EQUITY RESEARCH

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January 5, 2023

Arrowhead Pharmaceuticals, Inc.

We See Favorable Set-up Into AAT Data Next Week

Our view: SEQUOIA data is on Monday. Some noise is possible given small n/liver biopsy have limitations, but we are fundamental believers in the therapeutic hypothesis given the consistency across endpoints seen to date and endorsed by the FDA via BTD. Overall, we think the bogie of 50% regression in fibrosis vs 15% for placebo is achievable, and we like recent decision that data is at JPM-23 and not YE-22. Stock is +16% since then, but we continue to like the set up and see 80:20 PoS stock is +30%/-25% for high teens risk-adjusted upside.

Key points:

SEQUOIA Data On Monday Next Week - SEQUOIA top-line data is Monday next week. Recall, the trial has enrolled 42 patients randomized 2:1 to fazisiran (25 mg, 100 mg and 200 mg) or placebo. Key endpoints include biomarkers (liver/serum AAT, ALT, GGT, pro-C3), imaging (liver stiffness by FibroScan) and histology (PAS+D globules and fibrosis by METAVIR) but we expect investors to be laser-focused on fibrosis given likely the primary endpoint of the Phase III. Recall, of the 42 patients enrolled, 26 had liver fibrosis (<F4) at baseline. Such patients will receive a biopsy at baseline and at week 48, 72 or 96. Biopsies will be adjudicated by 3 independent pathologists.

Some Noise Possible, But We Are Fundamental Believers In The MoA - We think some noise is certainly possible given small n (only 6-12 patients on drug at the mid-/high-dose) and liver biopsies are notorious for sampling and intra-/inter- reader variability (link). However, we are fundamental believers in the therapeutic hypothesis that turning off the protein will make an impact for patients. The pathophysiology of the disease is well understood, and we like that prior data showed a signal that was consistent across all endpoints. On biomarkers, the 80-90% reduction in serum/liver AAT drove a material reduction in ALT/GGT (general markers of liver stress) and pro-C3 (fibro-genesis/disease progression). On imaging, a dose dependent reduction in liver stiffness was observed by FibroScan. On histology, an improvement was observed for both fibrosis and globule burden. Beyond prior data, we also think: 1) SEQUOIA has the benefit of a longer study (up to 96 weeks biopsy vs up to 48 weeks), 2) decision to present data during JPM Monday (likely to maximize visibility) instead of YE-22 is an indirect vote of confidence, and 3) TAK is clearly convinced as they submitted a Phase III design to the FDA before seeing SEQUOIA. Overall, we think the bogie of ~50% regression in fibrosis for the active arm (on par with prior data) vs 15-20% for placebo (as per prior natural history study) is achievable. On safety, FEV_1 remains a key theoretical risk, but we like flat lines reported so far.

Continued on page 2.

Outperform

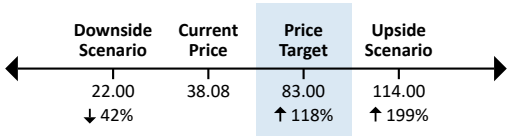
Speculative Risk

NASDAQ: ARWR; USD 38.08

Price Target USD 83.00

WHAT'S INSIDE	
☐ Rating/Risk Change	☐ Price Target Change
☐ In-Depth Report	☐ Est. Change
☐ Preview	☑ News Analysis

Scenario Analysis*



*Implied Total Returns

Key Statistics

Shares O/S (MM):	105.4	Market Cap (MM):	4,015
Dividend:	0.00	Yield:	0.0%
		Avg. Daily Volume:	941,490

RBC Estimates

FY Sep	2021A	2022A	2023E	2024E
Revenue	138.3	243.2	200.0	295.0
EPS, Ops Diluted	(1.36)	(1.67)	(2.18)	(1.92)
Revenue	**Q1**	**Q2**	**Q3**	**Q4**
2022	27.4A	151.8A	32.4A	31.6A
2023	35.0E	45.0E	55.0E	65.0E
EPS, Ops Diluted				
2022	(0.60)A	0.41A	(0.68)A	(0.80)A
2023	(0.66)E	(0.58)E	(0.51)E	(0.43)E

All values in USD unless otherwise noted.
Priced as of prior trading day's market close, EST (unless otherwise noted).

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For Required Conflicts Disclosures, see page 6

We Expect Uncontroversial Phase III Study Design - ARWR is also planning to present an outline of the Phase III study design, but we do not expect any major surprises: placebo-controlled, 200 mg Q12W likely the dose (recent changes on ct.gov suggests it is the dose picked in SEQUOIA for the OLE), the n likely in the ~100 range (recall SEQUOIA was planning to enroll 120 patients when considered potentially registrational) and fibrosis at one year likely the primary endpoint (with possible interim look at six months).

We See High Teens Risk-Adjusted Upside - Stock is +16% (vs +3% for the XBI) since announcement that data is at JPM-23 and not YE-22, but we continue to like the set up and see 80:20 PoS stock is +30%/-25% for high teens risk-adjusted upside.

Luca Issi, Ph.D. (212) 266-4089; luca.issi@rbccm.com

Income Statement

	Q1:21A	Q2:21A	Q3:21A	Q4:21A	2021A	Q1:22A	Q2:22A	Q3:22A	Q4:22A	2022A	Q1:23E	Q2:23E	Q3:23E	Q4:23E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E	2036E	2037E	2038E	2039E	2040E
Revenue	$21	$33	$46	$38	$138	$27	$152	$32	$32	$243	$35	$45	$55	$65	$200	$295	$456	$458	$1,109	$1,216	$1,586	$2,358	$3,100	$4,037	$4,555	$4,881	$5,079	$5,232	$5,382	$5,537	$5,688	$5,838
Collaboration revenue	$21	$33	$46	$38	$138	$27	$152	$32	$32	$243	$35	$45	$55	$65	$200	$220	$242	$266	$293	$322	$354	$390	$429	$472	$519	$571	$628	$690	$759	$835	$919	$1,011
A1AT																$75	$200	$1	$394	$216	$216	$291	$357	$378	$384	$390	$397	$403	$410	$417	$424	$431
APOC3																	$4	$28	$84	$178	$312	$487	$705	$898	$1,063	$1,210	$1,287	$1,316	$1,338	$1,361	$1,384	$1,408
ANG3																	$10	$61	$174	$352	$599	$921	$1,323	$1,811	$2,140	$2,252	$2,313	$2,376	$2,440	$2,506	$2,574	$2,644
HBV																	$0	$2	$14	$48	$105	$185	$287	$379	$449	$458	$455	$446	$434	$417	$386	$344
LPa									$0	$0						$0	$0	$100	$150	$100	$0	$85	$0	$100	$0	$0	$0	$0	$0	$0	$0	$0
Gross Profits	$21	$33	$46	$38	$138	$27	$152	$32	$32	$243	$35	$45	$55	$65	$200	$295	$454	$449	$1,084	$1,163	$1,495	$2,218	$2,897	$3,766	$4,234	$4,534	$4,719	$4,862	$5,005	$5,150	$5,292	$5,433
COGS																$0	$1	$9	$26	$53	$91	$141	$203	$271	$320	$346	$360	$369	$378	$387	$396	$405
Total operating expenses	$45	$61	$78	$103	$287	$91	$110	$105	$115	$422	$107	$109	$110	$112	$437	$509	$564	$593	$616	$635	$654	$673	$694	$714	$736	$758	$773	$788	$804	$820	$837	$853
R&D	$37	$45	$59	$66	$206	$66	$76	$72	$83	$297	$73	$74	$75	$76	$298	$313	$329	$345	$359	$370	$381	$392	$404	$416	$428	$441	$450	$459	$468	$478	$487	$497
SG&A	$9	$16	$18	$37	$81	$25	$34	$33	$32	$124	$34	$35	$35	$36	$139	$196	$236	$248	$257	$265	$273	$281	$290	$298	$307	$317	$323	$329	$336	$343	$350	$357
Income (Loss) From Op.	($24)	($28)	($32)	($65)	($149)	($63)	$42	($73)	($84)	($179)	($72)	($64)	($55)	($47)	($237)	($214)	($110)	($143)	$467	$529	$841	$1,544	$2,203	$3,052	$3,498	$3,777	$3,946	$4,074	$4,200	$4,330	$4,455	$4,580
Other income / expense	$3	$1	$2	$2	$8	$0	$3	$1	$2	$6					$0																	
Income (Loss) Before Tax	($21)	($27)	($30)	($63)	($141)	($63)	$44	($72)	($82)	($173)	($72)	($64)	($55)	($47)	($237)	($214)	($110)	($143)	$467	$529	$841	$1,544	$2,203	$3,052	$3,498	$3,777	$3,946	$4,074	$4,200	$4,330	$4,455	$4,580
Taxes									$3													$31	$44	$122	$140	$227	$316	$407	$588	$779	$713	$916
Net Income (Loss)	($21)	($27)	($30)	($63)	($141)	($63)	$44	($72)	($86)	($176)	($72)	($64)	($55)	($47)	($237)	($214)	($110)	($143)	$467	$529	$841	$1,513	$2,159	$2,930	$3,359	$3,550	$3,630	$3,667	$3,612	$3,551	$3,742	$3,664
Per share																																
Basic	($0.20)	($0.26)	($0.29)	($0.61)	($1.36)	($0.60)	$0.42	($0.68)	($0.81)	($1.67)	($0.66)	($0.58)	($0.51)	($0.43)	($2.18)	($1.92)	($0.97)	($1.27)	$4.14	$4.68	$7.45	$13.41	$19.13	$25.96	$29.75	$31.45	$32.16	$32.48	$32.00	$31.45	$33.15	$32.46
Diluted	($0.20)	($0.26)	($0.29)	($0.61)	($1.36)	($0.60)	$0.41	($0.68)	($0.80)	($1.67)	($0.66)	($0.58)	($0.51)	($0.43)	($2.18)	($1.92)	($0.97)	($1.27)	$4.14	$4.68	$7.45	$13.41	$19.13	$25.96	$29.75	$31.45	$32.16	$32.48	$32.00	$31.45	$33.15	$32.46
Weighted average shares (m)																																
Basic	103	104	104	104	104	105	106	106	106	105	109	109	109	109	109	111	113	113	113	113	113	113	113	113	113	113	113	113	113	113	113	113
Diluted	103	104	104	104	104	105	108	106	107	105	109	109	109	109	109	111	113	113	113	113	113	113	113	113	113	113	113	113	113	113	113	113

All values in millions of $USD, except per share
Source: Company reports, RBC Capital Markets estimates

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Key ESG questions

This section is intended to highlight key ESG discussion points relevant to this company, as well as our views on the outlook. Both the questions we highlight and our responses will evolve over time as the dialogue between management, analysts and investors continues to advance. We welcome any feedback on the topics.

	Our view
What are the most material ESG issues facing this company?	We believe the material ESG issues ARWR currently faces as a clinical stage company include clinical trial conduct, data transparency, and diversity of the management team, which are consistent with ones that affect the broader biotechnology sector.
Does the company integrate ESG considerations into its strategy?	We believe ARWR has continued to progress with aligning to ESG principles across several dimensions and is on a path toward a sustainable finance focus with an ecosystem of stewardship, value, and growth. ARWR is focusing on safe, reliable, and disease-modifying options from rare disease to more common CVD and liver disease indications where quality-of-life of patients is hindered and comes with considerable cost. ARWR is effecting positive change and productivity with a focus on treatments for rare disease (A1AT, ENaC), CVD (hypercholesterolemia, hypertriglyceridemia), and liver disease (NASH), with safe and effective outcomes, increased patient convenience, value, and lower system costs in our view.
How is the company managing data transparency and disclosures?	ARWR reports clinical data periodically at major medical meetings such as AASLD, EASL, ESCC, and AHA, and makes presentations and posters available on its website.
How is the company working to ensure board transparency and governance?	ARWR lists well-documented and transparent governance documents on its corporate website, which list guidelines to ensure good compliance, business conduct, and ethics, as well as corporate governance.

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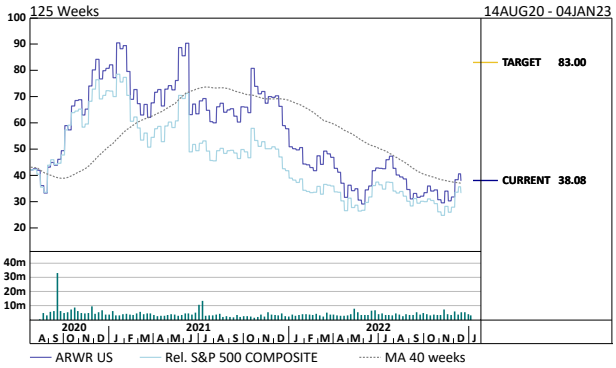
Target/Upside/Downside Scenarios

Arrowhead Pharmaceuticals, Inc.



Source: Bloomberg and RBC Capital Markets estimates for Target

Valuation

Our $83 price target is based on a DCF analysis that assumes a 10% WACC (same for all stocks in our coverage), 1% terminal growth rate (with a 0–2% range applied to our coverage depending on the relative maturity of platforms), 65% PoS for A1AT/APOC3/ANG3, 40% PoS for HBV, 35% for Lpa, and 20% for the platform. Non-PoS adjusted platform value is determined by the sum of the terminal value of each program. Our price target supports our Outperform, Speculative Risk rating. We assign a Speculative Risk qualifier given the unpredictability of future revenues and expenses, non-revenue generating status, and stock price volatility that could result in substantial upside/downside swings not anticipated in our valuation.

Upside scenario

Our upside scenario of $114 assumes 80% PoS for A1AT/APOC3/ANG3, 60% PoS for HBV, 50% for Lpa, 30% for ENaC, and 50% for the platform.

Downside scenario

Our downside scenario of $22 assumes all programs fail but APOC3/ANG3 (25% PoS) and the platform (10% PoS).

Investment summary

Platform De-Risked and Core Programs Poised for Success. We view the TRIM platform as increasingly validated given proven efficacy/benign safety. Despite COVID-19 delays, the A1AT program remains the most advanced and we think poised for success given validated nature of the target and impressive Phase II data. CV targets have shown early POC and we think: 1) APOC3 offers better dosing/safety vs. IONS; and 2) ANG3 offers better duration/route of administration vs. the antibodies (REGN). We view recent decision to pivot from small monogenic diseases (FCS/HoFH) to broader indications (MCM/mixed dyslipidemia/sHTG) as key to further increasing strategic value.

ARWR Best Positioned to Go Beyond Liver. ARWR is finding creative ways to drive tropism to tissue other than liver by optimizing the chemistry and targeting new receptors (i.e., integrins). In lung: the preclinical tox issue in ENaC is unfortunate, but ARWR remains committed to pulmonary with two new lung targets recently announced (RAGE and MUC5AC). In kidney, we view HIF2 as a promising target and note that top-line data in RCC has demonstrated target engagement and at least one patient achieved a partial response. In muscle, we are eager to get updates on upcoming CTA filing for DUX4 in FSHD. None of these programs are reflected in our base case and we view them as further optionality to the upside.

Non-Core Programs Partnered on Favorable Economics. In the HBV race (a polarizing subject of debate among investors) we believe that: 1) a functional cure will be achieved; 2) siRNA will be backbone of therapy; 3) ARWR/JNJ is furthest along; and 4) we think ARWR retains favorable economics (mid-teens royalties, $3.7b potential milestones). The Lpa program is behind IONS/NVS, but we think data so far has been solid, and we view decisions by NVS to start a CVOT trial and by AZN to partner with Silence as validating.

Sheer Volume of Shots on Goal Not Captured by Current Valuation. Overall, we think the sheer volume of shots on goal offers both diversification (risk spread across the portfolio) and a steady flow of read-outs that are not fully captured by current valuation.

Risks to rating and price target

Risks include clinical program execution, regulatory uncertainties, intellectual property risk, failure to demonstrate sustained efficacy in trials, potential emergence of a safety signal, competition, and long-term pricing pressure in the space.

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Company description

Arrowhead Pharmaceuticals, Inc. operates as a biopharmaceutical company. It develops medicines that treat intractable diseases by silencing the genes that cause them. The company was founded by R. Bruce Stewart in 1989 and is headquartered in Pasadena, CA.

Required disclosures

Conflicts disclosures

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RBC Capital Markets, LLC makes a market in the securities of Arrowhead Pharmaceuticals, Inc..

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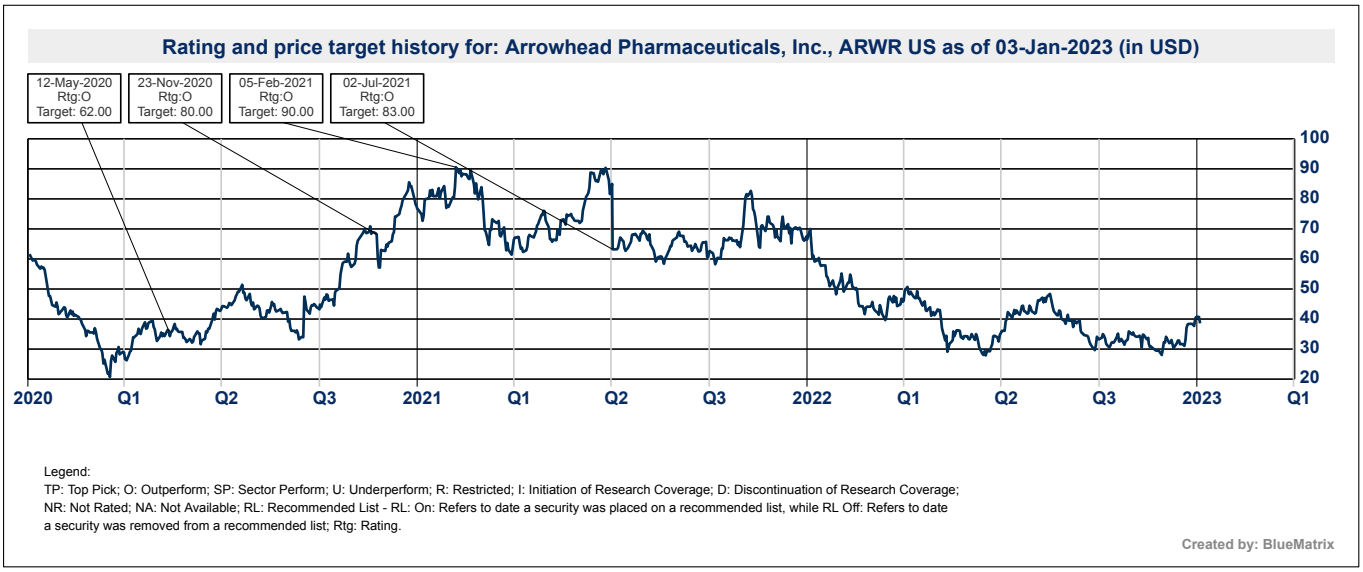
As of 31-Dec-2022

			Investment Banking Serv./Past 12 Mos.	
Rating	**Count**	**Percent**	**Count**	**Percent**
BUY [Outperform]	839	56.05	225	26.82
HOLD [Sector Perform]	603	40.28	151	25.04
SELL [Underperform]	55	3.67	3	5.45



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Arrowhead Pharmaceuticals, Inc.

Valuation

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qualifier given the unpredictability of future revenues and expenses, non-revenue generating status, and stock price volatility that could result in substantial upside/downside swings not anticipated in our valuation.

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