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15 Jan 2024 | **Opinion**

Stock Watch: Fewer Acquisitions Leave Many Behind

For Every Biotech Buyout There Will Be Several Left At The Altar

by Andy Smith

The biotech sector is so diverse that for every acquisition there will be at least one second-best. Even after years of independence following a drug approval, investors keep hoping that their pharmaceutical Prince Charming will arrive.

A Tall Order For The Pace Of M&A

December was a red-letter month for biotechnology companies as the large number of acquisitions that were ether completed or announced propelled the NASDAQ Biotech Index (NBI) skyward. (Also see "*Stock Watch: The Deal Flow Before Christmas*" - Scrip, 2 Jan, 2024.) I remember previous early Januarys sitting in coffee shops just up the hill from the J.P. Morgan Healthcare conference venue on the Sunday before registration and early Monday morning before the conference started reading of the blow-out earnings preannouncements and all the acquisitions that that had been saved up to coincide with the start of the conference. But after last December's red-letter month for biotech acquisitions, this January and the conference started off (and remained) lower key.

Regeneron's Damp Squib

There were some pre-announcements of fourth-quarter and full-year results but *Regeneron Pharmaceuticals, Inc.*'s* – although largely limited to its product for ophthalmic indications, Eylea (afibercept) – threatened to put a damper on the start of the week. US Eylea sales fell by 10% in the fourth quarter of 2023 on the same quarter of 2022 and by 7% on the third quarter of 2023 as Eylea was squeezed between biosimilar and off-label competition to other anti-VEGF agents on the one hand, and *Roche Holding AG*'s recently launched product Vabysmo (faricimab) on the other. Having once dominated the age-related macular degeneration (AMD) segment with

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Eylea, Regeneron had hoped that the higher dose 8mg version with its reduced intraocular injection frequency would help it regain the upper hand. That was until it received a complete response letter (CRL) in late June 2023 from the FDA that cited manufacturing concerns. (Also see "*Regeneron's CRL For High-Dose Eylea Benefits Roche, Vabysmo*" - Scrip, 28 Jun, 2023.)

Having worked with colleagues in pharmaceutical manufacturing and seen how quickly motivated management teams can resolve this type of issue, I invested in Regeneron last year after the CRL partially for its stock price to recover on a quick Eylea 8mg approval (which occurred in late August 2023), but also for the longer-term prospects of its anti-IL-4/IL-13 anti-inflammatory antibody Dupixent (dupilumab) partnered with *Sanofi* in the new potential indication of chronic obstructive pulmonary disease (COPD). (Also see "*Stock Watch: Full Approval And Surrogates Await Clinical Validation*" - Scrip, 4 Apr, 2023.) Like the earlier days of Eylea in AMD (and apart from the lower-cost off-label Avastin (bevacizumab) segment), where Regeneron led the market, clinical failures by *AstraZeneca PLC*'s and *GSK plc*'s* anti-IL-5 antibodies in COPD contrasted with Regeneron's two positive Phase III studies, thus holding out the prospect of a significant Dupixent sales expansion into COPD. Unfortunately, all this, and the rest of Regeneron's presentation at the conference, was thrown out with Eylea's preannounced bathwater as its fourth-quarter US sales also missed analysts' consensus estimates by nearly 2% and its stock price finished the first day of the conference down by over 1% against the NBI's rise by more than twice that margin. To cap a bad day for Regeneron, Eylea 8mg's first full quarter on the market also missed analysts' ambitious estimates by more than 3%.

Residual M&A

The NBI did well to finish in the black after the first day of the conference: the three acquisitions and licensing announcements seemed meager in comparison with December's bonanza and indeed the value and number of deals that had preceded previous conferences. The transactions announced just prior to the conference did, however, continue some of the themes of 2023.

Johnson & Johnson's $2bn acquisition of *Ambrx Biopharma, Inc.* continued the well-worn path of antibody-drug conjugate (ADC) deals that started back in 2019 when AstraZeneca PLC lit the fuse of the second-generation ADC firework.

Merck & Co., Inc.'s $680m acquisition of oncology company *Harpoon Therapeutics* was clearly on-message for a large cancer franchise with Harpoon's lead T-cell engager molecule in early clinical studies for the treatment of solid

J&J Makes Its Biggest Bet Yet On Antibody-Drug Conjugates With Ambrx Buyout

By Alaric DeArment

08 Jan 2024 CEO Joaquin Duato told the J.P. Morgan Healthcare Conference that the drug maker hopes the $2bn acquisition can make one of its lead candidates, ARX517, the first PSMA-directed ADC for prostate cancer. *Read*

tumors. Like Ambrx's early clinical-stage candidate for prostate cancer, the immaturity of these assets might not raise the anti-competitive hackles of the US Federal Trade Commission (FTC), which became more active during 2023 in scrutinizing the establishment of dominant therapeutic franchises formed when big pharmaceutical companies acquire biotech companies. In diving into T-cell engagers for oncology, Merck is taking a page from *Amgen, Inc.*'s* playbook with its $1.2bn acquisition of *Micromet, Inc.* in 2012. Merck's keenness for an acquisition to open the J.P. Morgan Healthcare conference hopefully included a closer study of that page because while Amgen's acquisition of Micromet was followed by Blincyto's (blinatumomab) approval in 2014 for acute lymphoblastic leukemia, Blincyto's third-quarter 2023 sales of $220m represented only 3% of Amgen's third-quarter total revenues. (Also see "*Merck & Co. Spears Another Acquisition With Harpoon*" - Scrip, 8 Jan, 2024.)

the full article here

The deal flow from the first day of the conference was rounded-out with *Novartis AG*'s two transactions – the up to $425m acquisition of early-stage *Calypso Biotech BV*, and the $185m up-front licensing transaction of two early-stage RNAi molecules from Shanghai Argo Biopharmaceutical. (Also see "*I.P. Morgan Day One: Novartis Reveals Two Deals, Pfizer's Bad Year, Bristol's Wobbly Growth*" - Scrip, 9 Jan, 2024.)

The M&A That Pharma Left Behind

In response to the lackluster deal flow on the first day of the conference, the NBI opened slightly down, but a late-in-the-day press article on Novartis's rumored and imminent bid for *Cytokinetics, Inc.* – after the latter's positive Phase III clinical trial announcement in December – propelled the NBI and Cytokinetics' stock to close up by over 2% and by 15%, respectively, by the end of that first day.

But not even GSK's second conference day acquisition of private UK respiratory company Aiolos Bio for up to $1.4bn was enough to maintain the NBI's momentum and the index closed the second day just into negative territory. Like Merck's acquisition of Harpoon, Aiolos was clearly on-message for a respiratory medicine powerhouse, but hopefully early enough in development of its asthma candidate not to attract the attentions of the FTC. GSK was rewarded by its stock rising by just under 2% in London on the second day of the conference. Aiolos was so early

Stock Watch: Cytokinetics – From Certain Villain To Possible Hero

By Andy Smith

08 Jan 2024

Investors' euphoria on Cytokinetics' positive Phase III study may be tempered by its high debt, pass-through royalties, entrenched competition and the FTC in the terms of any transaction.

– less than one hundred days since the company's formation – that social media commentators rightly wondered why GSK's business development machine could not have extended to *Jiangsu Hengrui Medicine Co., Ltd.* in China before, and even on better terms than, the then start-up Aiolos (whose lead product is licensed from Jiangsu Hengrui Medicine Co). (Also see "*GSK Takes A Deep Breath And Drops $1bn On Aiolos*" - Scrip, 9 Jan, 2024.)

Read the full article here

I view the acquisition of Aiolos for its TSLP inhibitor and GSK's following in the TSLP footsteps of Amgen and AstraZeneca as a back-handed complement on the intellectual property surrounding Regeneron's Dupixent. Dupixent's anti-IL-4/IL-13 mechanism in asthma and COPD is unique so far and companies have had to focus on other targets to address these inflammatory indications.

The bigger slap in the face from GSK's acquisition of Aiolos, however, was to those other much later-stage UK respiratory biotech companies whose investors had probably been patiently waiting for a conference acquisition announcement, but were left at the altar of continued losses, independence and an unpartnered product. The stock prices of *Synairgen plc* and *Verona Pharma plc* closed down by nearly 5% and 7%, respectively, on the day of GSK's acquisition of Aiolos. Also like Cytokinetics, RNAi company *Arrowhead Pharmaceuticals, Inc.* had been tipped for an imminent acquisition by its stockholders on social media before the conference, only to be ignored by Novartis (which has xRNA as one of its three emerging platforms) in favor of a Chinese RNAi transaction.

Pouring Cold Water On M&A

One of the stand-out absences from the conference deal flow was a big GLP-1 agonist or related transaction for the treatment of obesity or diabetes. Unlike ADCs, which had deal flow both sides of the year-end, the GLP-1 agonist transaction train is still to get going in 2024. But it was left to the CEO of Novartis, who, after disappointing Arrowhead holders, also dished out cold water on ADCs – with his preference instead for radiolabelled antibodies. In a TV interview at the end of the second day of the conference, and in answer to a question on Cytokinetics (with its market capitalization of over $8bn), he stated a preference for sub-$5bn acquisitions. With the rumored acquisition announcement failing to materialize, Cytokinetics stock finished the week of the conference down by nearly 9%, while the NBI was up by just 1%.

*Andy's pensions hold Regeneron, GSK and Amgen.

Andy Smith gives an analyst and investor's view on life science companies. He joined the independent research house Equity Development in October 2019 having previously been an analyst at Edison group and a Senior Principal in ICON PLC's Commercialization, Pricing and Market Access consulting

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