			
Enablex	Overactive bladder	Marketed	Merus
Several	Peripheral nerve repair	Marketed	AxoGen
POC diagnostic	Point-of-care diagnostic	Development	Wellstat Diagnostics
Roche Royalty Bearing Assets			
Herceptin	Breast cancer	Marketed	Roche
Avastin	Colon, lung, brain cancer	Marketed	Roche
Lucentis	AMD, RVO	Marketed	Roche
Xolair	Asthma	Marketed	Roche
Actemra	Rheumatoid arthritis	Marketed	Roche
Pertuzumab	Breast cancer	Phase III	Roche
T-DM1	Breast cancer	NDA / MAA filed	Roche
Obinutuzumab (afutuzumab; GA101)	NHL, CLL	Phase III	Roche
Ocrelizumab	Multiple sclerosis	Phase II	Roche
Lebrikizumab	Asthma	Phase II	Roche
Non-Roche Royalty Bearing Assets			
Auvi-Q	Anaphylaxis	Marketed	Kaleo Inc. (SNY)
EVZIO	Opioid overdose	Marketed	Kaleo Inc.
Tysabri	Multiple sclerosis	Marketed	Biogen/Elan
Cerdelga	Gaucher disease type 1	Marketed	Sanofi/ U of M
Solanezumab	Alzheimer's disease	Phase III	Eli Lilly
Daclizumab	Multiple sclerosis	Phase III	Abbott/Biogen
Farletuzumab	Ovarian cancer	Phase III	Eisai
Datoluzumab	Colorectal cancer	Phase II	Merck

Source: Company reports and RBC Capital Markets estimates

Exhibit 235: Income statement for PDLI

($ in MM; except per share)	2014E	Q1:15E	Q2:15A	Q3:15A	Q4:15E	2015E	Q1:16E	Q2:16E	Q3:16E	Q4:16E	2016E	2017E	2018E	2019E	2020E
Revenues:															
Total Royalties	486.9	127.8	116.9	119.2	96.8	460.7	107.2	11.9	0.0	0.0	119.1	0.0	0.0	0.0	0.0
Royalty rights - change in fair value	45.7	11.4	12.2	(4.3)	24.3	43.6	16.1	17.6	19.0	20.5	73.3	40.5	53.6	86.9	88.4
Interest revenue	48.0	10.5	9.0	9.1	9.4	38.0	10.1	11.0	11.9	12.8	45.7	40.3	23.2	6.9	1.8
License and Other	0.6	0.0	0.0	0.6	0.0	0.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total Revenues	581.2	149.7	138.1	124.6	130.5	542.9	133.4	40.5	30.9	33.3	238.0	80.9	76.9	93.7	90.2
Expenses:															
Cost of Royalty Revenues	0.0	0.0	0.0	0.0	0.0		0.0	0.0	0.0	0.0					
General and Administrative Expenses	34.9	7.7	7.4	8.5	0.5	24.0	5.1	5.5	6.0	6.4	23.0	24.0	25.0	26.0	26.0
Operating Income (Loss)	546.3	142.0	130.6	116.2	130.1	518.9	128.3	34.9	24.9	26.9	215.0	56.9	51.9	67.7	64.2
Other Income/(Expense), Net	(45.0)	(8.5)	(7.1)	(5.8)	(2.9)	(24.3)	(2.9)	(2.9)	(2.9)	(2.9)	(11.7)	(11.7)	(2.7)	0.3	0.3
Income Before Taxes	501.3	133.5	123.6	110.4	127.1	494.6	125.4	32.0	22.0	24.0	203.4	45.2	49.2	68.1	64.5
Income Tax Expense	179.0	49.0	45.3	40.9	44.5	179.7	43.9	11.2	7.7	8.4	71.2	13.6	13.5	17.0	16.1
Net income	322.2	84.5	78.3	69.5	82.6	314.9	81.5	20.8	14.3	15.6	132.2	31.6	35.7	51.1	48.4
EPS, Basic (GAAP)	$2.04	$0.52	$0.48	$0.42	$0.51	$1.93	$0.50	$0.13	$0.09	$0.10	$0.81	$0.19	$0.22	$0.31	$0.30
EPS, Diluted (GAAP)	$1.86	$0.50	$0.47	$0.42	$0.50	$1.89	$0.49	$0.13	$0.09	$0.09	$0.80	$0.19	$0.22	$0.31	$0.29
Dividend per common share	$0.60	$0.15	$0.15	$0.15	$0.15	$0.60	$0.15	$0.15	$0.15	$0.15	$0.60	$0.60	$0.60	$0.60	$0.60
Shares Outstanding, Basic	158.2	162.8	163.5	163.6	163.6	163.4	163.6	163.6	163.6	163.7	163.7	163.7	163.8	163.9	164.0
Shares Outstanding, Diluted	173.1	170.4	165.4	163.7	165.5	166.5	165.6	165.6	165.6	165.6	165.6	165.7	165.8	165.9	166.0

Source: Company reports and RBC Capital Markets estimates

Valuation

We arrive at our $6 price target using a product level DCF valuation. Our product level NPV assigns a value of ~$2/share to the Direct Flow Medical, Paradigm Spine, Kaleo, Careview, and Visc. Bros deal while assigning ~$2/share to the Ariad, Depomed, and Cerdelga royalty. We also include ~$2 for the Queens patent royalty and future deals.

Price target impediments

The biggest risks to our price target come from lower than forecast revenue generation, a dividend cut, or failure to successfully close and execute on future deals.

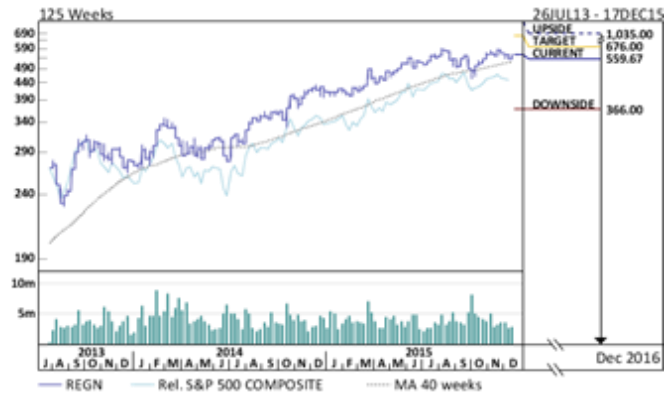
Regeneron Pharmaceuticals, Inc. (REGN)

Outperform

Price Target USD $676.00

Target/Upside/Downside Scenarios

Exhibit 236: Regeneron Pharmaceuticals, Inc.



Source: RBC Capital Markets estimates

Target price/base case

Our $676 per share price target includes Eylea at ~$437/share (US $316/share; EU $99/share; Japan $21/share). For the antibody platform/pipeline we value by individual product builds and by applying a probability adjusted sales multiple discounted back various periods, our value is $219/share ($58/ share for alirocumab, $15 for sarilumab, $66 for dupilumab and $80 for the rest). Next we value Zaltrap at $3/share, Arcalyst at $1/share, and cash/NOLs at $16/share.

Upside scenario

Our upside scenario of $1,035 assumes essentially no Eylea erosion in the outer years supported by the launch of combination drugs. This raises the value of Eylea in our model to $624/share. For the antibody platform/pipeline the value is $391/share ($143/ share for alirocumab, $30/ share for sarilumab, $138/ share for dupilumab and $80 for the rest), and the rest of the valuation items total ~$17/share.

Downside scenario

Our downside scenario of $366 assumes a flatter Eylea trajectory and strong competitor launches. This reduces the value of Eylea in our model to ~$208/share. For the antibody platform/pipeline, the value is $139/share, which assumes lower market shares than base case, and the rest of the valuation items total ~$17/share.

Investment summary

Our Outperform rating is based on ongoing and expected growth in Eylea sales, top- and bottom-line growth, potential longevity of the ophthalmology franchise, a robust late-stage pipeline with several potential blockbuster drugs, several earlier-stage compounds that remain below the radar, and a highly productive and industry-leading antibody-discovery engine. The company's landmark deal with Sanofi provides ~$160M/year to fund antibody discovery for eight years, gives Regeneron 50% of the profits, and defers all development costs until the partnership is profitable. Eylea can be a blockbuster product for several years even if a competitor drug is approved in 2019 or later, if the ophthalmology franchise is growing with combination therapy, and if visibility on several blockbuster potential products, including alirocumab for LDL-cholesterol, sarilumab for rheumatoid arthritis, and dupilumab for eosinophilic asthma and atopic dermatitis, is expected in 2016 and beyond. We view Regeneron as a core long-term biotech holding.

Potential catalysts for the stock

Our investment view is driven by:

- Quarterly results. Expectations stay high for "beats" and "raises" driven by Eylea data.
- Combination Eylea and PDGF-R or ANG2 Phase I data in 2016.
- Dupilumab Phase III data in 2016 and approval in 2016/2017.
- Pipeline progress and updates from earlier, proprietary Phase I and Phase II programs, which are synergistic with SNY partnered launches.
- Technological innovation leading to new or different approaches to treating various genetic and orphan disorders.

Risks to our investment thesis

- **Eylea competitors** could post better-than-expected results in wet AMD, RVO, or DME, and Eylea's sales ramp could be below expectations.
- **Alirocumab** could suffer clinical, regulatory, or commercial setbacks. Competition could prove tougher than expected.
- **Dupilumab and other pipeline candidates** could suffer clinical, regulatory, or commercial setbacks or face tougher-than-expected competition.
- **Expenses could stay high** and SNY could stop funding the pipeline.

Key questions and debates for REGN

1. Can Praluent (alirocumab; anti-PCSK9) launch to ramp and litigation deliver upside?	Both REGN and SNY have set low expectations by highlighting that coverage by payers takes time, the paradigm for when and to whom to prescribe needs to be established, sampling is in effect, and it is a competitive marketplace. There is a risk that sell side consensus estimates could come down but what would drive upside is if the anti-PCSK9 market achieves blockbuster status in 2016, if clinicians differentiate between the different atni-PCSK9 drugs conferring an advantage to a low dose option, if the once monthly dose is filed and possibly approved, the outcomes study is stopped for efficacy during the interim analysis, and if litigation with AMGN is settled on favorable terms, such as a single-digit royalty.
2. Are Eylea sales and market share likely to continue growing?	Both Eylea US and ex-US sales have been beating the consensus driven largely by the uptake in DME, which could be as big a market opportunity as wet AMD. Two-year Protocol data in early 2016 could confirm the efficacy seen at one year for Eylea, which began this run-up in DME sales and if it were to show further differentiation that could be upside to expectations. A competitor anti-PDGF read out is anticipated and should that combination fail to demonstrate a greater than 1-line improvement, then that is likely to be considered less disruptive to the anti-VEGF market. Finally, Eylea is also being combined with anti-PDGFR (REGN2176-3) and with anti-ang2 (REGN910-3) by REGN and if those trials are positive that too raises the value of REGN's ophthalmology franchise.
3. What do dupilumab Phase III trials need to show in order to drive upside?	Dupilumab is an internal focus and will get more external limelight in 2016. It is unique in atopic dermatitis indication where Phase III data are expected in 1Q:16. Asthma is more competitive but here too dupilumab is the only drug that improves FEV1. The Phase II pediatric study (age >=6 to <18) is also fully enrolled. For the Street to consider dupilumab a complete success, safety has to be clean since efficacy is largely assumed and combined this could be a positive event and hence a favorable catalyst for REGN shares.
4. After alirocumab, sarilumab and dupilumab, are there any meaningful pipeline candidates left to focus on near-term?	REGN advanced two other candidates, both proprietary, into late stage studies with REGN2222 for RSV in Phase III and fasinumab for osteoarthritis pain in Phase II/III. Data from one or both studies could be available in 2016. There are more proprietary candidates that could advance including those focused on metabolic, inflammation and allergy conditions and 2016 could also be the first year where data from REGN's oncology pipeline comes into focus.
5. What is the upside potential for REGN stock in 2016?	Shares have come off their highs as Praluent launch is expected to be slow and there is some uncertainty in 2016 from both commercial competition and clinical developments that could alter the ophthalmology and other landscapes. What drives upside is if Eylea continues to grow, Praluent approaches if not meets consensus, litigation with Amgen over anti-PCSK9 is settled, dupilumab data are clean and positive, and there is progress in the pipeline, especially the one or more programs focusing on Eylea combinations. Unexpected surprise would be if competitors suffer setback clinically or commercially, especially in the ophthalmology and LDL-C lowering arena.

Exhibit 237: Expected news flow for REGN

Timing	Expected News Flow	Program
Ophthalmology		
2015	Quarter comps/performance	Eylea, Lucentis
2H:15	Phase III data in DME (POLARIS)	Eylea, Lucentis, Avastin
YE:15/ 1H:16	Phase III 2-year update from Protocol T in DME	Eylea, Lucentis, Avastin
2016	Phase II data in non-infectious uveitis (SARILNIUSATURN)	Sarilumab (REGN88)
2H:15	Phase III data in DME (VIVID EAST)	Eylea
YE:15	Phase III 148-week data in DME (VIVID and VISTA)	Eylea
YE:15	EMA approval in BRVO	Eylea
YE:15	Phase I data in DME and wAMD	REGN910-3 (Eylea + anti-ang2)
2015	Initiate Phase III trials (?)	Competitor: DARPin (AGN)
2015/ 2016	Go/ no-go decisions for advancement	REGN910-3 (to Phase II)
Mid/ 2H:16	Phase III data in wet AMD	Potential competitor/ partner: Fovista (anti-PDGF) (OPHT)
2H:16/ 1H:17	Phase IV data in polypoidal choroidal vasculopathy (PLANET)	Eylea
2H:16/ 1H:17	Potential Phase II read out	REGN2176-3
1H/ 2H:17	Phase III data in DME (DRCRN: Protocol V)	Eylea
Mid/ 2H:17	Phase III data in wet AMD	Potential competitor/ partner: Fovista (anti-PDGF) (OPHT)
2017	Phase III Go/ no-go decisions for advancement	REGN2176-3

Source: Company reports and RBC Capital Markets estimates

Exhibit 238: REGN pipeline

Product	Stage	Indication	Partner
Eylea (VEGF Trap-Eye)	Marketed	Wet AMD (VIEW 1 and VIEW 2)	US proprietary/ Ex-US Bayer
	Marketed	Central retinal vein occlusion (COPERNICUS & GALILEO)	US proprietary/ Ex-US Bayer
	Marketed	Branched retinal vein occlusion (bRVO)	US proprietary/ Ex-US Bayer
	Marketed	Diabetic macular edema (DME)	US proprietary/ Ex-US Bayer
	Marketed	CNV of retina due to pathologic myopia (Asia)	US proprietary/ Ex-US Bayer
	Marketed	Diabetic retinopathy in patients with DME	US proprietary/ Ex-US Bayer
Arcalyst (rilonacept; IL-1 Trap)	Marketed	CIAS-1 Associated Periodic Syndrome (CAPS)	Proprietary
Zaltrap (Aflibercept)	Marketed	2nd-line metastatic colorectal cancer (VELOUR)	Sanofi-Aventis
	Phase III	1st-line metastatic colorectal cancer (AFFIRM)	Sanofi-Aventis
Praluent (Alirocumab/ REGN727 / SAR236553)	Pre-approval	LDL cholesterol	Sanofi-Aventis
Sarilumab (REGN88)	Phase III	Rheumatoid arthritis (TARGET, MOBILITY, ASCERTAIN)	Sanofi-Aventis
	Phase II	Non-infectious uveitis	Sanofi-Aventis
Dupilumab (REGN668 / SAR231893)	Phase III	Atopic dermatitis	Sanofi-Aventis
	Phase III planned	Asthma	Sanofi-Aventis
	Phase II	Nasal polyposis	Sanofi-Aventis
Fasinumab (REGN475; SAR164877)	Phase IIb/ III	Pain (knee, sciatic, pancreatitis, thermal injury, etc.)	Proprietary
REGN2222 (SAR438584)	Phase III	Respiratory syncytial virus (RSV)	Proprietary
REGN2176-3	Phase II	Wet AMD - Combo anti PDGFR-beta with EYLEA	US proprietary/ Ex-US Bayer
AVA-101	Phase II	Wet AMD	Avalanche
REGN1033 (SAR391786)	Phase II completed	Skeletal muscle disorders	Proprietary
REGN1908-1909	Phase I/II	Allergies	Proprietary
REGN910-3	Phase I	DME and wAMD	US proprietary/ Ex-US Bayer
REGN1500	Phase I	Metabolic disorders (HoFH/ HeFH) - patial hold women childbearing potentia	Proprietary
REGN1193	Phase I	Type 2 diabetes mellitus	Proprietary
REGN1979	Phase I	Anti CD20 and CD3 bispecific for cancer	Proprietary
REGN2810	Phase I	Anti PD1 for cancer	Proprietary
REGN1154	Phase I completed	Undisclosed	Proprietary
REGN1400	Phase I completed	Anti ErbB3 - Cancer	Proprietary

Source: Company reports and RBC Capital Markets estimates

Exhibit 239: Income statement for REGN

($ in millions, except per share) Fiscal Year Ends December	2014A	1Q:15A	2Q:15A	3Q:15A	4Q:15E	2015E	2016E	2017E	2018E	2019E	2020E
REVENUES:											
Eylea - US Sales	1,737.4	541.0	654.6	734.0	762.9	2,692.5	3,243.6	3,813.2	4,401.5	4,880.8	5,286.4
Arcalyst Sales	13.4	3.6	3.2	3.6	3.4	13.8	14.0	14.2	14.4	14.6	14.8
Total Product Related Revenues	1,750.8	544.6	657.8	737.6	766.4	2,706.3	3,257.6	3,827.4	4,415.9	4,895.5	5,301.3
Sanofi-aventis collaboration revenue	541.3	173.4	195.1	224.7	192.1	785.3	1,003.5	1,181.4	1,778.5	2,699.9	3,397.1
Bayer AMD Partnership	495.6	123.8	134.2	157.6	216.8	632.5	816.2	1,050.9	1,301.7	1,542.0	1,848.2
Technology licensing	31.9	27.8	11.5	17.5	21.0	77.8	80.7	82.9	88.8	95.2	102.1
Total Revenue	**2,819.6**	**869.6**	**998.6**	**1,137.4**	**1,196.2**	**4,201.9**	**5,158.0**	**6,142.6**	**7,584.9**	**9,232.5**	**10,648.7**
EXPENSES:											
Cost of Goods	129.0	42.6	60.9	67.2	76.6	247.2	248.4	201.3	232.2	257.4	278.7
Research and Development	1,271.4	343.1	390.3	425.9	437.0	1,596.4	1,721.4	1,871.4	1,971.4	2,071.4	2,171.4
Collaboration / Contract Manufacturing	76.0	41.4	28.0	41.9	51.0	162.2	206.2	247.5	307.8	359.0	423.4
SG&A	504.8	159.0	174.6	210.0	226.2	769.8	940.0	965.0	990.0	1,015.0	1,040.0
Expense Reimbursement to Sanofi	-	-	-	-	-	-	-	-	-	-	-
Total Expenses	1,981.1	586.1	653.8	745.0	790.7	2,775.5	3,116.0	3,285.2	3,501.4	3,702.7	3,913.5
Income from operations (EBIT)	**838.4**	**283.6**	**344.9**	**392.4**	**405.5**	**1,426.3**	**2,042.0**	**2,857.4**	**4,083.5**	**5,529.8**	**6,735.2**
Total Other Income	(62.7)	(7.0)	(16.9)	0.9	(8.3)	(31.3)	(13.0)	4.0	4.0	4.0	4.0
Other adjustments*	-	-	-	-	-	-	-	-	-	-	-
Pre-tax income	775.7	276.5	328.0	393.3	397.2	1,395.0	2,022.8	2,861.4	4,087.5	5,533.8	6,739.2
Taxes	427.7	200.5	133.4	182.9	139.0	655.8	708.0	1,001.5	1,430.6	1,936.8	2,358.7
Net Income (GAAP)	**348.1**	**76.0**	**194.6**	**210.4**	**258.2**	**739.3**	**1,314.8**	**1,859.9**	**2,656.9**	**3,597.0**	**4,380.5**
EPS Basic (GAAP)	$3.46	$ 0.74	$ 1.89	$ 2.04	$ 2.48	$7.15	$12.44	$17.02	$23.72	$31.33	$37.22
EPS Diluted (GAAP)	**$3.07**	**$0.66**	**$1.69**	**$1.81**	**$2.21**	**$6.38**	**$11.14**	**$15.29**	**$21.36**	**$28.28**	**$33.68**
Shares Outstanding - Basic	100.34	102.23	102.89	103.35	103.99	103.11	105.69	109.28	112.02	114.82	117.69
Shares Outstanding - Diluted	114.21	114.52	115.26	115.94	116.59	115.58	118.06	121.66	124.39	127.19	130.06
Net income (Non-GAAP)	**1,174.9**	**335.5**	**338.1**	**402.9**	**383.8**	**1,435.8**	**1,916.1**	**2,609.9**	**3,549.7**	**4,654.6**	**5,578.7**
EPS - Basic (non-GAAP with convert)	$11.71	$3.28	$3.29	$3.90	$3.69	$13.92	$18.13	$23.88	$31.69	$40.54	$47.40
EPS - Diluted (non-GAAP with convert)	**$10.30**	**$2.88**	**$2.89**	**$3.47**	**$3.29**	**$12.44**	**$16.25**	**$21.47**	**$28.55**	**$36.61**	**$42.91**
Shares outstanding - Basic	100.34	102.23	102.89	103.35	103.99	103.11	105.69	109.28	112.02	114.82	117.69
Shares outstanding - Diluted	114.21	116.51	116.98	116.01	116.59	115.58	118.06	121.66	124.39	127.19	130.06

Source: Company reports and RBC Capital Markets estimates

Valuation

We arrive at our $676 per share price target using a DCF/sum-of-the-parts analysis. We value Eylea at ~$437/share (US $316/share; EU $99/share; Japan $21/share). For the antibody platform/pipeline (includes alirocumab and dupilumab), which we value by individual product builds and by applying a probability adjusted sales multiple discounted back various periods, our value is $219/share ($58/ share for alirocumab, $15 for sarilumab, $66 for dupilumab and $80 for the rest). Next we value Zaltrap at $3/share, Arcalyst at $1/share, and cash/NOLs at $16/share.

Price target impediments

Risks to our price target include commercial uncertainty in the AMD and oncology space, and clinical and regulatory risks for pipeline programs, and potential legal risk from competitors, such as Roche.

SCYNEXIS Inc. (SCYX)

Outperform, Speculative Risk

Price Target USD $17.00

Target/Upside/Downside Scenarios

Exhibit 240: SCYNEXIS Inc.

Source: RBC Capital Markets estimates

Target price/base case

We value SCYX at $17 per share, which includes US and ROW sales of SCY-078. We assign a probability of success of 65% and a value of ~$7 per share to the US and $10 per share to the ROW opportunity. We assume a US launch in 2019 and an ROW launch in 2020. Currently, we assume that SCYX will sell SCY-078 in the US and a partner will commercialize these compounds outside the US. We forecast peak SCY-078 sales of $300–400MM in the US and $1.0–1.4B in the ROW.

Upside scenario

Our upside scenario of $30 includes ~$20 per share in value for the US opportunity and ~$10 per share in value for the ROW opportunity. We forecast peak SCY-078 sales of $1.0–1.1B in the US and $2.5–2.8B in the ROW. We assign SCY-078 a 65% probability of success and a discount rate of 15%, and use a terminal growth rate of -50%.

Downside scenario

Our downside scenario assumes that SCY-078 may not be successful clinically or commercially because either efficacy against resistant organisms was not borne out or it was not long-lasting or an unexpected adverse event was seen. Under such a scenario, shares would trade at roughly cash per share, which is currently $5.

Investment summary

Scynexis's (SCYX) SCY-078 treats systemic fungal infections via a new mechanism of action that attacks the fungal cell wall, a validated target. These infections are serious, have high rates of mortality, and rates of resistance to current drugs are rising. All currently available drugs have limitations, which allow SCY-078 to generate an attractive value proposition. The worldwide market for systemic anti-fungals is almost $4B. Roughly 600,000 patients are identified with invasive fungal infections and even more are treated. Phase I studies are completed for the oral version and in vitro and in vivo data show activity in organisms both susceptible and resistant to currently approved drugs. Next up is a Phase II for the oral and a Phase I for the intravenous form with data in 2015. A Phase II/III study in resistant patients could start in 2016 and potentially provide a more rapid path to the market. SCYX essentially owns all rights to SCY-078, which is patent protected through 2030, as well as to its anti-fungal pipeline. This leaves SCYX free to commercialize the products itself, partner on a global or regional basis, and/or sell the company.

Potential catalysts for the stock

- Phase II data for oral SCY-078 in 2016. Important catalyst as this will be the first time SCY-078 will be used in human patients.
- Phase I data for intravenous SCY-078 in 2016. Important as an intravenous does not yet exist and is needed to maximize the value of SCY-078 franchise.
- Phase II/III trial design in 2016. A sign-off from the FDA could determine the pace and potential path to the market.
- Phase II/III trial start in 2016 and data by YE:17/early 2018. A Phase II/III study in drug resistant patients could be the first proof that SCY-078 can achieve in patients what it is designed to do and has shown in in vitro and in vivo models.
- Business development activities in 2016. Non-core pipeline assets and even SCY-078 could be partnered, opportunistically raising non-dilutive capital.

Risks to our investment thesis

- Clinical studies for oral and intravenous SCY-078 could fail.
- Merck returned rights for SCY-078 back to SCYX. This raises the question of whether MRK saw anything lacking in SCY-078's clinical or commercial profile.
- Sales ramp of SCY-078 could lag expectations unless rates of resistance continue to rise.
- SCYX could fail to find a partner outside the US for SCY-078.
- Timelines are rapid and any delays could disappoint investors.

Key questions and debates for SCYX

1. Are new anti-fungal agents needed?	Resistance to currently available anti-fungal drugs is increasing and is expected to go up further as generics become available. SCY-078 is an enfumafungin derivative, which inhibits glucan synthase, a validated target for systemic fungal infections, but at the same time has the ability to work in echinocandin resistant organisms. The US FDA established the QIDP program to designate the development of important drug candidates of potent antibiotics and anti-fungal agents that can address drug-resistant organisms and SCY-078 has been granted the designation.
2. Does the oral SCY-078 formulation have value in of itself?	The challenge is that while azoles are available as an oral echinocandins are not, so theoretically, SCY-078 could be used as a step down therapy for IV echinocandins. However, to optimize the value of the SCY-078 both an oral and IV form should be developed.
3. Is SCY-078 Phase II oral step-down study on track?	While the Street has been concerned about whether or not the Phase II oral step down study remains on track, especially since SCYX has had to amend the protocol to facilitate recruitment, SCYX has maintained its guidance for completion in 1H:16. The objective is to evaluate oral SCY-078 as a step-down for patients who have been on an IV echinocandin for invasive Candida infections. SCYX has implemented protocol amendments to increase enrollment by: 1) opening additional US sites, 2) planning for sites outside the US, and 3) amending the protocol to allow higher enrollment, such as by changing lab criteria, among others.
4. When are SCYX shares expected to move?	While shares have been range-bound for some time, SCYX now has three clinical trials ongoing with data expected over the next three months. These include the Phase II oral step down study in systemic fungal infections, a Phase I study for the intravenous form, and a Phase II study with the oral form in VVC. All of these could have data giving the first evidence of clinical activity and should lead to value creation.
5. Could SCYX be a take out candidate?	The value proposition for novel anti-fungal drugs is similar to that of new antibiotics. Most companies that have successfully developed antibiotics or are developing them are larger biopharma companies with a target on the hospital. We think SCY-078 could fit well with those franchises.

Exhibit 241: Expected news flow for SCYX

Timing	Expected News Flow	Program
4Q:15	Initiate Phase I study with i.v. SCY-078	SCY-078
4Q:15	Initiate Phase II VVC with oral SCY-078	SCY-078
YE:15/ early 2016	Request QIDP designation for i.v. SCY-078	SCY-078
1H:16/ mid-2016	Phase II data from VVC study	SCY-078
1H:16/ mid-2016	Phase II results from oral SCY-078 step down study	SCY-078
Mid-2016	Phase I intravenous SCY-078 results	SCY-078
2H:16	Phase II/ III or pivotal study plans after meeting with the FDA	SCY-078
YE:16/ early 2017	Initiate Phase II/III i.v. to oral SCY-078 in relapsed/ refractory patients	SCY-078
YE:16/ early 2017	Initiate Phase III study for i.v. to oral SCY-078 in 1st line patients	SCY-078
2018	Phase II/III i.v. to oral data	SCY-078
2018	Potential NDA for SCY-078	SCY-078
YE:18/ 2019	Potential accelerated approval	SCY-078

Source: Company reports and RBC Capital Markets estimates

Exhibit 242: SCYX pipeline

Product	Mechanism	Stage	Indication
SCY-078	1,3 beta – glucan synthesis inhibitor	Phase II with oral formulation; Phase I with i.v. formulation	Invasive fungal infections caused by Candida and Aspergillus species
SCY-078		Phase II planned; Oral formulation	Vulvovaginal candidiasis (VVC)
SCY-635	Cyclophilin inhibitor	Phase IIa	Hepatitis C Virus (HCV)
SCYX-7158	Anti-parasitic	Phase I	Human African Trypanosomiasis (Sleeping sickness)
SCY-641	Cyclophilin inhibitor	Pre-Clinical	Dry Eye disease

Source: Company reports and RBC Capital Markets estimates

Exhibit 243: Income statement for SCYX

(in MM; except per share)	2014E	1Q:15A	2Q:15A	3Q:15A	4Q:15E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E
Revenue:														
SCY-078											49.5	84.0	122.6	165.5
Other Revenue	19.0	3.3	0.1	0.1	0.0	3.4	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8
Total Revenue	19.0	3.3	0.1	0.1	0.0	3.4	0.1	0.2	0.3	0.4	61.4	113.6	170.6	232.6
Operating expenses:														
Cost of Other Revenue	15.4	3.2			0.0	3.2			(0.3)	(0.2)	(0.1)		0.1	0.2
R&D	8.3	4.2	3.3	3.5	5.0	16.0	22.5	30.0	35.0	25.0	22.5	25.0	27.5	30.0
SG&A	7.6	2.2	3.3	4.1	3.3	13.0	14.0	15.0	16.0	17.5	20.0	25.0	31.3	31.3
Other	(0.2)													
Total Expenses	31.1	9.7	6.6	7.6	8.4	32.2	36.5	45.0	50.7	42.3	47.4	58.4	71.1	78.0
Operating income	(12.1)	(6.4)	(6.5)	(7.5)	(8.4)	(28.8)	(36.4)	(44.8)	(50.4)	(41.9)	14.0	55.2	99.5	154.6
Other:														
Amortization of deferred financing cost and debt discou	0.8													
Interest expense for beneficial conversion feature	0.0													
Interest expense-related party														
Interest expense	0.0	(0.0)		(0.0)		(0.0)								
Derivative fair value adjustment	(10.1)													
Other income	1.4		(0.0)		(0.1)	(0.1)	(0.0)	(0.1)	(0.1)	(0.1)	(0.2)	(0.4)	(0.6)	(0.8)
Income before Tax	(4.2)	(6.4)	(6.5)	(7.5)	(8.3)	(28.7)	(36.4)	(44.7)	(50.3)	(41.8)	14.2	55.6	100.1	155.4
Taxes											4.8	18.9	34.0	52.8
Net income (loss)	(4.2)	(6.4)	(6.5)	(7.5)	(8.3)	(28.7)	(36.4)	(44.7)	(50.3)	(41.8)	9.4	36.7	66.0	102.6
Discontinued Operations (loss)				(0.8)										
Derivative fair value adjustment	(10.1)	-	-	-	-	-	-	-	-	-	-	-	-	-
Net loss to common stockholders	(15.9)	(6.4)	(9.5)	(8.4)	(8.3)	(28.7)	(36.4)	(44.7)	(50.3)	(41.8)	9.4	36.7	66.0	102.6
EPS, Basic (GAAP)	($1.04)	($0.75)	($0.78)	($0.60)	($0.60)	($2.36)	($2.19)	($2.63)	($2.25)	($1.84)	$0.40	$1.55	$2.73	$4.16
EPS, Diluted (GAAP)	($2.69)	($0.73)	($0.76)	($0.59)	($0.59)	($2.32)	($2.15)	($2.59)	($2.22)	($1.81)	$0.40	$1.52	$2.68	$4.08

Source: Company reports and RBC Capital Markets estimates

Valuation

We value SCYX at $17 per share, which includes US and ROW sales of SCY-078. We assign a probability of success of 65% and a value of ~$7 per share to the US and $10 per share to the ROW opportunity. We assume a US launch in 2019 and an ROW launch in 2020. Currently, we assume that SCYX will sell SCY-078 in the US and a partner will commercialize these compounds outside the US. We forecast peak SCY-078 sales of $300–400MM in the US and $1.0–1.4B in the ROW. We currently assign no additional value to the earlier-stage pipeline. Finally, we assume product sales extend into 2030 and include a terminal value based on a terminal growth rate of -50% and a discount rate of 15%.

Price target impediments

Our price target is dependent solely on the clinical, regulatory, and commercial success of SCY-078. A Phase II study for SCY-078 is expected in 2015 and data expected in 2016. Failure to demonstrate efficacy or safety in the study would be a significant setback. Furthermore, any setbacks in regulatory approvals in the US or EU, delay in launch, failure to secure a partnership outside the US for SCY-078, increased competition or other limitations to the market potential of these products owing to either better efficacy and/or safety outcomes or pricing pressure due to the availability of generic drugs for glaucoma could negatively impact our valuation.

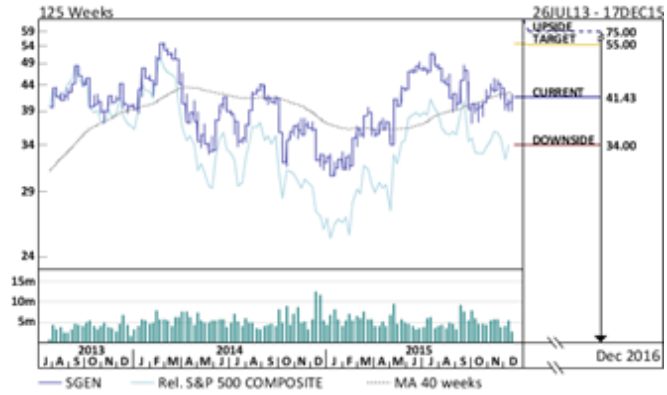
Seattle Genetics Inc. (SGEN)

Outperform

Price Target USD $55.00

Target/Upside/Downside Scenarios

Exhibit 244: Seattle Genetics Inc.



Source: RBC Capital Markets estimates

Target price/base case

Our $55/share price target is supported by a sum-of-the-parts analysis, which assigns ~$27 in value to Adcetris across HL, ALCL, DLBCL, CTCL, and PTCL and ~$28 to the pipeline. We include several proprietary and partnered programs in Phase I and Phase II studies as well as technology platform value. We value the pipeline on a probability-adjusted basis.

Upside scenario

Our $75/share upside scenario includes a higher uptake of Adcetris, including first-line, and proprietary pipeline products of $40 and $23, respectively; another ~$12/share comes from partnered program and value of the technology platform. There is room for further upside based on clinical, regulatory, and commercial catalysts that could cause us to increase our probabilities.

Downside scenario

In our downside scenario of $34/share, we assume a lower uptake of Adcetris of 70% of the base case and reduce the value of partnered and pipeline programs by 50% for potential setbacks or if pipeline productivity declines and exclude cash.

Investment summary

We view SGEN as a long-term and core biotech holding given its industry-leading antibody-drug conjugation (ADC) technology, a validated, rare, and coveted platform, a growing proprietary pipeline, multiple partnerships with leading biotechnology and pharmaceutical companies, robust late- and early-stage clinical pipeline, its retained product rights, and solid balance sheet. Ultimately, we believe SGEN will become a profitable, multi-product company, with sales and marketing infrastructure in the US, or it may be a target at some point for acquisition by a larger company looking to build a pipeline of antibody products in hematology/ oncology. News flow is likely to accelerate into 2016 and 2017 and data are expected from several Phase I, II, and III clinical trials from both proprietary and partnered drug candidates. Compendia listings, label updates, and data from investigator-sponsored studies (ISTs) could accelerate Adcetris sales as well.

Potential catalysts for the stock

Our investment view is driven by:

- **Modest growth in Adcetris sales** from additional indications, off-label use, or compendia listings**.**
- **Results from Phase III studies in HL,** newly diagnosed HL, relapsed/refractory CTCL and front-line CTCL in 2015-2017 and beyond.
- **Compendia listing and guideline inclusions.**
- **Phase II DLBCL updates** for Adcetris and SGN-CD19A in relapsed/refractory and newly diagnosed patients.
- **Phase I/II AML updates** for SGN-CD33A and SGN-CD19A.
- **Safety and activity data** from proprietary candidates SGN-75, SGN-19a, SGN-CD33a, and SGN-LIV1a**.**
- **Results in partnered programs** with Roche, Celldex, Progenics, Bayer, Astellas, Abbott, and others are in development and the timing of data remains unknown.
- **Data from several investigator sponsored studies.**
- **Potential licensing of technology** by additional partners.

Risks to our investment thesis

- **Phase III clinical trials could fail** to demonstrate compelling Adcetris safety and/or efficacy, especially relative to existing therapies.
- **New or unexpected side effects** could be identified.
- **Adcetris sales could lag expectations** across current and future indications due to safety, cost, reimbursement, or competitive concerns.
- **Partnered and/or proprietary programs** could fail**.**
- **Competing technologies could obviate the advantages** offered by SGEN's platform**.**

Key questions and debates for SGEN

1. What is the likelihood of competitors, such as checkpoint inhibitors, overtaking Adcetris?

Early data in relapsed/ refractory HL especially after Adcetris failure has been strong. Pivotal trials for both BMY's nivolumab and MRK's pembrolizumab are ongoing; however, earlier-stage use could require head-to-head data should Adcetris first-line study read out positive, could significantly raise the bar for any follower both in terms of efficacy but also trial design and time needed to complete the study. Furthermore, SGEN and Bristol-Myers Squibb are conducting a combination Adcetris + nivolumab study while the NCI is conducting a triple combination of Adcetris + nivolumab + ipilimumab in Hodgkin's Lymphoma.

2. Can Adcetris be combined with immuno-oncology drugs?

Combination studies in both HL and NHL/DLBCL are ongoing and at least one study in combination with ipilimumab has been reported and shown positive data with safety and tolerability. HL specialists we have spoken with would prefer to see how the combination works, especially if it has the potential to remove additional traditional chemotherapeutic agents from the treatment paradigm, but they do generally think Adcetris and immuno-oncology drugs are combinable.

3. Can Adcetris become a billion-dollar drug and does it matter?

The current trajectory for Adcetris to become nearly a $250M+ drug for its current indications alone, based on the most recently reported results. Approval or use in the post-transplant setting is likely to add another $100M-$200M, depending on the number of cycles given. Getting to the front-line setting would get Adcetris closer to the $1B mark overall. On a global basis Adcetris sales could approach $500M+ (Takeda pays royalties on ex-US sales).

4. Are CAR-T approaches likely to approve competitive against SGEN's pipeline candidates?

Chimeric antigen receptor (CAR) and T-cell receptor (TCR) approaches have demonstrated highly positive data in ALL, where SGEN is developing SGN-CD19A. The same target is also being used to evaluate the potential of CAR-T approaches in NHL/DLBCL. Furthermore, early stage work has been done in both HL and AML with other targets. So SGEN's pipeline is likely to see competition here, however, competitive data appears most compelling in ALL and then in NHL. Furthermore, SGEN's drugs could still be used in combination or before or after these competitive approaches so we do not see them as being pre-empted.

5. How is SGN-CD33A viewed by the Street?

The Street appears to have a mixed view in that there are a couple of high profile early stage AML studies with compelling data and SGN-CD33A data stacks up nicely vs. those other agents. We think more data that shows a compelling ORR/CR in combination plus a high margin of safety is likely to convince investors that 33A could become a backbone of anti-AML therapy.

6. What other pipeline candidates are meaningful catalysts and drivers for SGEN shares?

The number of clinical readouts is increasing from '16-'18 with Phase III data for Adcetris in CD30+ CTCL in '16, possibly Phase III data in front line HL and front line CD30+ MTCL in '17/'18. The front-line HL study could be particularly catalytic as it could help transform Adcetris into a blockbuster. The pivotal SGN-CD33A AML study could read out in '18 and the registrational SGN-CD19A r/r DLBCL in '17/'18. Many more Phase I studies in blood and solid tumor cancers could read out over the next 12-18 mo., starting with an interim look at the Phase I SGN-LIV1A study with an emphasis on results in triple negative breast cancer. HL and DLBCL Combination studies with nivolumab would also be of interest. The pipeline is expected to continue expanding with more INDs expected '16-'18+.

Exhibit 245: Expected news flow for SGEN

Timing	Adcetris: Expected News Flow	Program
2015	Quarterly financial results	Adcetris, expenses
YE:15	Initiate Phase I/II studies in HL and NHL	Adcetris + OPDIVO (nivolumab)
YE:15	Phase III AETHERA updated safety and efficacy info. @ ASH	Adcetris
YE:15	Phase II data in second line salvage setting and frontline in age 60+ @ASH	Adcetris
YE:15	HL data-5 year survival in r/r @ASH	Adcetris
YE:15/ 1H:16	Phase I data in CD30+ non-lymphomatous cancers	Adcetris
YE:15/ 1H:16	Phase I data in newly diagnosed, unfavorable risk HL	Adcetris +AVD
YE:15/ 1H:16	Potential Phase II data in newly diagnosed DLBCL	Adcetris + R-CHOP
YE:15/ 1H:16	Phase I data in patients with MF with variable CD30+	Adcetris
YE:15/ 1H:16	Phase I data in GvHD	Adcetris
YE:15/ 1H:16	Potential Phase I/II data in r/r HL (Adcetris+bendamustine)	Adcetris
YE:15/ 1H:16	Phase II data in r/r NHL	Adcetris + Rituxan
YE:15/ 1H:16	Approval/ label expansion in residual HL following ASCT	Adcetris
2015/2016	ECHELON-1 and -2 complete enrollment	Adcetris
2015/ 2016	Initiate randomzied Phase II study in CD30+ DLBCL	R + bendamustine +/ - Adcetris
2015/ 2016	Initiate pivotal Phase II/ III study in DLBCL	R-CHOP vs. Adcetris + R-CHP
Mid-2016	Phase III OS data from AETHERA	Adcetris
Mid/ 2H:16	Phase III data in CD30+ CTCL (ALCANZA)	Adcetris
Mid/ 2H:16	Phase II data in elderly untreated HL	Adcetris + chemo
Mid/ 2H:16	Phase II data in newly diagnosed HL in patients age 60 and higher	Adcetris
YE:16	sBLA for CTCL	Adcetris
YE:16	Phase I/ II data in HL and NHL	Adcetris + OPDIVO (nivolumab)
1H:17	Potential approval for CTCL	Adcetris
2016	ECHELON-2 complete enrollment	Adcetris
2016/ 2017	Phase II data in systemic lupus erythematosus (SLE)	Adcetris
Mid 2017	Potential final Phase II data in newly diagnosed DLBCL	Adcetris + R-CHOP
YE:17	Phase I data in GvHD	Adcetris
2017	Potential final Phase II data in r/r NHL	Adcetris + Rituxan
2017	Phase I data in r/r PTCL	Adcetris
2017	Potential Phase I/II data in r/r HL (Adcetris+bendamustine)	Adcetris
2017/ 2018	Potential Phase II dtaa in CD30+ DLBCL	R+ bendamustin +/ - Adcetris
2017/ 2018	Phase III data in MTCL (ECHELON-2)	Adcetris
2017/ 2018	Phase III data in front-line HL (ECHELON-1)	Adcetris

Source: Company reports and RBC Capital Markets estimates

Exhibit 246: SGEN pipeline

Product	Stage	Cancer Indication	Partner
Adcetris (SGN-35)	Marketed	Relapsed/refractory HL and ALCL	Millennium/Takeda
	Approved	Post-transplant Hodgkin lymphoma	Millennium/Takeda
	Phase III	Relapsed CTCL (MF, pcALCL) (ALCANZA Study)	Millennium/Takeda
		1st line HL (ECHELON-1; A+AVD vs. ABVD)	Millennium/Takeda
		Front-line MTCL (ECHELON-2)	Millennium/Takeda
	sBLA filed	Residual HL following ASCT (AETHERA)	Millennium/Takeda
	Phase II	CD-30+ cancers	Millennium/Takeda
		Relapsed/refractory NHL	Millennium/Takeda
		Diffuse large B-cell lymphoma (DLBCL)	Millennium/Takeda
	Phase I	Systemic lupus erythematosus (SLE)	Millennium/Takeda
	Phase I	1st line HL and ALCL (with chemo)	Millennium/Takeda
Anti-GCC ADC	Phase II	Gastrointestinal malignancies	Millennium/Takeda
SGN-CD19A	Phase I	Hematologic malignancies (NHL, CLL, ALL)	Proprietary
SGN-CD33A	Phase I	AML	Proprietary
SGN-LIV1A	Phase I	Breast cancer	Proprietary
SGN-CD70	Phase I	CD70 positive - NHL and renal cell carcinoma	Proprietary
SEA-CD40	Phase I	Multiple solid tumors	Proprietary
CDX-011 (Anti-GPNMB; CR011-vcMMAE; Glembatumumab vedotin))	Pivotal	Breast cancer, melanoma and squamous cell lung cancer	Celldex (Curagen)
Pinatuzumab (RG7593, DCDT2980S; anti-CD22)	Phase II	Non-Hodgkin's lymphoma	Roche (Genentech)
Polatuzumab (RG7596, DCDS4501A; anti-CD79b)	Phase II	Hematologic malignancies	Roche (Genentech)
PSMA ADC	Phase II	Prostate cancer	Progenics
RG7458 (anit-MUC16)	Phase II	Ovarian	Roche (Genentech)
Lifastuzumab (RG7599; DNIB0600A; anti-NaPi2b)	Phase II	NSCLC, ovarian	Roche (Genentech)
Adcetris+OPDIVO	Phase I/II	r/r HL	Bristol-Myers Squibb
	Phase I/II	r/r b-cell and t-cell NHL including DLBCL	Bristol-Myers Squibb
RG7450 (DSTP3086S; anti-STEAP1)	Phase I	Prostate cancer	Roche (Genentech)
RG7598	Phase I	Multiple myeloma	Roche (Genentech)
RG7600	Phase I	Cancer	Roche (Genentech)
RG7636	Phase I	Metastatic melanoma	Roche (Genentech)
RG7882 (DMOT4039A)	Phase I	Pancreatic or PROC	Roche (Genentech)
RG7841	Phase I	Refractory solid tumors	Roche (Genentech)
MN-IC	Phase I	Solid tumors	Bayer
AGS-163F (ASG-16M8F)	Phase I	Kidney cancer	Astellas (Agensys)
ASG-22CE (ASG-22ME)	Phase I	Solid tumors, including urothelial cancer	Astellas (Agensys)
AGS15E (ASG-15ME; anti-SLITRK6)	Phase I	Solid tumors (bladder and lung cancer)	Astellas (Agensys)
AGS67E	Phase I	Relapsed/ refractory lymphoid malignancies	Astellas (Agensys)
ABT-404	Phase I	Glioblastoma	Abbvie
A1mcMMAF (anti-5T4 ADC)	Phase I	Solid tumors	Pfizer
TF-ADC	Phase I	Solid tumors	Genmab
Not disclosed	Phase I planned	Not disclosed	Proprietary
ACTR products	Preclinical	TBD	Unum Therapeutics
SGN-CD19B	Preclinical	NHL	Proprietary
SGN-CD123A	Preclinical	AML	Proprietary
Anti-CD74	Preclinical	Not disclosed	Genmab
Not disclosed	Preclinical	Not disclosed	GlaxoSmithKline
Not disclosed	Preclinical	Not disclosed	Daiichi
Not disclosed	Preclinical	Hematologic malignancies	

Source: Company reports and RBC Capital Markets estimates

Exhibit 247: Income statement for SGEN

Fiscal Year Ends December	2014A	1Q:15A	2Q:15A	3Q:15A	4Q:15E	2015E	1Q:16E	2Q:16E	3Q:16E	4Q:16E	2016E	2017E	2018E	2019E	2020E
U.S./Canada Sales:															
Adcetris	178.2	48.9	55.1	59.1	60.9	223.9	62.3	64.8	67.3	79.1	273.4	329.9	414.1	491.2	562.0
Total Product Sales	**178.2**	**48.9**	**55.1**	**59.1**	**60.9**	**223.9**	**62.3**	**64.8**	**67.3**	**79.1**	**273.4**	**329.9**	**414.1**	**491.2**	**827.2**
Royalties	40.0	11.1	7.6	9.7	9.9	38.3	12.0	8.5	10.5	13.0	44.0	63.5	87.6	118.8	134.3
Contracts, licensing fees, and milestones	68.6	22.2	14.4	15.3	13.1	65.0	14.0	15.0	16.0	17.0	62.0	62.0	62.0	62.0	62.0
Total Revenues	**286.8**	**82.2**	**77.1**	**84.1**	**83.9**	**327.2**	**88.3**	**88.3**	**93.8**	**109.1**	**379.4**	**455.4**	**563.6**	**672.1**	**1,023.5**
Cost of goods	17.5	5.2	5.9	6.6	6.7	24.5	6.2	6.5	6.7	7.9	27.3	33.0	41.4	49.1	96.0
Cost of royalty	11.5	3.2	2.6	3.5	2.8	12.1	3.4	2.4	3.0	3.7	12.5	17.9	24.5	33.3	37.6
Research and development	230.7	63.4	85.7	70.8	80.1	300.0	81.0	83.0	84.0	87.0	335.0	350.0	360.0	370.0	380.0
Selling, general and administrative	104.3	32.1	30.3	29.7	32.9	125.0	32.5	33.5	34.5	37.0	137.5	145.0	150.0	155.0	160.0
Total Operating Expenses	**364.1**	**103.9**	**124.7**	**110.6**	**122.5**	**461.6**	**123.1**	**125.4**	**128.2**	**135.6**	**512.4**	**545.9**	**575.9**	**607.4**	**673.6**
Operating Income (Loss)	**(77.4)**	**(21.7)**	**(47.6)**	**(26.5)**	**(38.6)**	**(134.4)**	**(34.9)**	**(37.1)**	**(34.5)**	**(26.5)**	**(133.0)**	**(90.5)**	**(12.3)**	**64.7**	**349.9**
Interest income, net	1.2	0.1	0.1	0.1	0.8	1.0	0.1	0.1	0.1	0.2	0.5	0.8	1.0	1.1	1.2
Non-cash expenses															
Income before Tax	**(76.1)**	**(21.7)**	**(47.5)**	**(26.4)**	**(37.7)**	**(133.4)**	**(34.8)**	**(37.0)**	**(34.4)**	**(26.3)**	**(132.5)**	**(89.8)**	**(11.3)**	**65.8**	**351.1**
Provision for taxes														16.4	87.8
Preferred stock dividend (non-cash)															
Net Income (Loss)	**(76.1)**	**(21.7)**	**(47.5)**	**(26.4)**	**(37.7)**	**(133.4)**	**(34.8)**	**(37.0)**	**(34.4)**	**(26.3)**	**(132.5)**	**(89.8)**	**(11.3)**	**49.3**	**263.3**
EPS - Basic	($0.62)	($0.17)	($0.38)	($0.21)	($0.27)	($1.03)	($0.24)	($0.26)	($0.24)	($0.18)	($0.91)	($0.60)	($0.08)	$0.33	$1.72
EPS - Diluted*	**($0.62)**	**($0.17)**	**($0.38)**	**($0.21)**	**($0.27)**	**($1.03)**	**($0.24)**	**($0.26)**	**($0.24)**	**($0.18)**	**($0.91)**	**($0.60)**	**($0.08)**	**$0.31**	**$1.63**
Shares Outstanding - Basic (MM)	123.4	124.3	125.1	127.7	141.4	129.6	142.9	144.3	145.7	147.2	145.0	148.7	150.2	151.7	153.2
Shares Outstanding - Diluted (MM)	131.6	132.6	133.3	136.0	149.8	137.9	151.2	152.7	154.1	155.6	153.4	157.2	158.7	160.3	161.9
Fiscal Year Ends December	2014A	1Q:15A	2Q:15A	3Q:15A	4Q:15E	2015E	1Q:16E	2Q:16E	3Q:16E	4Q:16E	2016E	2017E	2018E	2019E	2020E
Adcetris (US)	178.2	48.9	55.1	59.1	60.9	223.9	62.3	64.8	67.3	79.1	273.4	329.9	414.1	491.2	562.0
Adcetris (EU)	181.8	55.3	38.1	48.5	49.7	253.8	27.6	115.1	181.8	253.8	324.9	404.7	511.5	551.5	584.7
Adcetris (WW)	360.0					466.1	162.8	259.1	360.0	466.1	566.5	680.0	837.3	891.9	940.2

Source: Company reports and RBC Capital Markets estimates

Valuation

Our $55/ share price target is supported by a sum-of-the-parts analysis, which assigns ~$27 in value to Adcetris across HL, ALCL, DLBCL, CTCL, and PTCL and ~$28 to the pipeline. We include several proprietary and partnered programs in Phase I and Phase II studies as well as technology platform value; however, we exclude net cash. We have product builds for Adcetris, and other later-stage proprietary/partnered candidates and the rest of the pipeline we value on a probability-adjusted basis

Price target impediments

Risks to our price target involve negative clinical or regulatory developments, significantly higher-than-expected toxicity for the company's conjugates, which could increase clinical development risk, and the loss of corporate partners.

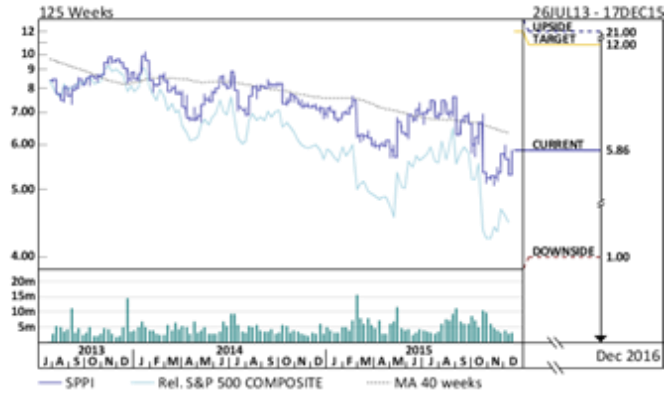
Spectrum Pharmaceuticals (SPPI)

Outperform, Speculative Risk

Price Target USD $12.00

Target/Upside/Downside Scenarios

Exhibit 248: Spectrum Pharmaceuticals.



Source: RBC Capital Markets estimates

Target price/base case

Price target/base case: $12. We arrive at our $12 price target using a product-level DCF valuation. Our product-level NPV assigns a value of ~$1/share to Fusilev and Zevalin, ~$1/share to Folotyn, ~$1/share to Beleodaq, ~$1/share to Marqibo and Melphalan, and ~$6/ share to SPI-2012. Earlier-stage pipeline candidates apaziquone and poziotinib at ~$2/share.

Upside scenario

Our upside scenario of $21 assigns a value of ~$3–4/share to Fusilev and Zevalin and $2/ share for Folotyn. We include Marqibo, Beleodaq, melphalan at ~$2–3/share and SPI-2012, apaziquone, poziotinib, and cash at $13/share.

Downside scenario

For our downside scenario of $1, we lower Fusilev and Zevalin values to ~$1/share and Folotyn to <$1/share. Next, we include Marqibo, Beleodaq and cash at <$1/share.

Investment summary

Spectrum is a cancer-focused biotechnology company with Folotyn, Zevalin, Fusilev, and Marqibo on the market, and belinostat recently approved, and an NDA for apaziquone expected. Most of these products also have or will have late-stage trials ongoing, which could read out in 2015/ 2016 and beyond. Spectrum's earlier-stage pipeline has several product candidates, including some in Phase II that target blockbuster-potential indications, which could help shift the Street's focus to the pipeline. The company's core business model is to in-license with favorable economics, develop, and sell hematology/oncology drugs, all of which can leverage its commercial infrastructure. In our view, risk-reward is favorable despite potentially declining Fusilev sales, given expected diversification from other marketed products, sales of new in-licensed, acquired, or developed products in 2015/ 2016, and additional upside from the pipeline.

Potential catalysts for the stock

Our investment view is driven by:

Folotyn and Beleodaq sales could continue to grow modestly, which would be viewed as a positive. Fusilev sales could stabilize, and if they do, that would be a positive driver.

Marqibo launch diversifies the top line and could beat currently low expectations.

Pipeline news flow in 2015-2016 could mean data from Phase II and II studies, which would be a driver for upside as the Street is not focused on it.

Business development is a catalyst although timing is uncertain, especially as SPPI has delivered two good deals (Marqibo and melphalan).

Risks to our investment thesis:

Sales of marketed products could lag expectations. In particular, Fusilev could continue to decline and Marqibo launch could disappoint.

Captisol encapsulated melphalan study could fail to meet the primary endpoint.

Pivotal or earlier-stage studies could fail.

Legal regulatory risk.

Business development activity could result in transactions that do not deliver a positive NPV.

Key questions and debates for SPPI

1. Can SPI-2012 be differentiated vs. pegfilgrastim?

SPI-2012 is a different molecule than pegfilgrastim and hence is a unique molecule and not a potentially substitutable biosimilar. In the Phase II study SPI-2012 showed quicker recovery and the question appears to be whether the FDA will allow a trial design that permits non-inferiority vs. pegfilgrastim while at the same time allowing for a superiority test vs. pegfilgrastim.

2. Will the FDA review apaziquone for the treatment of NMIBC?

The first step after the NDA being filed would be acceptance for review by the FDA, which would be considered a de-risking event. Since SPPI has initiated a Phase III study under an SPA, and there is a good chance the FDA could grant the apaziquone application an advisory committee review especially once enrollment in the confirmatory Phase III study achieves a certain threshold.

3. Is poziotinib going to be a differentiated HER inhibitor?

Data are early but poziotinib appears to be differentiated at least in patients with breast cancer. SPPI is planning further studies targeting breast cancer and data from that is more likely to show the Street what efficacy and safety profile for poziotinib could look like.

4. Is the competitive landscape for SPI-2012 going to become more challenging?

Management estimates the worldwide commercial opportunity for neutropenia treatments at $6B. While several biosimilars for Neulasta and Neupogen could be on the market, SPI-2012 is unique and a different molecule. Even a modest market share of 5-10% of the current neutropenia market could be a significant market opportunity for SPPI.

5. Does SPPI require further capital to fund its clinical programs?

We believe current cash is sufficient to fund ongoing studies; however, future studies and especially commercialization could require further capital. We also expect SPPI to remain opportunistic both about in- and out-licensing opportunities, which could also impact future cash needs. Last but not least, current product sales are also sufficient to support all or part of operational expenditures.

Exhibit 249: Expected news flow for SPPI

Timing	Expected News Flow	Program
2015	Quarterly comps/ sales performance	
Nov. 6, 2015	FDA meeting on CRL	Evomela
YE:15/ 1Q:16	FDA feedback on SPA	SPI-2012 (GCSF)
4Q:15	File NDA in NMIBC	Apaziquone
4Q:15	Initiate Phase III study	SPI-2012 (GCSF)
4Q:15	Finalize Phase II plans/ file IND	Poziotinib
YE:15/ 1H:16	Initiate Phase III study	Apaziquone
2015/ 2016	Potential business development activities	
2015/ 2016	Phase II data in NSCLC w/ resistance to 1st gen EGFR TK inhibitors	Poziotinib
2015/ 2016	Phase II data HER2+ gastric cancer	Poziotinib
1Q:16	NDA acceptance for review by the FDA	Apaziquone
1H/ 2H:16	Phase III data in newly diagnosed ALL	Marqibo
1H/ 2H:16	Phase II breast cancer study details	Poziotinib
1H/ 2H:16	Initiate Phase II breast cancer study	Poziotinib
Mid-2016	Decision on appeal in Fusilev vs. Sandoz (NVS) case	Fusilev
Sep. 12, 2016	Folotyn trial in P4 litigation	Folotyn
2016	Potential FDA AdCom	Apaziquone
2016	Phase II data in biliary cancer	SPI-1620
2016	Phase II data for mucositis in PTCL	Folotyn
2016	Phase II data in head & neck squamous cell cancer after platinum failure	Poziotinib
YE:16/ 1H:17	Phase III data in CD20+ DLBCL (OPTIMAL >60)	Marqibo
2016/ 2017	Potential FDA approval	Apaziquone
1H:17	Potential Phase III data in neutropenia	SPI-2012 (GCSF)
1H/ 2H:17	Phase II data in patients with brain mets from NSCL	Lucanthone
2017	Phase II data in 1st line monotherapy lung adenocarcinoma	Poziotinib
2017/ 2018	Phase III data in relapsed follicular lymphoma	Zevalin
2018	Potential FDA approval	SPI-2012 (GCSF)

Source: Company reports and RBC Capital Markets estimates

Exhibit 250: SPPI pipeline

Product	Indication	Status	Patent
Zevalin (ibritumomab)	1st-line consolidation in follicular NHL	Marketed	
	Relapsed / refractory low-grade or follicular B-cell NHL		
	Diffuse large B-cell lymphoma (ZEST)	Phase III	
	Relapsed DLBCL patients who get ASCT (SPINOZA)	Phase III	
	Rituxan refractory low-grade or follicular B-cell NHL with MGd	Phase II	
Fusilev (leucovorin)	Osteosarcoma	Marketed	Expires March 7, 2022 (inc. Hatch-Waxman extension)
	Colorectal cancer		
Folotyn	Peripheral T-cell lymphoma	Marketed	Jul. 16, 2022 (inc. Hatch-Waxman extension)
	CTCL	Phase I	
Marqibo	Philadelphia chromosome negative ALL in 2nd or higher relapse or for disease progression after two or more anti-cancer	Marketed	2024
	ALL (newly diagnosed)	Phase III	
	Diffuse large B-cell lymphoma (elderly patients)	Phase III	
Beleodaq (belinostat)	Peripheral T-cell lymphoma	Marketed	
	Non-small cell lung cancer (NSCLC)	Phase I	
Captisol enabled (CE) melphalan	Multiple myeloma, autologous transplant	NDA	2029
SPI-2012 (HM10460A)	Neutropenia	Phase II complete, Phase III planned	
Poziotinib	Breast, gastric, lung, and colorectal cancer	Phase II	
Apaziquone	Immediate instillation in non-muscle invasive bladder cancer (NMIBC)	Pre-NDA	
	Multiple instillations of intravesical apaziquone (MIIA)	Phase III on hold	
MGd	Radiation sensitizer with Zevalin	Phase II	
Ozarelix	Hormone dependent prostate cancer	Phase II	
Lucanthone	GBM/Brain metastasis	Phase II	
SPI-1620	NSCLC (Docetaxel +/- SPI-1620)	Phase II	
	Biliary cancer (2nd line)	Phase II	
MTRN-2696	Solid tumors (oral)	Phase I	
Orataxel	Solid tumors (oral)	Phase I	
SPI-014 (RenaZorb)	Hyperphosphatemia in ESRD	Phase I	
SPI-205	Chemo-induced neuropathy	Preclinical	

Source: Company reports and RBC Capital Markets estimates

Exhibit 251: Income statement for SPPI

($ in MM; except per share)	2014A	Q1:15A	Q2:15A	Q3:15A	Q4:15E	2015E	Q1:16E	Q2:16E	Q3:16E	Q4:16E	2016E	2017E	2018E	2019E
Product Sales														
Zevalin	22.3	4.2	4.8	4.8	4.2	18.0	3.4	3.6	3.8	4.0	14.7	14.7	14.7	14.8
Fusilev	105.7	20.2	14.3	11.1	7.8	53.4	8.0	5.0	3.0	2.7	18.7	6.5	3.3	1.6
Folotyn	47.6	9.3	12.2	8.7	10.4	40.7	9.5	11.0	10.5	11.2	42.2	43.8	45.4	47.1
Belinostat	4.9	2.8	1.7	2.6	2.1	9.2	2.0	2.5	2.3	3.1	9.9	11.5	13.2	14.9
Marqibo	6.2	1.9	2.1	1.3	1.9	7.2	1.9	2.1	2.1	2.1	8.2	9.3	10.5	11.8
CE Melphalan										2.5	2.5	5.0	10.0	15.0
SPI-2012													43.1	154.6
Apaziquone													26.9	55.0
Product sales, net	186.5	38.4	35.1	28.5	26.4	128.4	24.8	24.2	21.7	25.6	96.3	90.9	167.1	315.0
License and contract revenue	0.3	0.2	9.8	0.2			2.1	2.1	2.1	2.1	2.1	4.3		
Total Revenues	186.8	38.6	45.0	28.6	26.4	138.6	26.9	26.3	23.9	27.8	98.4	95.1	167.1	315.0
COGS	27.0	7.1	6.0	8.4	4.7	22.5	4.2	4.2	3.9	4.5	16.8	16.0	27.2	49.2
Research and Development Expenses	69.7	15.9	9.6	9.9	10.5	45.8	11.5	12.5	13.5	14.5	52.0	62.0	72.0	75.0
Sales, General and Administrative Expenses	97.4	23.3	22.6	19.4	19.7	85.0	19.3	19.4	19.5	19.8	78.0	81.8	90.0	103.5
Amortization of intangibles	24.3	14.0	6.9	6.9	0.5	28.3	2.0	2.0	2.0	2.0	8.0	7.0	5.0	5.0
Total Costs and Expenses	218.4	60.3	45.0	44.7	35.4	185.4	37.0	38.1	38.9	40.8	154.8	166.8	194.2	232.7
Operating Income (Loss)	(31.6)	(21.7)	(0.0)	(16.1)	(9.0)	(46.8)	(10.1)	(11.8)	(15.1)	(13.0)	(50.0)	(71.7)	(27.1)	82.3
Change in value of warrant liability	1.0	(0.5)	(0.1)	0.1	0.6									
Other income	(4.4)	(1.0)	0.1	(0.5)	1.9	0.4	0.5	0.5	0.5	0.5	2.0	1.6	1.7	1.8
Total other income	(12.0)	(3.8)	(2.3)	(2.7)	0.2	(8.6)	(1.8)	(1.8)	(1.8)	(1.8)	(7.1)	(7.5)	(5.9)	1.8
Income (Loss) before Tax	(43.5)	(25.4)	(2.4)	(18.8)	(8.8)	(55.4)	(11.9)	(13.5)	(16.8)	(14.8)	(57.1)	(79.2)	(33.0)	84.0
Provision for Income Tax	2.2	0.1	0.0	(0.1)		0.1								29.4
Net Income (Loss) - GAAP	(45.7)	(25.6)	(2.4)	(18.7)	(8.8)	(55.5)	(11.9)	(13.5)	(16.8)	(14.8)	(57.1)	(79.2)	(33.0)	54.6
EPS, Basic (GAAP)	($0.71)	($0.39)	($0.04)	($0.28)	($0.13)	($0.85)	($0.18)	($0.20)	($0.24)	($0.21)	($0.82)	($1.00)	($0.41)	$0.66
EPS, Diluted (GAAP)	($0.58)	($0.32)	($0.03)	($0.23)	($0.11)	($0.69)	($0.14)	($0.16)	($0.20)	($0.17)	($0.67)	($0.84)	($0.34)	$0.64
Shares Outstanding, Basic	64.5	64.9	65.5	65.9	66.2	65.6	67.5	68.9	70.2	71.6	69.6	79.1	80.7	82.3
Shares Outstanding, Diluted	79.2	80.0	80.6	81.0	81.3	80.7	82.6	84.0	85.3	86.8	84.7	94.0	95.8	85.8
EPS - Basic (Non-GAAP)	$0.31	($0.23)	$0.12	($0.12)	$0.03	($0.21)	($0.02)	($0.04)	($0.09)	($0.06)	($0.22)	($0.47)	$0.11	$1.17
EPS - Diluted (Non-GAAP)	$0.26	($0.23)	$0.10	($0.12)	$0.02	($0.21)	($0.02)	($0.04)	($0.09)	($0.06)	($0.22)	($0.47)	$0.09	$1.13

Source: Company reports and RBC Capital Markets estimates

Valuation

Price target/base case: $12. We arrive at our $12 price target using a product-level DCF valuation. Our product-level NPV assigns a value of ~$1/share to Fusilev and Zevalin, ~$1/share to Folotyn, ~$1/share to Beleodaq, ~$1/share to Marqibo and Melphalan, and ~$6/ share to SPI-2012. Earlier-stage pipeline candidates apaziquone and poziotinib at ~$2/share.

Price target impediments

Our price target is dependent primarily on the commercial success of Folotyn and Fusilev. Unfavorable legal/regulatory outcomes and any setbacks in market uptake or clinical development of Fusilev and Zevalin, Folotyn, or other pipeline product candidates could negatively impact our valuation. The biggest risk to Fusilev estimates is the potential for market share loss when generic leucovorin supplies fully return to the market. Upside could come from Apaziquone or other pipeline programs, price increase for marketed products, better-than-anticipated market penetration for Fusilev, and/or lower-than-forecast loss in Fusilev sales.

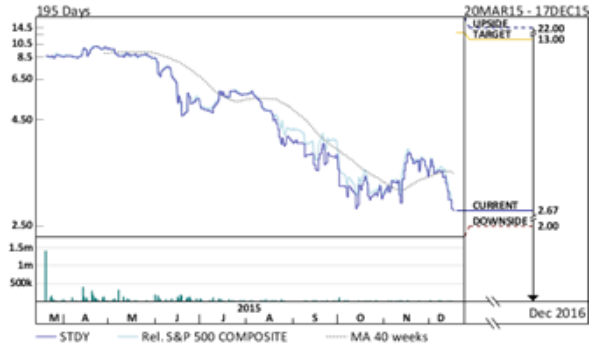
SteadyMed Ltd. (STDY)

Outperform, Speculative Risk

Price Target USD $13.00

Target/Upside/Downside Scenarios

Exhibit 252: SteadyMed Ltd.



Source: RBC Capital Markets estimates

Target price/base case

We value STDY at $13 per share, which includes US and ROW sales of Trevyent and AHPA products. We assign a probability of success of 60% and value of ~$12 per share to Trevyent. We assume a US launch in 2018 and an ex-US launch in 2019. For AHPA products, we assign a probability of success of 25% and value of ~$2 per share. We forecast peak Trevyent sales of $800–850M in the US and $100–150M in the ex-US in 2035 and AHPA peak sales of $700–800M in the US and $200–250M in the ex-US in 2035.

Upside scenario

Our upside scenario of $22 includes ~$18 per share in value for Trevyent and ~$4 for AHPA products. We forecast peak Trevyent sales of $1.2–1.3B in the US and $150–200M in the ex-US in 2035. We forecast peak AHPA product sales of $1–1.2B in the US and $300–400M in ex-US in 2035. We assign a probability of success of 60% for Trevyent and 25% for AHPA products, a discount rate of 15%, and use a terminal growth rate of -50%.

Downside scenario

Our downside scenario assumes that Trevyent may not be successful commercially due to a perceived lack of equivalent efficacy and convenience to Remodulin. Under this scenario, we assume that STDY will be valued at cash per share of $2. In this scenario, we also do not assign any value to any AHPA products.

Investment summary

We believe STDY shares offer the potential for upside, as Trevyent uses STDY's proprietary formulation of preservative-free treprostinil in its proprietary PatchPump to create what is essentially a safer, easier to dose, and more convenient version of Remodulin, a $550M+ drug approved for the treatment of PAH. STDY has sought a bio-waiver and is using the 505(b)(2) pathway to receive approval for Trevyent without conducting any clinical trials, which is an approach that has precedence. STDY will file an NDA in 3Q:16 and expects to hear back from the FDA by YE:17. There are 24,000 patients in the US alone who are eligible to receive prostacyclin therapy, yet only 3,000 are on subcutaneous or intravenous treprostinil (Remodulin), which leaves room for a better product to gain market share and potentially expand the market.

STDY owns 100% of the rights to Trevyent worldwide and patent protection extends into 2035, which means that the company is free to launch Trevyent itself, partner it, or sell it. The pipeline includes both proprietary pain products, for which STDY could also seek a bio-waiver approach, and the PatchPump technology, which could apply to several approved and in-development product candidates, and is available for partnering.

Potential catalysts for the stock

- **Phase I data for ketorolac AHPA in 4Q:15.**
- **Orphan drug designation for Trevyent in 2016.** This would be an important catalyst, as it could foretell the advantages conferred by Trevyent and a shorter-review cycle.
- **NDA filing for Trevyent in 3Q:16.** Acceptance of the NDA for review could signal that the FDA is still comfortable with the bio-waiver approach.
- **NDA decision by YE:17.** Potential approval is likely at the earlier end if the orphan drug designation is granted.

Risks to our investment thesis

- **FDA or other regulatory agencies could request clinical data.** This could significantly delay Trevyent approval timelines and increase the cost of development.
- **United Therapeutics (UTHR) could sue STDY and delay product launch.** STDY's Trevyent does not infringe on UTHR's patents. Nevertheless, the lawsuit could create uncertainty around when Trevyent could be launched.
- **STDY could fail to find a partner for Trevyent.** A partner outside the US is preferable.
- **Sales of Trevyent could lag expectations.** Although the bio-waiver approach is a quick and efficient way to approve a drug, clinicians could be reluctant to use a drug without seeing clinical efficacy and safety.

Key questions and debates for STDY

1. Is Trevyent on track for a 3Q:16 NDA filing?

STDY started manufacturing registration stability lots (RSLs) in November to generate the required data to support a Trevyent NDA submission. Manufacturing issues originally delayed the NDA filing, but the company has communicated some confidence that the data they are generating will be sufficient for a 3Q:16 submission.

2. Will Trevyent receive orphan drug designation?

The Office of Orphan Products Development originally did not grant orphan drug designation to Trevyent. Without disclosing what the additional information was, STDY provided additional data to the Orphan Drug Office and expects a decision in 1Q:16. Being granted orphan status is likely an important catalyst.

3. Is filing of the IPR review by the USPTO for Remodulin meaningful?

The key point is that STDY believes it has freedom to operate so in essence the IPR is an insurance policy. The US PTO could decide in 2Q:16 if the IPR challenge is accepted for review and that would trigger a 12-month review period. STDY filed the IPR against UTHR's '393 patent relating to prostacyclin derivative preparation in Oct. UTHR has 90 days to respond to IPR from filing date (10/2), and then the PTO has another 90 days to decide whether they will actually conduct a review.

4. What will be the design of the Phase II ketorolac trial?

To conserve resources STUDY is going to focus on the development of ketorolac over bupivacaine. A Phase II trial is expected in 2H:16; however, final confirmation on design and scope is a function of agreements with the FDA.

5. Will STDY require more capital?

Based on our estimates, STDY could require further capital prior to getting approval for or commercializing Trevyent and successfully developing further pipeline candidates.

Exhibit 253: Expected news flow for STDY

News Flow

Timing	Description	Product
4Q:15	Conduct PK studies	Ketorolac AHPA
YE:15/ 1Q:16	Submit IND	Bupivacaine AHPA
YE:15/ 1Q:16	Update on orphan drug discussions	Trevyent
1Q:16	Conduct PK studies	Bupivacaine AHPA
YE:16	Submit MAA in PAH with partner(s)	Trevyent
3Q:16	Submit NDA in PAH	Trevyent
4Q:16/ 1Q:17	FDA acceptance of NDA to review or not	Trevyent
2016/ 2017	Conduct registration study	Bupivacaine AHPA
2016/ 2017	Conduct registration study	Ketorolac AHPA
4Q:17	Potential FDA approval	Trevyent
Late 2017	Generic treprostinil entry from Sandoz and TEVA	Competitor: Remodulin
2017	Submit NDA and MAA	Bupivacaine AHPA
2017	Submit NDA and MAA	Ketorolac AHPA
2017/ 2018	Launch Trevyent in the US	Trevyent
2018	Launch Trevyent in the EU	Trevyent
2018	Launch Ketorolac AHPA or Bupivacaine AHPA	Ketorolac AHPA/ Bupivacaine AHPA

Source: Company reports and RBC Capital Markets estimates

Exhibit 254: STDY pipeline

Product	Indication	Stage
Trevyent	Pulmonary arterial hypertension (PAH)	Pre-NDA
Bupivacaine AHPA	Pain	Pre-IND
Ketorolac AHPA	Pain	Pre-IND

Source: Company reports and RBC Capital Markets estimates

Exhibit 255: Income statement for SPPI

($ in MM; except per share)	2014A	1Q:15A	2Q:15A	3Q:15E	4Q:15E	2015E	1Q:16A	2Q:16A	3Q:16E	4Q:16E	2016E	2017E	2018E	2019E	2020E	2021E	2022E
Revenue																	
Trevyent	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4.4	23.1	49.1	130.1	193.2
AHPA	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	14.0	28.8	59.3	121.8
Ex-US Royalties																	
Trevyent	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	1.3	2.7	6.9
AHPA	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.3	2.6	5.1
Other	0.0	0.0	0.0	0.4	0.4	0.8	0.4	0.4	0.4	0.4	1.6	0.8	0.0	0.0	0.0	0.0	0.0
Total Revenue	**0.0**	**0.0**	**0.0**	**0.4**	**0.4**	**0.8**	**0.4**	**0.4**	**0.4**	**0.4**	**1.6**	**0.8**	**4.4**	**37.4**	**80.5**	**194.6**	**327.0**
Operating expenses																	
COGS	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.1	6.7	11.7	28.4	47.3
R&D	12.9	4.4	5.4	4.8	5.6	20.2	5.7	6.0	6.5	6.8	25.0	28.8	14.4	7.2	3.6	1.8	1.8
SG&A	2.9	1.1	1.4	1.5	1.6	5.6	1.7	1.8	2.0	2.2	7.7	20.5	40.0	59.0	78.9	96.5	106.2
Other	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total operating expenses	**15.8**	**5.5**	**6.8**	**6.3**	**7.1**	**25.8**	**7.4**	**7.8**	**8.5**	**9.0**	**32.7**	**49.3**	**55.5**	**72.9**	**94.2**	**126.7**	**155.2**
Operating Income (Loss)	**(15.8)**	**(5.5)**	**(6.8)**	**(5.9)**	**(6.7)**	**(25.0)**	**(7.0)**	**(7.4)**	**(8.1)**	**(8.6)**	**(31.1)**	**(48.5)**	**(51.1)**	**(35.5)**	**(13.7)**	**67.9**	**171.8**
Other income (expenses)																	
Financial expense	(3.0)	0.1	(0.1)	0.1	0.1	0.2	0.1	(0.1)	0.1	0.1	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Other	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total other income (expense)	**(3.0)**	**0.1**	**(0.1)**	**0.1**	**0.1**	**0.2**	**0.1**	**(0.1)**	**0.1**	**0.1**	**0.2**	**0.2**	**0.2**	**0.2**	**0.2**	**0.2**	**0.2**
Pretax Income	(18.8)	(5.4)	(6.9)	(5.9)	(6.6)	(24.8)	(6.9)	(7.5)	(8.0)	(8.5)	(30.9)	(48.3)	(50.9)	(35.3)	(13.5)	68.1	172.0
Accretion convertible preferred shares																	
Income tax expense	(0.2)	(0.1)	0.0	(0.1)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	(23.8)	(60.2)
Net income (loss)	**(19.0)**	**(5.6)**	**(6.9)**	**(6.0)**	**(6.6)**	**(24.8)**	**(6.9)**	**(7.5)**	**(8.0)**	**(8.5)**	**(30.9)**	**(48.3)**	**(50.9)**	**(35.3)**	**(13.5)**	**44.2**	**111.8**
EPS - Basic (GAAP)	**($44.15)**	**($4.35)**	**($0.51)**	**($0.44)**	**($0.48)**	**($2.35)**	**($4.35)**	**($0.54)**	**($0.33)**	**($0.35)**	**($1.29)**	**($1.39)**	**($1.44)**	**($0.86)**	**($0.32)**	**$1.04**	**$2.57**
EPS - Diluted (GAAP)	**($44.15)**	**($4.35)**	**($0.51)**	**($0.44)**	**($0.48)**	**($2.35)**	**($4.35)**	**($0.54)**	**($0.33)**	**($0.35)**	**($1.29)**	**($1.39)**	**($1.44)**	**($0.86)**	**($0.32)**	**$0.99**	**$2.47**
Shares (basic)	0.5	1.5	13.5	13.6	13.7	10.6	13.8	13.9	24.0	24.2	24.0	34.7	35.3	41.1	41.9	42.7	43.6
Shares (diluted)	7.3	3.0	15.0	15.1	15.2	12.1	15.4	15.5	25.6	25.8	25.6	36.3	37.0	42.7	43.6	44.5	45.3

Source: Company reports and RBC Capital Markets estimates

Valuation

We value STDY at $13 per share, which includes US and ROW sales of Trevyent and AHPA products. We assign a probability of success of 60% and value of ~$12 per share to Trevyent. We assume a US launch in 2018 and an ex-US launch in 2019. For AHPA products, we assign a probability of success of 25% and value of ~$2 per share. We assume a US launch in 2019 and an ex-US launch in 2020. Currently, we assume that STDY will sell both Trevyent and AHPA products in the US and that a partner will commercialize these compounds outside the US. We forecast peak Trevyent sales of $800–850M in the US and $100–150M ex-US in 2035 and AHPA peak sales of $700–800M in the US and $200–250M ex-US in 2035. Finally, we assume product sales extend into 2035 and include a terminal value based on a terminal growth rate of -50% and a discount rate of 15%.

Price target impediments

Our price target is dependent solely on the clinical, regulatory, and commercial success of Trevyent and AHPA products. Assuming the FDA's acceptance of Trevyent under Section 505(b)(2), approval is expected in 2016. Failure to secure approval without clinical trials would be a significant setback, as testing STDY products through clinical trials would delay launch and would be costly. Furthermore, any other setbacks in regulatory approval in the US or EU, delay in launch, failure to secure a partnership outside the US, reimbursement, increased competition, or other limitation to the market potential for Trevyent could negatively affect our valuation.

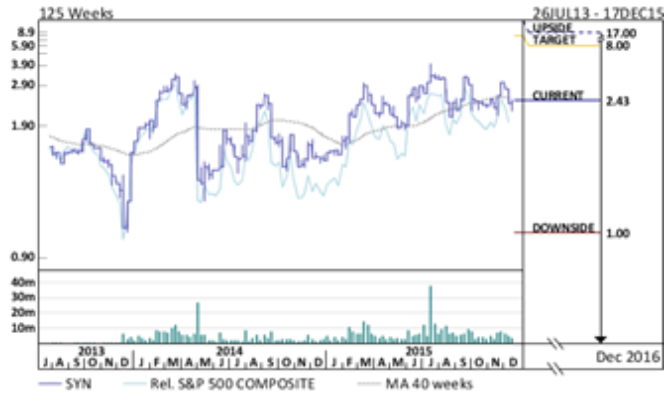
Synthetic Biologics (SYN)

Outperform, Speculative Risk

Price Target USD $8.00

Target/Upside/Downside Scenarios

Exhibit 256: Synthetic Biologics.



Source: RBC Capital Markets estimates

Target price/base case

We value SYN at $8 per share. We assign a probability of success of 60% and a value of $4 per share to SYN-004 in CDI. For SYN-010 in IBS-C, we assign a probability of success of 55% and a value of $4 per share. We assume that both products launch (US) in 2019. Finally, we assume product peak sales in 2031 for the US and EU. We include a terminal value based on a terminal growth rate of -50% and a discount rate of 15%.

Upside scenario

Our upside scenario values SYN at $17 per share and includes SYN-004 sales in CDI for ~$10 per share and SYN-010 for ~$6.40 share. We forecast peak SYN-004 sales of ~$2.3B+ and SYN-010 of $3.4B+ for the US and ex-US. For the US, we assign the same probability of success as for the base case.

Downside scenario

Our downside scenario of $1 per share assumes that SYN may not be successful in clinical trials of SYN-004 and SYN-010. Under such a scenario, cash per share is ~$1.

Investment summary

We believe SYN shares offer the potential for significant upside given multiple shots on goals with at least two clinical-stage candidates addressing high unmet needs that leverage the microbiome. SYN-004 is in Phase II studies for the prevention of C. Difficile infection (CDI) with existing proof-of-concept data in earlier-stage and first-generation compound available. SYN-010 is in Phase II studies for the treatment of irritable bowel syndrome with constipation (IBS-C) with promising proof-of-principle data. Both SYN-004 and SYN-010 could achieve blockbuster status in their respective indications. Both also have the potential to expand to additional indications.

Potential catalysts for the stock

Our investment view is driven by:

- SYN-010 and SYN-004 Phase II data in 2015 and 2016. This is the first look into the activity.
- SYN-010 and SYN-004 Phase III clinical trial initiation in 2016 and 2017. Updates on Phase III study design for IBS-C and/or CDI and timelines to data are key.
- SYN-010 Phase III data in IBS-C in 2017. Efficacy studies could read out within one year while safety studies could take longer.

Risks to our investment thesis

- Clinical studies for SYN-004 in CDI and SYN-010 in IBS-C or development of earlier-stage programs could fail.
- SYN could fail to find a partner for its therapeutic candidates.
- Sales of products could lag expectations. Without differentiation, clinicians and payers could be slow to adopt SYN-004 and/or SYN-010, putting their assumed blockbuster potential at risk.

Key questions and debates for SYN

1. Can SYN-004 prevent CDI without affecting antibiotic efficacy?

SYN-004 is designed to break down beta-lactam antibiotics in the gut to protect the gut microbiome. Since it is not absorbed into systemic circulation, it is expected not to affect the efficacy of beta-lactam antibiotics administered intravenously, as shown by the recently completed Phase IIa study. Evidence also exists from the first-generation compound with Phase I and Phase II data as well as from Phase I studies of SYN-004.

2. Is methane production an accepted biomarker for IBS-C? What is needed for SYN-010 approval?

Methane production as a biomarker for IBS-C appears to be gaining traction and could easily garner greater acceptance by clinicians and regulators as SYN delivers more clinical data in IBS-C. However, while breath methane levels may be helpful in enrolling or enriching trials, the FDA is likely to require clinical endpoints such as bowel movement, constipation and pain, similar to what has been required for other IBS-C drug approvals.

3. Will data from the ongoing Phase II studies for SYN-010 and SYN-004 lead to the start of Phase III programs?

The ongoing Phase IIb study for SYN-004 is a large, randomized study that is going to show both efficacy and safety outcomes. We believe data from that study could be sufficient to advance to a Phase III study. The ongoing Phase II studies of SYN-010 will also measure clinical endpoints along with breath methane levels. Depending on the level of clinical benefit seen, SYN could advance the IBS-C program into a Phase III pending FDA discussion.

4. Will SYN require more capital prior to bringing SYN-004 and SYN-010 to the market?

Phase II studies should be completed with current cash and results assuming they are positive could be value creating events. However, conducting the Phase III studies and then commercializing the candidates could require more capital, where SYN could have several options available, including partnership(s) for one or both agents as well as other pipeline candidates.

5. What is the probability that timelines can slip?

Phase II studies in CDI and IBS-C for the lead candidates are ongoing. Once the Phase III program begins after successful Phase II trials, we think timelines for SYN-010 should be relatively straightforward since it is a well-trodden path. SYN-004 is more novel in its indication so it could take more work to finalize clinical trial design and patients recruit.

Exhibit 257: Expected news flow for SYN

Timing	Description	Product
YE:15	Phase II data in IBS-C (breath methane)	SYN-010
YE:15	Phase IIa data in CDI	SYN-004
1Q:16	Phase II data in IBS-C (extension phase)	SYN-010
1Q:16	Phase II data in CDI with PPI	SYN-004
Mid-/ 2H:16	Phase IIb data in CDI	SYN-004
2H:16	End of Phase II meeting	SYN-010
YE:16	Initiate Phase III trial in IBS-C	SYN-010
2017	Initiate Phase III trial in CDI	SYN-004
YE:17/ 1H:18	Phase III results in IBS-C	SYN-010
2018/ 2019	Phase III data in CDI	SYN-004

Source: Company reports and RBC Capital Markets estimates

Exhibit 258: SYN pipeline

Product	Stage	Indication	Partner
SYN-004	Phase II	C.difficile infection (CDI) /Antibiotic-associated diarrhea (AAD)	
SYN-010	Phase II	Irritable bowel syndrome with constipation (IBS-C)	Cedars-Sinai Medical Center
Trimesta	Phase II	Relapsing-remitting multiple sclerosis	
	Phase II	Cognitive dysfunction in multiple sclerosis	
SYN-005	Phase I	Pertussis (whooping cough)	Intrexon Corporation, The University of Texas at Austin

Source: Company reports

Exhibit 259: Income statement for SYN

($ in millions, except per share) Fiscal Year Ends December	2014A	1Q:15A	2Q:15A	3Q:15A	4Q:15E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E
Revenue														
SYN-004	-	-	-	-	-	-	-	-	-	22.36	45.84	93.98	192.69	395.05
SYN-010	-	-	-	-	-	-	-	-	-	6.27	19.63	40.32	124.31	255.65
Ex-US Royalties	-	-	-	-	-	-	-	-	-	-	-	-	-	-
SYN-004 - Ex-US royalties	-	-	-	-	-	-	-	-	-	-	2.98	5.96	11.95	23.93
SYN-010 - Ex-US royalties	-	-	-	-	-	-	-	-	-	-	1.38	2.77	5.57	16.78
Other	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Total Revenue	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**28.63**	**69.83**	**143.04**	**334.51**	**691.41**
Operating expenses														
R&D	14.49	6.49	7.51	10.05	8.51	32.55	47.50	65.00	85.00	60.00	20.00	10.00	5.00	5.00
SG&A	6.01	1.71	2.22	1.60	1.96	7.50	11.10	15.92	27.08	60.00	85.00	97.50	102.38	107.49
Acquired in-process R&D	-	-	-	-	-	-	-	-	-	-	-	-	-	-
COGS	-	-	-	-	-	-	-	-	-	4.29	9.82	20.15	47.55	97.60
Other	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Total operating expenses	**20.50**	**8.21**	**9.73**	**11.65**	**10.47**	**40.05**	**58.60**	**80.92**	**112.08**	**124.29**	**114.82**	**127.65**	**154.93**	**210.10**
Operating Income (Loss)	**(20.50)**	**(8.21)**	**(9.73)**	**(11.65)**	**(10.47)**	**(40.05)**	**(58.60)**	**(80.92)**	**(112.08)**	**(95.67)**	**(44.99)**	**15.40**	**179.59**	**481.31**
Other income (expenses)														
Interest income	0.00	0.00	0.00	0.00	0.00	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
Interest expense	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Other	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Total other income (expense)	**0.72**	**(4.15)**	**(3.89)**	**4.14**	**0.00**	**(3.90)**	**0.01**	**0.01**	**0.01**	**0.01**	**0.01**	**0.01**	**0.01**	**0.01**
Pretax Income	**(19.78)**	**(12.36)**	**(13.62)**	**(6.77)**	**(9.73)**	**(42.49)**	**(57.13)**	**(79.44)**	**(110.61)**	**(94.19)**	**(43.51)**	**16.87**	**181.06**	**482.79**
Income tax expense	-	-	-	-	-	-	-	-	-	-	-	(5.90)	(63.37)	(168.98)
Net income (loss)	**(19.78)**	**(12.36)**	**(13.62)**	**(6.77)**	**(9.73)**	**(42.49)**	**(57.13)**	**(79.44)**	**(110.61)**	**(94.19)**	**(43.51)**	**10.97**	**117.69**	**313.81**
EPS - Basic (GAAP)	**($0.32)**	**($0.17)**	**($0.19)**	**($0.08)**	**($0.11)**	**($0.53)**	**($0.58)**	**($0.70)**	**($0.88)**	**($0.65)**	**($0.29)**	**$0.07**	**$0.77**	**$2.00**
EPS - Diluted (GAAP)	**($0.32)**	**($0.17)**	**($0.19)**	**($0.08)**	**($0.11)**	**($0.53)**	**($0.58)**	**($0.70)**	**($0.88)**	**($0.65)**	**($0.29)**	**$0.07**	**$0.69**	**$1.81**
Shares (basic)	61.9	72.7	72.7	86.0	89.2	80.1	97.9	113.1	125.4	144.9	147.8	150.8	153.8	156.9
Shares (diluted)	61.9	72.7	87.2	87.6	104.0	87.9	113.0	128.7	141.1	160.8	163.8	167.0	170.1	173.4

Source: Company reports and RBC Capital Markets estimates

Valuation

We value SYN at $8 per share. We assign a probability of success of 60% and a value of $4 per share to SYN-004 in CDI. For SYN-010 in IBS-C, we assign a probability of success of 55% and a value of $4 per share. We assume US launch in 2019. Finally, we assume product peak sales in 2031 for the US and EU. We include a terminal value based on a terminal growth rate of -50% and a discount rate of 15%.

Price target impediments

Our price target is dependent solely on the clinical, regulatory, and commercial success of SYN-004 and SYN-010 in CDI and IBS-C, respectively. We expect data from Phase II studies of SYN-010 and SYN-004 in 2015 and 2016 and progress to Phase III studies in 2016 and/or 2017. Failure to demonstrate efficacy or safety in one or both of these studies would be a significant setback to our forecasts. Furthermore, any setback in regulatory approvals for CDI or IBS-C, delay in launch, especially in the US, failure to secure a partnership outside the US or possibly in the US for one or both products, increased competition or other limitations to the market potential, such as resistance by clinicians or payers to use or price, could negatively affect our valuation.

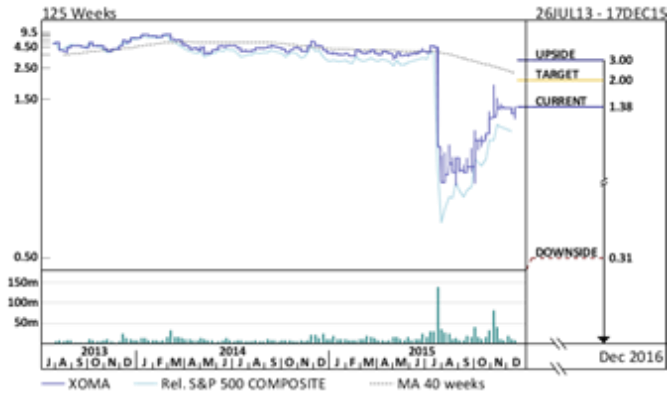
XOMA Corporation (XOMA)

Sector Perform, Speculative Risk

Price Target USD $2.00

Target/Upside/Downside Scenarios

Exhibit 260: XOMA Corporation.



Source: RBC Capital Markets estimates

Target price/base case

We arrive at our $2 price target using a product level DCF valuation. Our product level NPV assigns a value of ~$2 / share for pyoderma gangrenosum with a 35% probability of success.

Upside scenario

Upside scenario: $3. Our upside scenario assumes similar values for gevokizumab in pyoderma gangrenosum with higher market potential as well as a probability adjusted sales multiple based sum-of-the-parts valuation for the pipeline.

Downside scenario

Our downside scenario assumes pipeline programs do not succeed leaving cash per share of $0.31.

Investment summary

An investment in XOMA is predicated on the assumption that its lead drug, gevokizumab (XOMA 052), will be successfully developed for any one of several potential indications, such as pyoderma gangrenosum, where Phase III trials are ongoing, or other pipeline programs. Though the pipeline is under review, several planned and ongoing studies targeting orphan indications increase the likelihood of success and potentially provide a path to expedited approval.

Potential catalysts for the stock

Our investment view is driven by:

- Faster-than-forecast enrollment in pyoderma grangreosum.
- Phase III NIU data in 2015/2016.
- Pivotal trial data from pyoderma gangreosum in 2016/2017.
- Data from one or more of several ongoing proof-of-concept studies.

Risks to our investment thesis

- Slower than anticipated clinical trial enrollment.
- Clinical setbacks for ongoing pivotal studies.
- Failure of pipeline to advance
- Inability to execute on business development and pay down debt obligations.

Key questions and debates for XOMA

1. Is there clinical potential left in XOMA's pipeline?

XOMA is now focusing its clinical program on endocrinological disorders, such as XOMA 358 for hypoglycemia due to hyperinsulinemia, an ultraorphan indication. The company has pivoted to this area because it seems less competitive and mostly seeded with large biopharma players. XOMA 213 is in development for hyperprolactinemia. Phase III studies for gevokizumab in pyoderma gangrenosum are also ongoing, although XOMA's outlook appears more cautious.

2. What are the potential catalysts?

For XOMA 358, A Phase II study in patients with congenital hyperinsulinism is enrolling with the goal to lower the activity of the insulin receptor, while another Phase II in bariatric surgery is planned for 1Q:16. Both could potentially have data in 2016, which would serve as potential catalysts for the stock. In addition, XOMA 213 for hyperolactenemia could also have data in 2016/2017.

3. Does XOMA have enough cash to push clinical programs forward?

XOMA ended September with $32M in cash, but pro forma cash balance could be closer to $74M with recent business development activities, such as licensing its TGF beta antibody program with Novartis and XMetA with Novo Nordisk. The company believes this cash is enough to fund operations into 2017.

Exhibit 261: Expected news flow for XOMA

Timing	Expected News Flow	Program
YE:15	Initiate Phase II in congenital hyperinsulinism	XOMA 358 (XMetD)
YE:15	Initiate Phase II in post-bariatric surgery hyperinsulinism	XOMA 358 (XMetD)
2015/ 2016	Initiate Phase II proof of concept study in hyperprolactinemia patients	XOMA 213 (LFA 102)
2015/ 2016	Potential outlicensing	XOMA 089, biodefense portfolio, XMetA
2016/ 2017	Potential Phase II data in congenital hyperinsulinism	XOMA 358 (XMetD)
2016/ 2017	Potential Phase II data in post-bariatric surgery hyperinsulinism	XOMA 358 (XMetD)
2016/ 2017	Potential Phase II data in hyperprolactinemia	XOMA 213 (LFA 102)
2H:16/ 1H:17	Pivotal data in neutrophilic dermatoses (pyoderma gangrenosum)	Gevokizumab
2017	Potential BLA for pyoderma gangrenosum	Gevokizumab
2017/ 2018	Potential Phase II data in diabetic nephropathy	Gevokizumab
2018	Potential approval in pyoderma gangrenosum	Gevokizumab

Source: Company reports and RBC Capital Markets estimates

Exhibit 262: XOMA pipeline

Product	Stage	Indication(s)	Partner(s)
Gevokizumab	Phase III discontinued	Behcet's disease (Phase III failed), non-infectious uveitis (NIU), NIU controlled	Servier continues NIU
	Phase III	Pyoderma Gangrenosum	
	Phase II	Diabetic nephropathy	Servier
	Phase II	Schnitzerl's syndrome	Servier
XOMA 358	Phase II planned	Congenital hyperinsulinism	
XOMA 213 (LFA102)	Phase II planned	Prolactinoma, anti-psychotic induced hyperprolactinemia	
XOMA 129 (XMetD FAB)	Pre-clinical	Acute severe hypoglycemia	
XOMA 089	Pre-clinical	TGF beta for cancer	
XMetA (INSR)	Pre-clinical	Short-acting reversal of insulin	
Anti-PTHr	Pre-clinical	Hyperparathyroidism, malignancy induced hypercalcemia	
Anti-ACTH	Pre-clinical	Cushing's disease	

Source: Company reports and RBC Capital Markets estimates

Exhibit 263: Income statement for XOMA

($ in millions, except per share)	2014A	Q1:15A	Q2:15A	Q3:15E	Q4:15E	2015E	Q1:16E	Q2:16E	Q3:16E	Q4:16E	2016E	2017E	2018E	2019E
REVENUES:														
Aceon Revenue	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
License and collaborative fees	5.7	0.3	0.9	0.6	1.1	3.0	0.3	0.3	0.3	0.3	1.0	2.0	2.0	2.0
Contract and other revenue	13.2	2.4	1.6	1.4	2.6	8.0	1.0	1.0	1.0	1.0	4.0	4.0	4.0	2.0
Gevokizumab sales (US)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	12.7	57.0
Royalties (Gevokizumab ex-US)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.9	12.4
Total Revenues	**18.9**	**2.7**	**2.5**	**2.1**	**3.7**	**11.0**	**1.3**	**1.3**	**1.3**	**1.3**	**5.0**	**6.0**	**21.6**	**73.4**
EXPENSES:														
Research and development	80.7	20.0	19.7	17.6	12.0	69.3	8.0	6.0	6.0	6.0	26.0	30.0	25.0	30.0
General and administrative	19.9	5.2	5.1	5.6	3.5	19.4	2.5	2.3	2.0	2.0	8.8	10.0	11.0	12.0
Other expenses	0.1	0.0	0.0	2.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total Operating Expenses	**100.7**	**25.2**	**24.8**	**25.8**	**15.5**	**88.7**	**10.5**	**8.3**	**8.0**	**8.0**	**34.8**	**40.0**	**37.3**	**47.7**
Operating Income (Loss)	**(81.8)**	**(22.6)**	**(22.2)**	**(23.7)**	**(11.8)**	**(77.7)**	**(9.3)**	**(7.0)**	**(6.8)**	**(6.8)**	**(29.8)**	**(34.0)**	**(15.7)**	**25.7**
Total Other Income (Expense)	43.5	0.9	(1.5)	23.2	(26.4)	(3.9)	(1.0)	(1.0)	(1.0)	(1.0)	(4.0)	(2.9)	(2.4)	(1.9)
Income before Tax	**(38.3)**	**(21.7)**	**(23.8)**	**(0.5)**	**(38.2)**	**(81.6)**	**(10.3)**	**(8.0)**	**(7.8)**	**(7.8)**	**(33.8)**	**(36.9)**	**(18.1)**	**23.8**
Provision for taxes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	8.1
Net Income (Loss)	**(38.3)**	**(21.7)**	**(23.8)**	**(0.5)**	**(38.2)**	**(81.6)**	**(10.3)**	**(8.0)**	**(7.8)**	**(7.8)**	**(33.8)**	**(36.9)**	**(18.1)**	**15.7**
GAAP EPS - Basic	($0.36)	($0.19)	($0.20)	($0.00)	($0.30)	($0.68)	($0.08)	($0.06)	($0.06)	($0.06)	($0.24)	($0.20)	($0.09)	$0.07
GAAP EPS - Diluted*	($0.36)	($0.19)	($0.20)	($0.00)	($0.30)	($0.68)	($0.08)	($0.06)	($0.06)	($0.06)	($0.24)	($0.20)	($0.09)	$0.07
Shares Outstanding - Basic (MM)	107.4	116.2	117.5	118.6	129.1	120.4	129.8	130.4	131.1	131.7	142.8	188.0	211.8	216.0
Shares Outstanding - Diluted (MM)	115.3	147.1	148.4	149.5	160.1	151.2	160.7	161.4	162.1	162.7	172.2	195.2	219.0	223.3

Source: Company reports and RBC Capital Markets estimates

Valuation

We arrive at our $2 price target using a product level DCF valuation. Our product level NPV assigns a value of ~$2/share to gevokizumab with a 35% probability of success in PG. Pipeline success would be an upside driver.

Price target impediments

Risks to our price target include: (1) clinical risk for gevokizumab in pivotal program and POC trials; (2) regulatory risk in the pivotal program; and (3) financing risk, although we expect no additional capital raises until data readouts from gevokizumab warrant further investment.

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