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J.P. Morgan Notebook Day 1: Pfizer, Gilead, Alnylam, Novartis, Sarepta, Deal Trends And Cell Therapy Challenges

by Jessica Merrill

News and notes from the 2019 J.P. Morgan Healthcare Conference. Pfizer CEO Bourla underscores need for scientific and commercial innovation, Gilead makes M&A a priority, Novartis' new R&D chief reflects on first meeting with CEO Narasimhan, Sarepta CEO Ingram clarifies regulatory path for micro-dystrophin, J.P. Morgan outlines deal and macro biopharma trends in 2019, and cell therapy panel discusses manufacturing challenges.

Pfizer's Bourla Debuts As CEO In The Grand Ballroom

Pfizer Inc.'s new CEO Albert Bourla made his debut at the J.P. Morgan Healthcare Conference, appearing in the Grand Ballroom with Worldwide President-R&D Mikael Dolsten in a fireside chat format. Bourla set the stage for a smooth transition from Ian Read.

"Things are changing in Pfizer now, but not because the leader is changing. In fact, things are changing because the previous leader was very successful."

Pfizer should be on track for a solid growth trajectory after cycling through the loss of exclusivity (LOE) for *Lyrica* (pregabalin) expected in late June 2019. The company secured a pediatric exclusivity, extending US market exclusivity until June 30.

"Following that, we have a virtual LOE-free period until 2026," Bourla said.

But he acknowledged the gathering headwinds known as US drug pricing pressure. Big pharma in particular is facing top-line growth challenges as the price increases they take on mature marketed drugs, long an important driver of growth for the industry, come under scrutiny.

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Bourla said the drug industry needs to think about new ways to deliver drugs to patients affordably.

"Our strategy to achieve this top-line growth can be simplified into three words: innovating for growth," he said. That means scientific innovation and commercial innovation, he said, referring to innovative ways to address market access and affordability issues.

Pfizer is planning to increase its R&D spend in 2019, which it plans to offset by holding its selling and administrative costs steady, despite some planned increases to consumer advertising and promotions. The company has been in the midst of a restructuring to eliminate some mid-level managerial roles.

"We expect that in 2019 this reallocation will be in excess of $500m as a result of the reductions that we are doing," Bourla said.

US Drug Pricing: What A Difference A Year Makes

By Jessica Merrill

02 Jan 2019
Drug makers were optimistic going into 2018 about the political climate and drug pricing environment, but the outlook is more tenuous heading into 2019. Now is the time when industry raises prices on mature, marketed drugs and it's unclear how those hikes may be tempered or what the backlash might be.

Read the full article here

Gilead Makes M&A Its Top Capital Allocation Priority In 2019

In the wake of the recently revealed $74bn acquisition of *Celgene Corp.* by *Bristol-Myers Squibb Co.*, many companies at J.P. Morgan are being asked about their merger and acquisition strategies, and *Gilead Sciences Inc.* notes that M&A is a top priority this year. (Also see "*Bristol Values Celgene's Hematology, Immunology Portfolio At $74bn, But Does It Price In Risk?*" - Scrip, 3 Jan, 2019.)

Gilead Executive Vice President and Chief Financial Officer Robin Washington said during the company's fireside chat at the meeting when J.P. Morgan analyst Cory Kasimov asked about Gilead's capital allocation strategy in 2019 that, "first and foremost, we're focused on M&A in scientifically differentiated assets in our core therapeutic areas, including oncology, inflammation, [non-alcoholic steatohepatitis (NASH)] and other liver diseases. And we remain optimistic and very engaged at looking a lot of different opportunities in that area."

Washington also said the company will return money to its investors via dividends and share repurchases. "And, finally, we do have some debt that we'll continue to repay ... but overall M&A and focusing on growth is our primary area of focus from a capital standpoint."

Kasimov asked the CFO how Gilead thinks about doing deals across the spectrum of small-cap to large-capital biopharma companies or if it all depends on the science at potential acquisition targets or partners.

"I think for us, it's always been primarily about following the science and we think that's where we excel to the greatest extent, where we've been able to make the biggest scientific differentiation," Washington said. "If we find assets that also give us top-line revenue in addition to very deep pipelines, those are golden eggs and we'll continue to look for those."

Alnylam Posts A Good First Full Onpattro Quarter

Alnylam Pharmaceuticals Inc. reported ahead of its Jan. 7 presentation at the J.P. Morgan Healthcare Conference that global net product sales for its small interfering RNA (siRNA) therapeutic *Onpattro* (patisiran) for polyneuropathy associated with hereditary transthyretin-mediated (TTR) amyloidosis totaled $11m-$12m in the fourth quarter of 2018 – its first full quarter on the market in the US. This was in line with Jefferies analyst Maury Raycroft's forecast of $10.9m in fourth quarter Onpattro sales.

The drug has a hefty wholesale acquisition cost (WAC) of $450,000 per year, but the company has entered into or is negotiating value-based agreements (VBAs) with several US payers that have ensured access for patients with the rare disease TTR amyloidosis.

Alnylam announced, and CEO John Maraganore noted during his J.P. Morgan presentation, that the company has VBAs in place with Harvard Pilgrim Healthcare, Humana and another top five US payer. It also is negotiating VBAs with 15-plus other commercial payers, which – if all completed – would cover more than 90% of commercial lives in the US. Alnylam said more than 200 patients in the US and EU have been treated with Onpattro in the commercial setting as of the end of 2018.

Alnylam Offers Flexible Value-Based Deals For Breakthrough RNAi Drug Onpattro

By Emily Hayes

11 Aug 2018
The commercial team is on board and ready to market the first FDA-approved RNAi therapeutic patisiran for hereditary transthyretin-mediated amyloidosis.

Read the full article here

"It's early days, but I think we're off to an incredible start with the launch," Alnylam President Barry Greene told *Scrip* in an interview. "Most importantly, the physician and patient experiences we're hearing about are good. We're already hearing from physicians that patients on commercial drug, after two or three doses, are feeling better."

He noted that: "We are not facing payer headwinds. In fact, the payers, because of our value-

based agreement approach, have been working with us to help get patients on drug," including the five biggest commercial payers in the US and the Veteran's Administration.

"Of course, the big unknown is just how many patients are out there, how quickly can we find them, and that will remain an unknown for a while. As long as we keep finding patients and getting them on drug, I think Onpattro will be a very important program," Greene said.

He said about 3,000 hereditary TTR amyloidosis patients have been diagnosed in the US, but the epidemiology of the disease suggests there are as many as 20,000, but at that size the hereditary form of the disease will remain an orphan indication. However, the wild-type form of TTR amyloidosis is larger and growing as more doctors, especially cardiologists, actively work to diagnose the disease.

"At every cardiology conference, it's starting to become a bigger topic," Greene said. "It used to be if someone came in with something that looked like heart failure, it was heart failure. They were given the normal calcium channel blockers, beta blockers and sent off on your way. Now they're actually looking for amyloid and the cardiologists have the tools to look."

Alnylam is looking to expand Onpattro's label into the treatment of cardiomyopathy associated with TTR amyloidosis via the APOLLO B clinical trial kicking off in mid-2019 with data expected in 2020 or 2021. The HELIOS A trial for follow-on drug vutrisiran was initiated in 2018 with data expected in 2020. The company also intends to launch an outcomes trial known as HELIOS B, but it hasn't provided any timelines yet for that study.

"We want to be the company that helps patients with TTR amyloidosis with all aspects of the disease," Greene said. "In the shorter term, the successful launch of Onpattro in hereditary patients with TTR polyneuropathy is our key focus in the US, Europe, Asia and Latin America. We've launched in the US. We should get pricing negotiations under way throughout this year and into next year in Europe. We plan on launching in Japan later this year and then Brazil late this year, early next year."

How Did Novartis Woo R&D Chief Tsai? It All Started With A Conversation at J.P. Morgan

Novartis AG's new Head of Global Drug Development and Chief Medical Officer John Tsai talked to *Scrip* about the energized R&D engine at the company, pipeline catalysts and plans for business development. But he also talked about how surprised he was to find himself working at Novartis – and in Basel, Switzerland – having been recruited from *Amgen Inc.*. He joined the company in May, taking over the position held by now-CEO Vas Narasimhan. (Also see "*Appointments: Novartis And GSK Announce New R&D Heads, LNC Therapeutics Gets A New CEO, Plus Announcements From Zelluna and BC Platforms* " - Scrip, 19 Apr, 2018.)

It all started one year ago at the J.P. Morgan conference in 2018, shortly after he had been contacted by the Swiss company.

"They contacted me and said that Vas was going to be the new CEO," he said. "When I received that text, I said that is great that a physician is going to be the new CEO, but did you know that I just purchased my home and closed on it in California."

But he was encouraged to at least talk to Narasimhan at J.P. Morgan and the two hit it off. "It turned out to be … a discussion around pipeline, bringing in new therapies, talking about data and digital, how we can transform the way we develop drugs, how we can bring back more to society – and everything was fully aligned with what I wanted to do and what I had passion for," Tsai said. "Next thing you know I was in Basel interviewing and then May 1, I was starting, and I was thinking how can this be?"

As for what it's like to have the former R&D chief as your boss, Tsai said he welcomes the experience. "I have always thought about it as having the best two minds to think about how do you develop drugs, because what better way than to have your mentor challenge you."

[Editor's note: More to come about Tsai's vision for R&D at Novartis in an upcoming issue of Scrip.]

Sarepta Provides Clarity On Micro-Dystrophin Regulatory Path

Sarepta Therapeutics Inc. is anxious to get its micro-dystrophin gene therapy program for Duchenne muscular dystrophy (DMD) to patients as quickly as possible – and now it has clarity on the program from the US FDA. In an opening session at J.P. Morgan, CEO Doug Ingram said the company met with the FDA to discuss the path forward in the fourth quarter and has initiated a 24-patient placebo-controlled trial, focusing on the functional benefits.

But that trial is running with clinical supply, and the company will need to run a confirmatory trial using commercial supply, which left some investors confused about what that could mean for the launch timeline. The company's stock price fell 4.7% to close at $110.02 on Jan. 7. Ingram said the company would be able to initiate a trial using commercial supply by the end of 2019.

In an interview, Ingram clarified that the timeline for launching hasn't changed. "The timelines remain the same for us, our goal limited only by building the appropriate amount of manufacturing capacities to execute our placebo-controlled trial and then commence our commercial supply registration trial toward the back half of 2019, all with the goal, if we are successful, of having a therapy that could be serving the community by the end of 2020."

He couldn't say how big the trial would need to be, but noted that it would be a multi-center trial, with sites in the US and Europe.

Investors were also hoping the company might be able to present the first biopsy data from a Phase I/IIa study of MYO-101, a gene therapy developed in partnership with *Myonexus Therapeutics Inc.* for limb-girdle muscular dystrophy 2e (LGMD2e). Those data were not available yet, though they will be important to informing how the company moves forward with a broad program in LGMD. Sarepta in-licensed rights to five gene therapy programs for different LGMDs from Myonexus in May for $60m up front. (Also see "*Deal Watch: Genentech Gets Down In The Dirt With Lodo Therapeutics*" - Scrip, 11 May, 2018.)

"We are going to look at the data for our 2e program and if it looks good, we are going to meet with the agency and talk through the path forward for that program," Ingram said in the interview. "And, we've got to get going on our other programs as well."

While each of the individual indications for the rare and deadly disease are small, the limb-girdle umbrella of diseases represents a significant opportunity, representing about the same size as the DMD opportunity, he said.

Transglobal Pharma Consolidation Will Continue In 2019

With the year kicking off with the mega-merger of Bristol-Myers Squibb and Celgene and *Eli Lilly & Co.*'s acquisition of *Loxo Oncology Inc.*, J.P. Morgan bankers predict that more deals will be done.

Opening up the J.P. Morgan Healthcare Conference, with a record 484 companies presenting and more than 9,000 delegates attending, Michael Gaito and Michele Colocci, global co-heads of health care investment banking, painted a fairly optimistic vision for 2019 even though the US industry faces some geopolitical challenges.

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

Their optimism is underpinned by new product launch trends supporting healthy volume growth, offsetting lingering patent expiry concerns, and that the pharma launch pipeline continues to be robust.

Capital deployment and the need to increase exposure to higher growth markets will continue to drive industry consolidation. “US corporates remain flush with cash from tax reform and a strong economic cycle. However, end of cycle forces and market volatility may create increasing need

and opportunity for strategic deals, while investors may push for increased capital return and utilization to improve their returns," noted Gaito.

"Cross-global consolidation will continue as companies seek global leadership in key therapeutic areas and end-markets and increased exposure to higher growth markets, especially in the US and emerging markets," added Colocci.

Dark clouds on the horizon, however, include concerns associated with health care costs. The FDA continuing to push for generics approvals (a record 971 generics were approved or tentatively approved in 2018), the Trump administration proposing alternative Medicare drug reimbursement models, such as an international pricing index, and new health care price transparency requirements for hospitals in 2019 could have a negative impact, the bankers noted. Other 2019 challenges include US/China trade tensions and the political risks present in Europe, such as the impact of Brexit or Italian fiscal policy.

Interestingly, while companies such as Bristol-Myers and Lilly have opted to double down on specific therapeutic areas, Novartis AG CEO Vas Narasimhan intends to retain a broader therapeutic focus, supported by strong lead brands and important late-stage opportunities. He is not a fan of the mega-deal either, preferring instead to maintain a disciplined approach to value-added bolt-ons. In 2018, Novartis spent about $15bn on such acquisitions while completing more than 100 collaborative and licensing deals.

Celgene Et Al. Tackle 'Weakest Links' In Cell Therapy Supply

Executives from Celgene and other biopharma companies stressed the need to get better control over manufacturing and delivery of cellular therapies during a panel on the commercialization of cell therapies in oncology at the Biotech Showcase, which is held in San Francisco's Hilton Union Square and Parc 55 Hilton in parallel with the J.P. Morgan meeting at the Westin St. Francis.

In the final question of the panel, the panelists were asked what the weakest links in the supply chain were that need the attention of the industry.

Manufacturing has emerged as an important differentiating factor for commercial success of chimeric antigen receptor T-cell (CAR-T) immunotherapies. (Also see "*The Case For CAR-T Grows As Responses Hold Up Longer Term*" - Scrip, 20 Dec, 2018.)

Celgene's Joanna Beck said that the changing paradigm of how physicians deliver care is presenting challenges. Treatment centers are now becoming an extension of the [sponsor] company, because staff members have to be trained specifically in how to deliver therapies.

"I think that is a big change and it is not completely under our control. It will take a lot of work to train and certify all those treatment centers," said Beck, executive VP, global pharmaceutical

development and operations.

Beck added that sponsors need to work together to strengthen that link and try to harmonize delivery of therapies at treatment centers as much as possible. (Also see "*CEO of New UK Cell And Gene Therapy Hub Says 'All Systems Are Go'* " - Scrip, 11 Sep, 2018.)

Steven Kelly, president and CEO of Philadelphia-based CAR macrophage developer *Carisma Therapeutics Inc.*, said he was not so sure his company was at a stage where he could answer that question, but that two things concerned him, especially in the solid tumor space – cost of goods and capacity. Approvals of cell therapies in solid tumors would mean significantly bigger patient populations than for hematology indications, resulting in higher costs for the health care system and greater demands for manufacturing enough supply.

"I am hoping everyone solves that before we get there," the exec said, to laughter in the packed audience at the 8 a.m. session. (Also see "*Autolus Raises $80m To Take T-Cell Engineering To The Next Level*" - Scrip, 26 Sep, 2017.)

Panelist Christopher Vann, chief operating officer at London-based T-cell therapy developer *Autolus Ltd.* called for fully integrated supply, delivery and training.

There is not one rate-limiting step to address followed by another when it comes to the supply chain, rather there is a "whole slew of items" to address, said Maria Fardis, president and CEO of *Iovance Biotherapeutics Inc.* in San Carlos, Calif., a mid-stage company developing autologous tumor-infiltrating lymphocytes. (Also see "*Iovance Biotherapeutics CEO On TIL Immunotherapy For Solid Tumors*" - Scrip, 22 Nov, 2017.) In the long term, it's good to own your own manufacturing facility, though you wouldn't want to spend money up front until you know the FDA agrees with your strategy, she said.

Mike Ward also contributed to this report.