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J.P. Morgan Day Two: Playing Up Potential In The Year Ahead

by Scrip Team

Daily notebook from the J.P. Morgan Healthcare Conference: Small and mid-size companies take the stage to lay out their guidance for the year, while big pharma is pushed on strategy and business development. Updates from GSK, Mirati, Sarepta, Amgen and US FDA commissioner Robert Califf.

R&D Whiplash At GSK

GSK plc CEO Emma Walmsley made her debut at J.P. Morgan five years ago, outlining an ambitious strategy to turn the company into an oncology powerhouse. That vision has not become a reality and now it appears, from Walmsley's comments this year that the company is ready to take the hit on the chin.

Oncology as a priority therapeutic area received hardly a passing mention, while infectious disease and HIV were highlighted as key areas of investment.

"Infectious disease and HIV represent around two-thirds of our pipeline and are our primary focus for R&D," Walmsley said. Immunology, respiratory and oncology remain areas of investment, but with a "pragmatic approach."

Though GSK has long had a solid foundation in vaccines and HIV, it is still quite a different story than the strategy Walmsley outlined in 2018 after becoming CEO and recruiting Hal Barron to oversee R&D, with a primary goal of rebuilding in oncology. (Also see "*Walmsley Takes On Oncology: Can GSK Become A Power Player?*" - Scrip, 16 Jan, 2018.) Barron has since left, succeeded by Tony Wood, whose early career was in immunology and antiviral drug development. (Also see "*GSK's New Research Chief Begins Leadership With Expanded Genomics/AI Alliance*" - Scrip, 18 Oct, 2022.)

In November, the company's oncology goals took a big hit when the multiple myeloma therapy Blenrep (belantamab mafodotin) was withdrawn from the US market after the Phase III trial meant to confirm the accelerated approval failed to meet the primary endpoint of progression-free survival. (Also see "*Blenrep US Withdrawal Is A Big Blow To GSK's Blockbuster Hopes*" - Scrip, 22 Nov, 2022.)

Meanwhile, the company's Shingrix vaccine for shingles has been a big growth driver and the company has another big opportunity in vaccines in respiratory syncytial virus (RSV). The company's RSV vaccine for older adults is pending at the FDA with action expected by 3 May.

Califf Laments Shift To Ex-US Trials

US Food and Drug Administration commissioner Robert Califf was the keynote speaker to open the second morning of the J.P. Morgan Healthcare Conference on 10 January – and took the opportunity to get a point across to industry about relying on clinical trials that are run outside the US for drugs intended for the US population.

"I'm 100% in favor of globalization. I'm 100% opposed to offshoring as a financial arbitrage," he said. "We're seeing much more of the clinical trial enrollment coming from low-income countries."

Clinical trials run outside the US have become a hot button regulatory issue after the FDA pushed back on approving drugs tested in populations that aren't representative of the US last year. The agency declined to approve *Eli Lilly and Company*/*Innovent Biologics, Inc.*'s PD-1 inhibitor sintilimab because the application was based primarily on data from China, a decision that had implications for several other drug makers that are investing in Chinese-developed drugs. (Also see "*Foreign Data: Sintilimab's Development Shows What Not To Do When Pursuing US Approval*" - Pink Sheet, 16 Feb, 2022.)

"The reasons I emphasize I'm in favor of globalization ... [is] we're only 4% of the world's population, so China, India, Africa, those people should all be doing clinical trials," Califf said. "But the idea that we're offshoring is a financial arbitrage, and the money is being made by selling the products here in the US, where the trials are not being done. I don't think that's a good way to do things."

"It's not good for our economy," he said. "We're also seeing it in supply chains. It's not good for our national security."

Califf also discussed ways companies should counter misinformation about products online. (Also see "*US FDA Mulls Granting Regulated Industry Flexibility To Respond To Misinformation*" - Pink Sheet, 10 Jan, 2023.)

Amgen's Deal Strategy Unchanged After Big Horizon Buy

Amgen, Inc. came to the J.P. Morgan Healthcare Conference in 2022 eager to execute deals of all sizes as it rebuilds a portfolio suffering from multiple losses of exclusivity (LOEs) and anticipating future biosimilars and generics of key products. (Also see "*Amgen CEO Bradway On Deals: Good (Smaller) Opportunities Are Vast*" - Scrip, 11 Jan, 2022.) With the LOE of osteoporosis blockbuster Prolia (denosumab) in 2025 and oral psoriasis therapy Otezla (apremilast) in 2028, the company is still in the market for a wide range of deals even after the December announcement that it will pay $27.8bn for rare disease player Horizon Therapeutics plc. (Also see "*Amgen To Enhance Rare Disease Franchise With $27.8bn Horizon Takeover*" - Scrip, 12 Dec, 2022.)

"We'll continue to look across a range of opportunities to acquire external innovation and also to license external innovation," CEO Bob Bradway said during the Q&A following his 9 January J.P. Morgan presentation. "We think the environment now is well-suited to business development opportunities and ... we think we've put the company in position to capitalize on that, and we want to continue to capitalize on that."

Both Bradway and executive vice president of research and development David Reese reiterated Amgen's stance that the company's capital allocation priorities haven't really changed.

"Priority one, innovation, whether it's internal or external, we want the best innovation that can be had in the world," Reese told *Scrip*. He noted that the company also is committed to maintaining and growing the dividends it pays investors and returning its balance sheet to current levels of debt by 2025.

In terms of deal-making priorities, Reese said, "I would say the aperture remains wide in the sense that in R&D our core focus remains inflammation, general medicine – largely cardiometabolic disease, and then oncology. So those areas, or areas that I would consider strategically adjacent, would be the focus. And then we're open to a range of opportunities from platform technologies in very early preclinical work through molecules at various stages of clinical development or even marketed molecules."

The Horizon transaction and capital allocated to that deal does not signal any abrupt changes in Amgen's deal-making plans, he added.

Galapagos Regroups After Busy 2022

Galapagos NV CEO Paul Stoffels used the firm's slot at J.P. Morgan to say the company is keen on making a couple more deals, be they acquisitions or in-licensing.

Former chief scientific officer at Johnson & Johnson, Stoffels took over at the troubled Belgian biotech in April and he has been busy refocusing the company. "We went through a big change this year," he pointed out, noting that the acquisitions of *CellPoint B.V.* and *Abound Bio,*

Inc. propelled into next-generation cell therapy, marking its entry into oncology, "and we might do more. First we regroup, make this work and then take the next steps." (Also see "*Looking To Learn From Past Failures, Galapagos Pivots To Immunology And CAR-T*" - Scrip, 7 Nov, 2022.)

He added that "acquisitions always are somewhat more complicated because you have to integrate the company ... but we also will look at licensing where we can bring assets in the immunology and the oncology space." Stoffels stressed that while the CellPoint and Abound may suggest a pivot very much towards cancer, "we want to keep a balance, we have a very strong immunology team and capabilities in small molecules which we don't want to leave behind."

The CEO has overseen cuts in the workforce, with 200 jobs shed, and the termination of the company's fibrosis and kidney disease programs. "At the moment, we have done everything we needed to do on the clearing-out," he said, noting that a Phase II trial with investigational CFTR inhibitor GLPG2737 in patients with autosomal dominant polycystic kidney disease will be completed.

Topline results from the study, named MANGROVE, are expected in the first half of 2023 and if successful, Galapagos will out-license the program. "If this works, we have a commitment to make sure that it goes forward [but] it is probably best in somebody else's hands than ours," Stoffels said.

Mirati Unveils Three-Pronged Launch Plan For Krazati

In a 9 January presentation at J.P. Morgan, *Mirati Therapeutics, Inc.* highlighted its strategy for the upcoming launch of its first product, the KRAS inhibitor Krazati (adagrasib). The drug won US approval in December for second-line treatment of KRAS G12C-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC), setting it up for head-to-head competition with Amgen, Inc.'s Lumakras (sotorasib). (Also see "*Mirati's Krazati Is Second KRAS Inhibitor To Market, But At Higher Price*" - Scrip, 13 Dec, 2022.)

CEO David Meek revealed the firm has three main priorities for the Krazati launch. Firstly, "we want to drive Krazati trial and adoption by educating oncologists on the drug's overall response rate, progression-free survival data, overall survival data and finally, CNS penetration," he said. The firm is also concerned with improving accessibility and affordability for patients, and Meek noted work had been underway for more than a year to this end.

Mirati also hopes to expand the eligible patient population for Krazati beyond its current label. "We've got compelling evidence for multiple tumor types and multiple lines of therapy and we're combinable with checkpoint inhibitors," Meek explained.

The company is enrolling second-line plus KRAS G12C-mutated advanced colorectal cancer patients into a Phase III trial studying Krazati plus cetuximab. Mirati also reiterated its plans to

convert its Phase II KRYSTAL-7 trial into a pivotal study for first-line GC12+ NSCLC with a tumor proportion score of less than 50%.

As for the rest of its pipeline, Meek emphasized Mirati would prioritize assets with the "highest opportunity for capital." The firm revealed it had ended 2022 with around $1.1bn, which should support its activities over the next two years.

Sarepta Approaches Cash Positivity With Expected SRP-9001 Approval

Sarepta Therapeutics, Inc. predicts sales of its Duchenne muscular dystrophy (DMD) gene therapy product could reach $4bn, if approved by the US FDA later this year, and make the firm cash positive in 2024.

During a 9 January presentation at J.P. Morgan, CEO Doug Ingram said "2023 will be a bellwether, not merely for Sarepta, but for families with DMD." The FDA has a 29 May review deadline for SRP-9001, which works by delivering the gene that encodes for micro dystrophin to the muscle tissue.

Meanwhile, a separate confirmatory trial of the asset, EMBARK, is under way with a readout penciled in for the fourth quarter of the year. Sarepta admitted it had not yet heard from the FDA regarding a potential advisory committee review but said it was nonetheless preparing for one.

The company also unveiled preliminary fourth quarter earnings as part of the presentation. Sarepta ended 2022 with cash and cash equivalents of around $2bn, down from $2.1bn at the end of the previous year. Net revenues for 2022 are expected to total $843.3m, driven by the consistent performance of its three RNA-based antisense therapies for DMD, Exondys 51 (eteplirsen), Vyondys 53 (golodirsen) and Amondys 45 (casimersen). This would represent a 32% increase on 2021 revenues and surpass management's prior guidance of $825m-$840m.