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J.P. Morgan Notebook Day 2: Biogen, GSK, Bluebird, Roche, Amgen, Biohaven, Lilly And FDA's Gottlieb

by Mandy Jackson

Daily round-up of news and notes from the 2019 J.P. Morgan Healthcare Conference in San Francisco: Biogen may be looking for gene therapy partner, Lilly CEO says Loxo is just the start, GSK plays up its BCMA, Amgen vows to put money into deals, Biohaven readies oral CGRP inhibitor to compete, and Roche talks value-based payments.

Is A Gene Therapy Partnership Next For Biogen?

Biogen Inc. has made a lot of early initiatives in gene therapy but nothing concrete has come out of the effort. The most notable setback has been a delay getting a gene therapy for spinal muscular atrophy (SMA) into the clinic, while rival *Novartis AG* has gotten its SMA gene therapy AVXS-101 all the way to the FDA. Novartis acquired its gene therapy with the $8.7bn acquisition of *AveXis Inc.* last April, a deal some Biogen investors wished at the time that the big biotech had done instead, since AVXS-101 will be a threat to Biogen's own *Spinraza* (nusinersin). (Also see "*Biogen's SMA Ambitions Run Up Against A New Deep-Pocketed Rival*" - Scrip, 9 Apr, 2018.)

Biogen had no update on the gene therapy program for investors at the J.P. Morgan Healthcare Conference, noting only that it continues to be in dialogue with the FDA on the investigational new drug application (IND).

In an interview, Chief Medical Officer Alfred Sandrock reaffirmed the company's commitment to moving forward with the gene therapy. He also said Biogen is interested in gene therapy more broadly, but might look to build into the area with a partner.

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"There are a lot of elements," he said, referring to everything from development to manufacturing. "We are aware of what is going on and we are looking at everything. It is likely that we will want to partner."

Alnylam, Novartis, Sarepta, Deal Trends And Cell Therapy Challenges

And, he said partnering is core to Biogen's R&D engine. "We did 10 deals in the last two years. We doubled our clinical pipeline," he said. "*Ionis Pharmaceuticals Inc.*is a partnership, and that is a great example of a partnership."

GSK On Why My BCMA Is Better Than Your BCMA

GlaxoSmithKline PLC is making big investments in oncology, including with the $5.1bn acquisition of *Tesaro Inc.* announced in December, and the company pushed an aggressive development plan for high-value opportunities at J.P. Morgan. Both of the late-stage therapies it is focusing on, with the Tesaro-owned PARP inhibitor *Zejula* (niraparib) and the anti-BCMA antibody-drug conjugate GSK '916, are in highly competitive areas of drug development.

In an interview, Oncology Therapeutic Area Head Axel Hoos outlined why he thinks GSK's B-cell maturation antigen (BCMA) product will have an edge over the competition in multiple myeloma, including the chimeric antigen receptor T-cell (CAR-T) therapy bb2121 from *Celgene Corp.*/*bluebird bio Inc.* and multiple bispecific antibodies in development. BCMA drugs were a hot area at the American Society of Hematology (ASH) meeting last year. (Also see "*ASH Preview: BCMA-Targeting CAR-Ts And Bispecifics Hog The Spotlight*" - Scrip, 28 Nov, 2018.)

"The key item here for me is utility," Hoos said. "This is an antibody-drug conjugate. You can scale it up fast. You can enroll patients quickly and you can make the drug available really quickly. The utility alone is a massive advantage."

And GSK has worked aggressively to speed up the clinical development timeline for the product, putting it neck-and-neck with bb2121, which Celgene/bluebird plan to file in 2019. GSK anticipates it will be on track to file in third-line or later multiple myeloma in the second half of 2019, and Hoos said his ambition is for it to reach the market in mid-2020, based on results from the DREAMM-1 trial.

CEO Emma Walmsley also highlighted the BCMA development program as an example of how the company is moving forward with multiple clinical trials across various patient populations at the same time. The company simultaneously is moving ahead with pilot studies in combination with the standard of care in second-line and first-line multiple myeloma.

GSK also talked about enthusiasm for Zejula, where the company also faces stiff competition

with *AstraZeneca PLC*/*Merck & Co. Inc.*'s leading PARP inhibitor *Lynparza* (olaparib). But GSK believes it could have an edge in first-line ovarian cancer when its Phase III PRIMA study reads out late this year. The study is recruiting all comers, whereas Lynparza was approved for first-line maintenance in BRCA-mutated patients in December. (Also see "*First-Line Ovarian Cancer Approval Solidifies Lead For AstraZeneca's Lynparza* " - Scrip, 19 Dec, 2018.) The broader opportunity in ovarian cancer could represent three times the commercial opportunity. "That alone carries the acquisition," Hoos said.

Bluebird Sets $2.1m Price Ceiling For Lentiglobin

bluebird bio Inc. CEO Nick Leschly made the case during the company's Jan. 8 presentation at J.P. Morgan for an innovative value-based installment pricing model for its *Lentiglobin* gene therapy, and suggested the price will be under $2.1m.

Lentiglobin (lentiviral beta-globin gene transfer) is under review in the European Union for transfusion-dependent beta-thalassemia and is expected to be cleared in the US in 2020 for that indication. (Also see "*Bluebird 'Turns A Corner' With Lentiglobin Gene Therapy, Tests Remain*" - Scrip, 18 Jun, 2018.) Lentiglobin is also in development for sickle cell disease. (Also see "*Gene Therapy's Next Big Challenge: Manufacturing* " - Scrip, 11 Dec, 2018.)

Under the plan detailed at the meeting, payers would pay for the therapy over five years. The first 20% would be paid up front while the rest would be paid in annual installments – but only if treatment is successful, based on a reduction in the number of blood transfusions – and there would be no payments after five years.

Leschly explained at J.P. Morgan that the total value of the therapy is estimated at about $4m, taking into account quality of life for the patient, extension of life, cost offsets (which vary between the US and Europe), and the societal value. But bluebird is basing its pricing strategy on what it calls "intrinsic value," including quality of life and extension of life and returning the rest to the health care systems. The CEO stressed, however, that value is not the same thing as price and the price has not been fixed yet.

The company wants to be transparent about how it is thinking about pricing and it aims to have the treatment available to as many patients possible. Toward that end, bluebird does not believe in pricing a therapy high just because you can, and the plan is to have no price increases above the consumer price index, the exec said.

There are many challenges with the new model, including questions about how to define and track outcomes, what happens when patients change payers and how to handle Medicaid/Medicare best price calculations, but the company has some ideas on how to address these, Leschly said.

Leerink analyst Mani Faroohar said in a Jan. 8 note that his firm has been modeling the launch price of $1.2m in the US and $0.9m in the EU, both of which are significantly below the $2.1m price ceiling cited by the company. "The proposed plan allows for upside to our pricing assumptions, though the value-based agreement would couple payments to patient outcome – a net positive in our view," Faroohar said.

"However, 80% of the cost of gene therapy would be at risk, and while the data for LentiGlobin has been promising in our view, long-term durability is still an unknown and lower than expected durability could erode the assumed price," the analyst added.

Loxo Deal Doesn't Limit Lilly's Deal Capacity

Lilly CEO David Ricks and Chief Financial Officer Joshua Smiley re-emphasized that even after the $8bn acquisition of *Loxo Oncology Inc.* announced a day earlier, Lilly has plenty of financial capacity to do additional deals this year.

"What we've said is we're not limited on capacity; the company's in a good cash flow-generating position," Ricks said during his J.P. Morgan fireside chat. "We have very low levels of debt and a high [credit] rating. We see ourselves having quite a bit of capacity do more deals. We're agnostic whether they're collaborations or M&A."

Lift-Off For Lilly In Cancer Genetics With Loxo Buy

By Kevin Grogan

07 Jan 2019
The New Year is just a week old but the biopharma merger and acquisitions merry-go-round is already spinning furiously as Lilly now steps in with a proposal to buy Loxo.

Read the full article here

Ricks was asked if a very large transaction to create massive scale, like *Bristol-Myers Squibb Co.*'s $74bn acquisition of Celgene Corp. announced in the days leading up to the conference, would be of interest to Lilly, but the CEO dismissed the idea that such a deal add worthwhile value. (Also see "*Bristol Values Celgene's Hematology, Immunology Portfolio At $74bn, But Does It Price In Risk?*" - Scrip, 3 Jan, 2019.)

"We don't see it. I think scale probably destroys more value than it creates, particularly in R&D functions," Ricks said. "What matters, really, is differentiation of assets. So the question is, either can you add value to validated assets, like Loxo, or can you create your own assets that have differentiated effects for patients. If you do that consistently, I'm not sure what investing in scale gets you. As a manager, it seems like a big distraction from your core business and as a scientist it's even more of a distraction." (Also see "*Bristol/Celgene Made Perfect Sense, But Doesn't Promise Big M&A Year, EY Says*" - Scrip, 8 Jan, 2019.)

Smiley addressed the question similarly, noting that "our analysis continues to support that we're going to win through innovation, not through cost synergies or somehow benefit from scale." The CFO noted that "you can't merge your way" to better ability to negotiate with payers, because consolidation among commercial insurers and pharmacy benefit managers in the US has shifted the power in reimbursement negotiations in the payers' direction.

However, Smiley added, the opportunity to do smaller acquisitions of validated drug candidates is increasing as the massive wave of innovation that's swept through the biopharma industry has resulted in novel approaches maturing to the point where small companies have to think about commercialization and whether they can handle that challenge on their own. Also, recently declining valuations for drug developers has made some deal targets more attractive.

"We announced a big deal this week, but we're still excited to look for others," Smiley said.

It's worth noting that Lilly is still committed to reinvesting in its own pipeline and in external innovation even at a time when the company is facing pricing headwinds. Ricks noted in the fireside chat that various pricing pressures will result in mid-single-digit net price reductions across the commercial portfolio.

However, the company has added enough new drugs – 10 in the past five years – that increased revenue from those products is making up the difference and then some. Ricks said Lilly expects its revenue to increase 4%-5% in 2019. (Also see "*Lilly's New Year Resolution: Make New Launches Into Blockbusters* " - Scrip, 20 Dec, 2018.)

Amgen Vows To Spend As Another Neulasta Biosimilar Launches

Amgen Inc. CEO Robert Bradway signaled at J.P. Morgan that the company is ready to do deals in 2019 – and he and Chief Financial Officer David Meline noted in the Q&A following the firm's Jan. 8 presentation that Amgen has considerable resources to put forth across a variety of transactions.

"I'd say heading into the volatile environment that we're all living in in 2019, we feel well-prepared to manage through the volatility, but also to harness the incredible array of opportunity that we see arising not just at Amgen, but across the industry," Bradway said at the start of his formal remarks.

The CEO later reiterated during the Q&A that Amgen will look beyond its considerable in-house, genomic data-driven research and development organization for new assets. Exec VP-R&D David Reese noted that Amgen has gone from 15% of its drug candidates having some human genetic validation to now three-fourths of candidates at the time of translational development. Also, improvements to R&D efficiency has shortened the development process for the company's drugs by as much as three years.

"At a high altitude, we would like to invest in innovation," Bradway said. "I think at the last three J.P. Morgan conferences we've articulated our desire to look at a wide range of targets, wide range of opportunities – large and small, licensing and acquisition, and that continues to be the case," he added.

Meline noted during the Q&A that Amgen ended the third quarter with $30bn in cash, giving the company "very strong capability to both invest in the business, which is our first priority, including acquiring – if you look at the history of the company, 50% of our products and sales have come from some history of acquisitions – so, we continue to be very interested in adding to the portfolio, and we're in the fortunate position to be able to do that without constraining ourselves."

That cash position also will enable Amgen to continue buying back some of its stock and paying dividends to investors, he added.

The company is under pressure to bring more products through R&D and into the commercial market, whether through internal discovery and development programs or through external opportunities, because of competition for some of its blockbuster products, including the neutropenia therapy *Neulasta* (pegfilgrastim).

Bradway noted in his main J.P. Morgan presentation that despite biosimilar competition for the product, *Neulasta OnPro* – the on-body injector drug/device version of the biologic – continues to hold a 60% share of the market. Just how long that share will hold up remains to be seen, however.

Coherus BioSciences Inc. has now launched its biosimilar *Udenyca* (pegfilgrastim-cbqv) in the US after promising in November that it would bring the product to market in January at a 33% discount to the original product.

"At 33% discount to Neulasta's list price – and parity to Mylan, but with likely unencumbered supply – near-term 10%+ share is likely, with potential for 30%+ share longer term. We believe at 10% share ($200-$250m) breakeven will occur while allowing substantial investment," Cowen analyst Ken Cacciatore said in a Jan. 8 Coherus note about Udenyca's launch.

Coherus Gears Up For January Udenyca Launch, Prices Biosimilar At 33% Discount To Neulasta

By Mandy Jackson

09 Nov 2018
Buoyed by the market share held by biosimilars of the short-acting neutropenia drug Neupogen, Coherus hopes its Udenyca price, contracts and services will give its biosimilar a significant share of the market for the longer-acting Neulasta.

Read the full article here

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Biohaven Readies To Compete With Allergan's Oral CGRP Inhibitor

Biohaven Pharmaceutical Holding Co. Ltd. is preparing to go head-to-head with a formidable competitor in the migraine headache space – *Allergan PLC* – with its oral CGRP inhibitor rimegepant after gathering Phase III data for the *Zydis* fast-dissolving tablet formulation developed through a partnership with *Catalent Inc.*

Biohaven intends to submit both the regular tablet and Zydis formulations of rimegepant for US FDA approval in the first half of 2019, following just months behind a filing for Allergan's oral GGRP inhibitor ubrogepant. Allergan CEO Brent Saunders said during his Jan. 7 J.P. Morgan presentation that the company will file for approval of ubrogepant "imminently."

Both candidates have been developed for acute treatment of migraine as opposed to the anti-CGRP biologics that were approved for prevention of migraine headaches in 2018: Amgen/Novartis' *Aimovig* (erenumab), *Teva Pharmaceutical Industries Ltd.*'s *Ajovy* (fremanezumab) and *Eli Lilly & Co.*'s *Emgality* (galcanezumab). (Also see "*Migraine Market Gets Competitive With Second, Third CGRP Inhibitor Launches*" - Scrip, 9 Nov, 2018.)

Scrip spoke with Biohaven CEO Vlad Coric at the conference and he described the Phase III results for the Zydus formulation of rimegepant as "phenomenal" and "better than imagined," largely because the company saw separation between placebo and the fast-dissolving drug starting at 15 minutes after the medicine was administered with durability of up to 48 hours. Ubrogepant doesn't act as fast and has shown efficacy only as long as 24 hours, Coric said, which he attributed to the Allergan drug's four-hour half-life as opposed to rimegepant's eight to 12 hours.

Also, patients treated with the fast-dissolving CGRP inhibitor did not require rescue medications or a second dose, while Allergan reported use of rescue medicines or administration of a second dose of ubrogepant in its Phase III program – a data point that Biohaven has been talking up since March when it reported Phase III data for the original formulation of rimegepant. (Also see "*Biohaven Posts Positive Migraine Results, But Investors Are Wary*" - Scrip, 26 Mar, 2018.)

Biohaven intends to simultaneously seek approval for both formulations of its drug, but the company expects its faster-acting version to be the better seller. Coric noted multiple advantages of the Zydis formulation, such as migraine patients – who often experience nausea and vomiting – not needing to take the fast-dissolving tablet with water. Also, given that 85% of migraineurs are women, the fact that rimegepant remains in the blood for a day or two versus biologics that are in the body for weeks or months is attractive to younger patients who may be trying to get pregnant. The on-demand use of the drug also is attractive for women who generally only experience migraines around menstruation, further limiting how often the medicine is in their system.

The company has an intranasal version of the CGRP inhibitor BHV-3500 in early-stage development that could provide efficacy in as quickly as five minutes.

"The injectables are going to educate patients and doctors about how great this mechanism is for migraine," Coric said. "We will leverage the marketing of the antibody companies."

Amgen CEO Robert Bradway said during his Jan. 8 J.P. Morgan presentation that more than 18,000 doctors have written prescriptions for Aimovig since its launch last year and more than 150,000 patients are on the preventative therapy.

FDA Commissioner Clarifies Regulatory Route For Gene Therapies For Neurodegenerative Diseases

The US FDA will soon clarify the regulatory pathways and evidentiary requirements for gene therapies for neurodegenerative diseases based upon a treatment's intended effect, Commissioner Scott Gottlieb said Jan. 8.

In a keynote address to the J.P. Morgan conference, Gottlieb said the agency intends to distinguish when a gene therapy for a neurodegenerative disease might be able to use the accelerated approval pathway – such as in the case of a treatment with curative intent – versus when a more conventional development approach might be necessary – such as for a therapy aimed at treating symptoms.

"We're going to be putting out a guidance document that sort of articulates the divide when it comes to neurodegenerative diseases so to have a policy focused specifically on neurodegenerative disease, and we plan to talk in more detail about that in a statement we're going to put out within the next week," Gottlieb said.

The commissioner's remarks suggest such a policy announcement could come in the midst of the partial government shutdown that has limited the agency's activities since Dec. 22. (Also see "*Shutdown Week Three: Sponsors With Upcoming User Fee Dates Should Start Sweating*" - Pink Sheet, 7 Jan, 2019.) Gottlieb delivered his keynote address at J.P. Morgan remotely, rather than in person, because of the lapse in agency appropriations.

[Editor's note: For more on Gottlieb's remarks at JPM, see our sister publication Pink Sheet.]

Roche: Value-Based Pricing Coming Surely … But Slowly

Roche is eager to engage in value-based pricing, but there are still challenges around implementation, particularly in the US, Chief Financial Officer Alan Hippe said during the firm's Jan. 8 Q&A session.

With value-based pricing there are a lot of prerequisites – databases, for example – and it's not so easy to implement, the exec said.

"Let's see what the ideas will be, and what the future pricing environment in the US will look like. But one thing that, in my opinion, is relatively obvious is that it will take quite a bit of time until you get there. I don't really expect a revolution in the short term when it comes to pricing the US; I expect an evolution and I expect it will take quite some time until we have the instruments available," Hippe said.

Roche elaborated after the session that regarding value-based contracts, it would welcome a system where pricing of a medicine could be based on different indications, regimens and outcomes, and is working hard to be part of the solution.

The company points out that in the US it is currently piloting several value-based contracts with individual payers and has put forward ideas on this topic to the federal government. In Europe, Roche has been working on this with a number of countries, a spokesperson said.