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J.P. Morgan Notebook Day 2: Bourla Feels Pfizer's Underappreciated, GSK Prepares For Myeloma First And More

by Mandy Jackson

Daily round-up from the J.P. Morgan Healthcare Conference in San Francisco: GSK's first-in-class oncology opportunity, Pfizer's Bourla on underappreciated pipeline, AstraZeneca's Enhertu pricing, Amgen's genomics push, Lilly filters through deals and Medicxi's de Rubertis teases big pharma CEOs about M&A.

Albert Bourla On What The Street Has Wrong About Pfizer

Pfizer Inc. CEO Albert Bourla is one year into the job and tried to impress upon J.P. Morgan Healthcare Conference attendees at a fireside chat in the Grand Ballroom at San Francisco's Westin St. Francis how much the company's innovative R&D business has changed. Pfizer is set to update investors on 2019 financials and 2020 forecasts on 28 January, but Bourla said there is a lot of upside in the company's longer-range pipeline that Wall Street analyst forecasts aren't taking into account.

For example, in vaccines he said that while there are some forecasts for Pfizer's 20-valent pneumococcal vaccine, analysts aren't accounting for a *Clostridium difficile* vaccine in Phase III that will read out later in 2020, a meningococcal vaccine in Phase II, and a maternal vaccine for respiratory syncytial virus (RSV) in Phase II.

"In rare diseases, I know the Street projects the growth of tafamidis and now they increased Vyndaqel projections, but I haven't seen anyone having numbers for our gene therapy," Bourla said. Pfizer surprised investors with the success of its early launch of the Vyndamax/Vyndaqel

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(tafamidis) franchise last year for wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM). (Also see "*Pfizer Vyndaqel Launch Surprises With An Early Burst Out Of The Gate*" - Scrip, 29 Oct, 2019.)

conference in San Francisco and read additional coverage of the meeting here:

I.P. Morgan Notebook Day 1: No Big Deals, But Plenty Of Pipeline, Commercial Highlights

Bourla said also that Pfizer is poised to be a leader in gene therapy, but rarely gets the credit for that on Wall Street. The company has three gene therapies in clinical development, two more it gained through business development with *Vivet Therapeutics* and *Therachon AG* and another seven in preclinical development, he said. Pfizer paid $340m in May for Therachon, gaining a Phase I gene therapy for short-limbed dwarfism. (Also see "*Pfizer Grows In Rare Disease With $810m Dwarfism Company Buy*" - Scrip, 9 May, 2019.) Also in 2019, the company gained an option to buy Vivet, which was advancing a treatment for Wilson disease toward the clinic at the time. (Also see "*Pfizer Buys Option For Vivet In Latest Gene Therapy Tie-Up*" - Scrip, 20 Mar, 2019.)

"We are building in Sanford here in the US, the largest gene therapy manufacturing capacity in the world, and there's nothing, I think, in the projection of the Street about that," Bourla said. Pfizer announced last year a $500m investment in the construction of a gene therapy manufacturing facility in Sanford, NC.

In Pfizer's immuno-inflammation franchise, he said the company has five different JAK inhibitors in development across 10 different indications. "Only one of them I have seen some minor projections in the Street analysts," he said. "I can go on and on. What I want to say is that there is a significant gap."

Some of the responsibility falls to Pfizer, he said, which hasn't shone a big enough spotlight on the innovation going on. He announced the company will have its first R&D day in many years on 31 March. He also told investors that they can expect Pfizer to spend more on R&D going forward as a percent of sales because the company plans to continue the same level of R&D investment even after it spins out the Upjohn business into a merger with *Mylan NV*. (Also see "*Upjohn/Mylan: Will "Potential Moderate Growth" Lure Investors?*" - Scrip, 29 Jul, 2019.)

The result is that Pfizer will go from being one of the lowest R&D spenders as a percentage of sales to one of the highest. Pfizer spent 14.8% of revenues on R&D in 2018.

First-In-Class Launch Will Test GSK's Cancer Credentials

GlaxoSmithKline PLC is gearing up for the anticipated approval and launch of belantamab mafodotin, a first-in-class treatment for multiple myeloma that represents an important next stage in GSK's reinvention, since it is one of six anticipated new drug or line extension approvals

in 2020.

Presenting at the J.P. Morgan conference, CEO Emma Walmsley recapped GSK's progress in transforming its product portfolio and internal culture during the last few years, stressing that "we have much more to do."

Belantamab is especially important as it will be a test of the company's re-entry into oncology, which it effectively exited in 2014 under previous CEO Sir Andrew Witty. *(Also see "GSK Gears Up For Three Cancer Launches In 2020" - Scrip, 5 Nov, 2019.))*

GSK hasn't launched a new cancer treatment since the melanoma combination of Mekinist (trametinib) and Tafinlar (dabrafenib) seven years ago, and that means it is now busy with a recruitment drive to rebuild its commercial expertise in the field.

Belantamab is an antibody-drug conjugate and the first drug to be submitted to the US Food and Drug Administration that targets B-cell maturation antigen (BCMA) in patients with relapsing and refractory multiple myeloma.

The drug may reach the market before any of its competitors, but two chimeric antigen receptor T-cell (CAR-T) therapies – *bluebird bio Inc.* and *Bristol-Myers Squibb Co.*'s bb2121 and JNJ-4528 from *Johnson & Johnson* and *Legend Biotech Corp.* – are not far behind. Bristol anticipates filing its CAR-T candidate for FDA approval during the first half of 2020. (Also see "*Bristol's CAR-T Strategy Comes Into Focus With Two Near-Term Filings*" - Scrip, 10 Dec, 2019.)

GSK's head of R&D Hal Barron has singled out belantamab for rapid development, and told investors at J.P. Morgan that its registrational DREAMM2 study produced "quite impressive" data. This remark skirts round that the fact that the overall response rate (ORR) in the trial stood at just 31% – down a long way from the 60% ORR seen in an earlier study and far below the 100% response rate reserved to date with JNJ-4528. There also are safety concerns regarding the eye condition keratopathy.

At the same time, GSK can point to belantamab's advantages over CAR-T therapies, including convenience, cost and toxicities.

GSK's commercial head Luke Miels also outlined the company's efforts to build a new oncology organisation by hiring experienced sales reps.

"What we've tried to do is, from a strategic level right down to an operational level in the key markets, hire people who really know this area," Miels said. "Of course, there's a few mergers and things which are also disruptive, which put people into the marketplace who may not have naturally been out there looking, and we've taken advantage of that. So, I feel very comfortable

with the teams that we've built."

GSK's oncology portfolio includes ovarian cancer treatment Zejula (niraparib), purchased in the $5.1bn acquisition of Tesaro Inc. that closed last year, plus multiple internal and partnered candidates that are central to the company's growth for the next five to 10 years.

AstraZeneca On Launching Enhertu

The launch of *AstraZeneca PLC*'s Enhertu (trastuzumab deruxtecan) for metastatic HER2-positive breast cancer is expected to be a blockbuster, and exec VP-Oncology Business Unit David Fredrickson talked to *Scrip* at the J.P. Morgan Healthcare conference about the launch.

The drug, partnered with *Daiichi Sankyo Co. Ltd.*, received accelerated approval from the US Food and Drug Administration on 20 December based on Phase II data, including a notable progression-free survival benefit in patients who have run through other treatment options. The market is expected to be a competitive one, however, with *Seattle Genetics Inc.* poised to launch tucatinib, a medicine that works differently but has also shown strong efficacy, in 2020. (Also see "*Data For Two HER2-Positive Breast Cancer Drugs Impress, Including On Overall Survival*" - Scrip, 11 Dec, 2019.)

Getting to the market first could be an advantage gaining traction, Fredrickson said, though he expects both Enhertu and tucatinib will become part of the treatment paradigm for advanced breast cancer patients. "New options are good for patients always," he said. But, he noted, "the way I see things playing out is we are launched and we are available today." Positive early experience with the medicine is what will carry the most weight going forward from a competitive standpoint, he said, as that is what will drive more uptake longer term.

AstraZeneca and Daiichi are also poised to take advantage of patients who are waiting for a new option. "We do see and expect there are going to be some bolus of patients that are out there that are being treated with chemotherapy today," Fredrickson said, though he said he doesn't expect any patients who are responding to treatment with existing therapy would switch.

Enhertu does appear to carry a premium price tag. Leerink analyst Andrew Berens said in a 23 December note that the price per patient is approximately $13,300 per month, which would be $159,600 annually. Analysts at Datamonitor Healthcare calculated the wholesale acquisition cost at approximately $172,295 per year for an 80kg patient, given that dosing is weight based.

AstraZeneca wouldn't confirm the WAC for Enhertu, however, a contrary move given the push more recently by big pharma to be more transparent on pricing. Fredrickson said the price is in line with the value it offers and on parity with other innovative drugs in breast cancer.

Lilly Pans For Gold, Filtering Out The Sand From External R&D Gems

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Scrip spoke with *Eli Lilly & Co.* senior vice president and chief scientific officer Daniel Skovronsky about various programs in the company's research and development pipeline, which Lilly continues to fill with both internally discovered assets and externally sourced programs. The company was the only big pharma to announce a significant M&A deal around the start of the J.P. Morgan Healthcare Conference when it said on 10 January it would buy *Dermira Inc.* for $1.1bn.

"It's a deal that's perfectly lined up with our strategy of bolt-on acquisitions where the science is good, the probability of success is high, addressing a major unmet medical need in one of our therapeutic areas," Skovronsky said. "By the time you get through all of those filters, there's not too many deals that look like that, so we were really excited about this opportunity and pleased to announce the deal."

> ***Lilly's Paying $1.1bn For Itch Advantage With Dermira's Lebrikizumab***
>
> By Joseph Haas
>
> 10 Jan 2020
> Making a large acquisition heading into the JP Morgan Healthcare Conference for the second consecutive year, Lilly is buying Dermira and its Phase III atopic dermatitis drug lebrikizumab, setting up a competition with Sanofi's Dupixent.
>
> *Read the full article here*

Lilly also came to J.P. Morgan in January 2019 with another big deal – the $8bn acquisition of *Loxo Oncology Inc.*, leading to the recent formation of a new oncology R&D unit helmed by Lilly executives who came to the company through the Loxo deal. (Also see "*Lilly Taps Loxo Execs To Bring Back That Biotech Feeling*" - Scrip, 5 Dec, 2019.)

"Probably I spend more than half of my time here at J.P. Morgan doing business development – meeting with companies and scouring for great opportunities," Skovronsky said. "They're hard to find; we have to look at a lot of things to find a Loxo or a Dermira. I wish that we had more. I would happily do deals like these more often, but our standards are high."

He said Lilly is looking for good science, which includes drug mechanisms of action that are understandable and will translate into a high probability of success in areas of significant unmet need within the company's therapeutic areas – oncology, immunology, diabetes and neuroscience.

"And then the final big screen is on value," Skovronsky continued. "We have to be able to acquire things at a price that while fair for the company being acquired still creates value for our shareholders. Usually that's about Lilly seeing something that others don't see or being willing to create some upside on the asset through our unique capabilities. Dermira checked all those boxes this year as Loxo did last year."

Asking prices for such assets, he noted, “are also high in all areas, but probably particularly in oncology, and at the same time competition is high. We are competing against our peers, and sometimes companies larger than us, to get the best assets and the best companies.”

Amgen Looks To Capitalize On Investments In Genomics

Amgen Inc. CEO Bob Bradway said in his 14 January presentation at the J.P. Morgan Healthcare Conference that the company’s three most important words this year are execution, execution and execution. Commercial execution is key as the company continues to feel the impact of biosimilar and generic competitors for some of its biggest blockbusters, but newer products still are struggling to make up for the revenue gap. (Also see "*Amgen’s Q3 Sales Beat Consensus, But Two Key New Drugs Fell Short*" - Scrip, 29 Oct, 2019.)

Execution also is important for the company’s research and development pipeline, where Amgen hopes its investments in *deCode genetics EHF* and other genomics capabilities will pay off through more efficient R&D processes and faster successes. (Also see "*'Beautiful baton pass' as Amgen picks up deCODE to validate drug targets* " - Scrip, 11 Dec, 2012.)

“We consider that we are the industry-leading company when it comes to integrating human genetics into our discovery research, and we significantly expanded those efforts through collaborations completed in 2019,” Bradway said. “In addition, we're very focused on using next-generation proteomics technologies to enable us to combine information with our genetics portfolio to characterize the pathways in biology that we think are relevant for disease.”

Scrip spoke on the sidelines of J.P. Morgan with Amgen executive vice president of research and development David Reese about the three strategic imperatives that the company’s R&D effort is focused on across Amgen’s three therapeutic areas – cardiovascular disease, immunology and oncology – including the use of genomics to bring medicines to the market faster.

First, the company is working on improving its success rate, where genomics and proteomics efforts are being used to not only identify new drug targets, but also identify appropriate patients for clinical trials. Second is reducing the development cycle time of getting a drug from discovery to the market, which takes about 10-14 years now, and Amgen has shaved about three years off of that process. Third is taking into consideration earlier in development barriers that keep patients from getting access to new drugs.

“We need to be sure the drugs we’re developing and the evidence packages will allow drugs to get to the people that need them,” Reese said. “We’re infusing that thinking in R&D, internally and in partnering. That doesn’t mean the commercial group is determining what research is done. We want hand-in-glove thinking. We want to make sure patients get our drugs and that we generate a return that allows us to continue to invest in R&D.”

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Karyopharm CEO Says Xpovio Launch Is 'Better Than Expected'

Karyopharm Therapeutics Inc. gave an early look at sales to date for its multiple myeloma drug Xpovio (selinexor) on 13 January, a day before CEO Michael Kauffman presented at the J.P. Morgan Healthcare Conference, and the executive told *Scrip* the launch "has been going a bit better than expected."

The US Food and Drug Administration approved Xpovio, a selective inhibitor of nuclear export, on 3 July for relapsed or refractory multiple myeloma patients who have gone through at least four prior lines of therapy. Karyopharm said sales totaled $17m-$18m in the fourth quarter versus analyst consensus of $15m; sales for 2019, starting with Xpovio's launch on 9 July, totaled $30-$31m for the fiscal year.

"To date, the payer community has been pretty receptive; they understand how sick these patients are," vice president Ian Karp said. "We haven't seen denials for this drug – it just hasn't been a hurdle."

> ***Karyopharm's Xpovio In Multiple Myeloma Priced At $22,000 Per Four-Week Cycle***
>
> By Joseph Haas
>
> 03 Jul 2019
> Immediate interaction with US FDA after stressful advisory committee facilitated accelerated approval in fourth-line myeloma, company says. Four different dosing regimens will be priced at $22,000 for four weeks.
>
> *Read the full article here*

More than 550 doctors have prescribed Xpovio and more than 1,400 prescriptions have been filled as of 31 December.

Next up for Karyopharm may be a second indication in relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after at least two prior multi-agent therapies and who are ineligible for stem cell transplantation, including chimeric antigen receptor T-cell (CAR-T) therapy; the company submitted an application to the US FDA in December for this indication and will file later this year for European approval, following submission in early 2020 for multiple myeloma.

Also, results from the Phase III BOSTON study testing Xpovio in combination with Velcade (bortezomib) in second-line multiple myeloma are expected in early 2020, and if positive it will be filed with the FDA in 2020. Karp noted that this indication will expand the patient population eligible for treatment from 6,000 to 32,000 patients in the US.

Karyopharm expects results from the Phase III SEAL study in patients with advanced, unresectable, dedifferentiated liposarcoma – Xpovio's first solid tumor indication – in mid-2020 with an FDA filing expected this year. Completion of enrollment in the Phase III SIENDO study of Xpovio as maintenance therapy in endometrial cancer patients expected this year.

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The Last Laugh On Biopharma M&A

Truth be told, biopharma is a pretty serious business and light-hearted moments have been in short supply at the J.P. Morgan conference this year.

Meeting this unmet need on the second day of the conference was Francesco De Rubertis, co-founder and partner at Medicxi. The venture capital firm has many of the great and good from biopharma advising its investment plans, and enticed some of these big names to its event at a hotel away from the conference, high up on San Francisco's Nob Hill.

De Rubertis was leading a discussion about "New Shapes of the Pharma Industry in the Next Decade" with three industry heavyweights: Giovanni Caforio, CEO of Bristol-Myers, newly enlarged by the $74bn acquisition of *Celgene Corp.*; Jennifer Taubert, EVP, worldwide chairman, pharmaceuticals at Johnson & Johnson, and Vas Narasimhan, CEO of *Novartis AG*, one of the sector's most prolific M&A practitioners.

The conversation about business and M&A strategy was proceeding as normal until De Rubertis deadpanned: "So can you please tell us the names of the companies you are going to acquire?"

This raised a big laugh from the audience, who like everyone else attending J.P. Morgan were wondering when the next big M&A deal was going to land, since the conference kicked off without any large deals being unveiled.

Narasimhan eventually asked the biotech venture capitalist: "I have a question for you, Francesco. So, do you feel like a lot of biotech valuation expectations have gotten really out of hand?"

Francesco allowed the laughter to subside before answering simply: "No, I don't think so!"

[Editor's note: This article has been updated to correct the date of approval for AstraZeneca's Enhertu.]