EQUITY RESEARCH FIRST GLANCE

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Arrowhead Pharmaceuticals, Inc.

A Year Of Execution Ahead, With Early A1AT Filing Possible

Outperform
Speculative Risk
NASDAQ: ARWR; USD 53.79
Price Target USD 83.00

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

We caught up with ARWR. No landmark binary this year (maybe a positive in this tape) and the focus remains on execution. On A1AT (biomarkers/ biopsy in 2Q22/3Q22), early filing is viewed as "a flyer", but we think possible given SOC approved on similar evidence. On CV, pivotal for FCS is ongoing and Phase IIb for sHTG/LDL are designed to move quickly into pivotal. ENaC animal tox is ongoing and two new lung candidates will be announced. Reiterate OP given strategic value of siRNA (three prior M&As) and a rich pipeline that balances de-risked liver targets with higher risk/reward extra-hepatic assets.

A1AT: Early Filing Remains Possible Ahead Of Phase III - On A1AT, recall impressive open label data was shared last year (2002 trial - link) and randomized study (SEQUOIA) will read out circulating A1AT in 2Q22 and liver biopsy in 3Q22. FDA meetings are planned after each of these data points, and ARWR reiterated that regulators are: 1) likely to ask for a confirmatory Phase III and 2) equally focused on efficacy and safety as respiratory issues are always a theoretical concern given MoA. Overall, we agree that running Phase III is base case, but also note that: 1) the molecule has breakthrough therapy designation, 2) data to date suggests a clear impact on fibrosis (6/9 patients had a 1+ stage improvement, data adjudicated by three independent pathologists - link1/2), 3) no safety signals to date (FEV_1 unchanged out to week 72, albeit one case of dyspnea in a COPD patient), and 4) augmentation therapy (current SOC) was approved on similar number of patients (Glassia approved on a 50 patient trial, ARWR will have similar numbers when 2002 trial data is combined with SEQUOIA).

CV: Pivotal For FCS Started, Phase IIb For sHTG/LDL Designed Pragmatically - On APOC3, Phase III for FCS has started (12-18 months to enroll plus 10 months to read out the primary endpoint) and two Phase IIb are ongoing in patients with high triglycerides or mixed dyslipidemia. Both studies are exploring different doses (10 mg, 25 mg, 50 mg) with only two injections per patient, which will allow to quickly pick a dose/ dose frequency for Phase III. On ANG3, Phase IIb in mixed dyslipidemia is also ongoing and ARWR notes that exploring both APOC3 and ANG3 for this indication is justified by different clinical profile (APOC3 lowers trigs/ boost HDL, ANG3 lowers LDL). Overall, we like the CV pipeline given: 1) de-risked targets (APOC3 validated by IONS's Waylivra, ANG3 by REGN's Evkeeza), 2) both targets are wholly-owned and offers optionality for non-dilutive funding, 3) potential for approval on biomarkers alone, at least in most severe patients (genetically defined or patients with very high TG/ LDL) and 4) differentiation (IONS is ahead on APOC3, but ARWR will dose less frequently).

Lung: ENaC Tox Findings and New Targets To Be Announced - ENaC is still on voluntary clinical pause and long-term primate studies are ongoing to help contextualize prior rat findings (link).

Continued on page 2.

Results will help determine if the issue is species specific, or due to volume overload. If the latter, ARWR notes that a novel molecule with higher potency has been identified and can drive similar PD effect at much lower volumes. Two novel targets will be announced this year (in-person KOL event in NYC in Feb/March possible pending omicron) and ARWR notes that one of them will have a secreted biomarker that would facilitate PK/PD modeling (ENaC does not have such a biomarker). On possible indications, ARWR notes that CF, asthma, COPD, IPF or viral infections are all viable options.

RCC: HIF2 Data At Higher Doses At ASCO-GU On Feb 19th at 10 am - Longer-term follow-up and first look at the highest dose (1,050 mg weekly) will be presented at ASCO-GU on Feb 19th at 10 am (link). Prior data was mixed given only one PR (65% tumor shrinkage by RECIST) and noisy evidence of target engagement (reduction in HIF2 seen in 7/9 patients, KD ranging from -9% to -82%). ARWR notes that MRK's approved HIF2 (Welireg) also showed delayed responses, but we continue to view HIF2 as upside and not currently in our model. ARWR also acknowledges that oncology requires an expertise that is currently not in-house and the goal is to show PoC for the platform and attract a partner.

Muscle: DUX4 To Start Phase I In 1H22 - ARWR notes promising preclinical data showing ability to prevent tamoxifen-induced expression and revert FSHD-like phenotype in mice (improvements in body weight/muscle fibrosis/motor function). Phase I trial (SAD/MAD) will start in 1H22.

HBV: More Data In 2022, JNJ To Begin A Trial in HDV - More HBV data will be presented this year (likely EASL/AASLD), and ARWR notes that JNJ has recently decided to explore siRNA for Hepatitis delta, where approval just on circulating viral levels is possible (evidence of functional cure not needed).

Lpa: AMGN May Start Pivotal By YE22 - On Lpa, AMGN will read out Phase II data in 1H22 and pivotal trial could start by YE22, pending end of Phase II meeting with the FDA.

Reiterate Outperform - We reiterate OP, given strategic value of siRNA (three prior acquisitions - DRNA for $3.3b by NOVO, MDCO for $9.7b by NVS and Sirna for $1.1b by MRK) and a rich pipeline (10 programs in the clinic) that balances de-risked liver targets with higher risk/reward extra-hepatic assets.

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.

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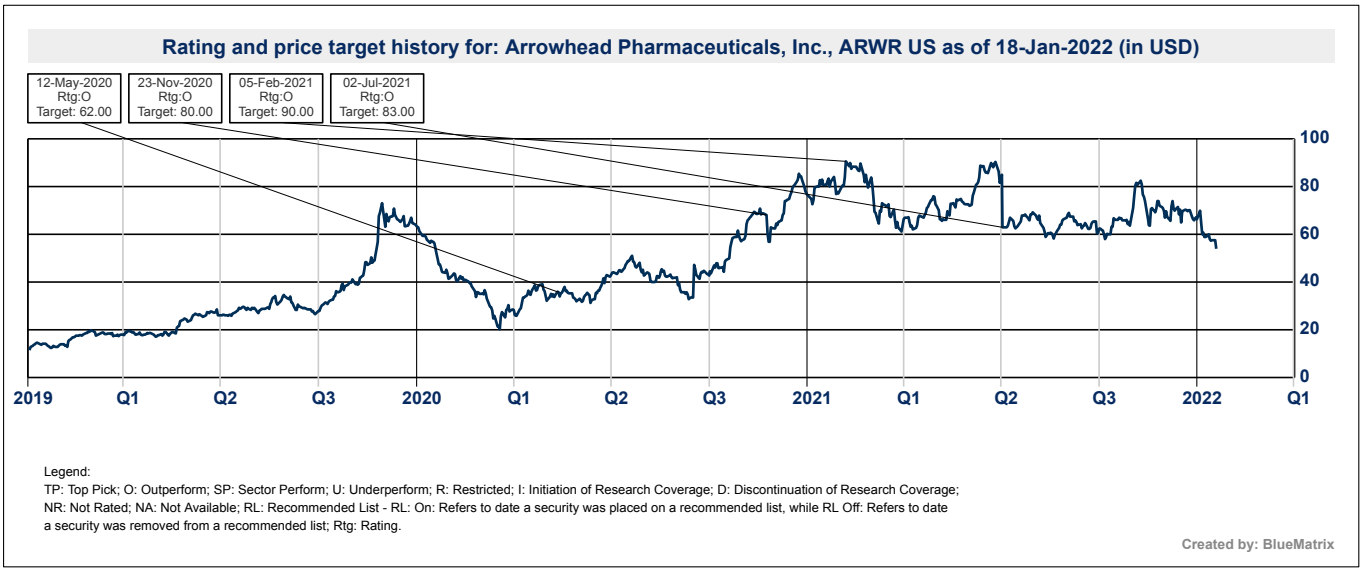

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Arrowhead Pharmaceuticals, Inc.

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.

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