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J.P. Morgan Notebook Day 3: Biotech Feeling Government Shutdown, AstraZeneca, Denali, Allergan, Aptinyx, Sangamo

by Jessica Merrill

Daily round-up of news and notes from the 2019 J.P. Morgan Healthcare Conference in San Francisco: AstraZeneca's net prices set to slide in 2019; biotechs ponder disasters from government shutdown; Denali moves into gene therapy; Sangamo clarifies partnering strategy; and *Scrip* talks to Allergan and Aptinyx about upcoming NMDA data releases.

AstraZeneca: 2019 Net Price Decreases

AstraZeneca PLC's 2019 net prices on average across the portfolio will decrease versus 2018, Senior VP-Market Access Rick Suarez said in an interview at J.P. Morgan.

The industry is under pressure from the public and legislators when it comes to list price increases. HHS Secretary Alex Azar launched a thread on Twitter Jan. 9 berating companies for continuing to raise list prices. Many drug makers did raise list prices in January as they generally do, but so far, many of those price increases have been more tempered. (Also see "*US Drug Pricing: What A Difference A Year Makes* " - Scrip, 2 Jan, 2019.)

Industry would rather focus on net prices, i.e. after rebates, which are often significantly lower than list prices. But list price still matters, especially to patients in high-deductible plans who have to pay upfront.

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"When we start having discussions that are truly focused on just a list price, we are not really getting to the core of what some of the challenges are that patients might have in terms of the cost of the pharmacy counter," Suarez said.

AstraZeneca is trying to increase pricing transparency and is looking at novel ways of pricing drugs, largely value-based reimbursement agreements with payers, which AstraZeneca has pursued proactively across its portfolio, he said. (Also see "*AstraZeneca's 13 Outcomes-Based Contracts Show "Proactive" Engagement On New Models*" - Scrip, 31 May, 2017.)

The exec said one good thing to come out of the focus on drug prices by the Trump administration has been opening up the discussion on how drugs are priced, paid for and reimbursed. (Also see "*Trump's Drug Pricing Blueprint: An Administrative Vs. Legislative Breakdown*" - Pink Sheet, 12 Jun, 2018.)

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

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

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By Cathy Kelly

11 May 2018
The reform 'blueprint' might actually live up to its hype.

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Biotech Bemoans Impact Of Government Shutdown

Industry is wary of the effects of the US government shutdown – mindful of potential pitfalls if it becomes prolonged – execs said during a Jan. 9 panel at the Biotech Showcase, held in parallel with J.P. Morgan.

The battle between President Trump and Congress members over funding for a wall along the border between the US and Mexico resulted in a partial government shutdown starting Dec. 22. (Also see "*Shutdown Week Three: Sponsors With Upcoming User Fee Dates Should Start Sweating* " - Pink Sheet, 7 Jan, 2019.) The US FDA has continued to review filings using carryover funding, but this is expected to dry up in February.

New NDA filings are not being accepted and there is no transparency about how long this might last, execs said on a Biotech Showcase panel about the "intersection of policy and sentiment."

An announcement that Lauren Silvis – chief of staff for US FDA commissioner Scott Gottlieb – would not be participating in the panel as planned kicked off a discussion about the impact of the

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shutdown. Gottlieb himself was set to give a keynote address at J.P. Morgan, but delivered his speech remotely instead. (Also see "*J.P. Morgan Notebook Day 2: Biogen, GSK, Bluebird, Roche, Amgen, Biohaven, Lilly And FDA's Gottlieb*" - Scrip, 9 Jan, 2019.)

During the Biotech Showcase panel, Joe Panetta, president and CEO of Biocom, a life sciences trade association in Southern California, said members of his organization are reporting that they are not able to submit filings as planned. "We have folks who want to file NDAs and can't file NDAs," he said.

And it's unclear how long the standoff could go on. "We are in an industry where that kind of uncertainty doesn't help," Panetta pointed out.

Into 2019: Risk, Uncertainty And A Return To Product Focus

By Brian Chapman

09 Jan 2019

In view of the political and regulatory threats and opportunities likely to emerge in 2019, for those in the medtech industry, it pays to be vigilant, advises ZS' Brian Chapman. And while some new tech entrants appear to represent a threat to established medtech players, their emergence in general promises significant opportunities for savings and innovation in health care. At the same time, there will likely be a short-term return to both old medtech industry values, and to major M&A.

Read the full article here

Glycomimetics Inc. CEO Rachel King commented that she just heard from a banker that two initial public offerings that were set to launch after the J.P. Morgan meeting are on hold. Timing is everything for capital formation and delaying the launch of a roadshow is a "disaster," she said.

Jonathan Leff, a partner at Deerfield Management, said that the shutdown is a reminder of how "overwhelmingly dependent the whole industry of biotech and drug development is on government." He noted, "It's a symbiotic relationship."

A prolonged government shutdown has "enormous" implications for biotech, perhaps more so than any other industry because of that "extraordinary level of inter-dependency," he said. Many things are affected, including FDA reviews, research funding and patents – the list goes on and on.

"Past government shutdowns have turned out to be bit of a yawn because they have gone on for a week or two and that gets absorbed into the system. But if this goes on for a long time I think we will see all kinds of impacts – even beyond the ones we are thinking about today," Leff said.

Denali's Gene Therapy Moves

Denali Therapeutics Inc. is moving into gene therapy for neurodegenerative diseases, one of the

most exciting but most challenging areas of drug development. In an interview at J.P. Morgan, Chief Operating Officer and co-founder Alex Schuth talked about how the neuroscience specialist thinks it can address one of the big challenges with gene therapy in neurodegenerative diseases.

"There has been tremendous progress in gene therapy in recent years," he said. "One of the challenges is still to deliver gene therapy to the brain and that is where we see one of our core competencies – around the blood brain barrier."

The company announced a partnership Jan. 9 with *Sirion Holdings Inc.*, a developer of viral vector-based gene delivery technologies, to develop adeno-associated virus (AAV) vectors to get therapeutics to cross the blood-brain barrier, with the aim of developing a broad portfolio of product candidates for neurodegenerative disease.

Denali has a high-profile pedigree, founded by a group of former Genentech scientists and launched in 2015 with funding from venture backers Flagship Ventures and ARCH Venture Partners, so the industry will certainly be keeping an eye on its progress. (Also see "*Denali Builds Neurodegeneration Pipeline Through Discovery, Collaborations And Lots Of Cash*" - Scrip, 26 Aug, 2016.)

NMDA Modulator Data Coming Soon From Allergan, Aptinyx

Allergan PLC's Phase III data for its NMDA modulator rapastinel, expected in the first half of 2019, will be an important milestone for the company this year as well as a meaningful one for newly public *Aptinyx Inc.*, which was spun out of the drug's original developer *Naurex Inc.*

Rapastinel is an intravenously administered drug in development for major depressive disorder (MDD) with three Phase III studies testing the therapy as an adjunct to standard-of-care treatments. Data from all three clinical trials are expected during the first half of this year. If successful, the trials will support regulatory filings in the second half of 2020.

Allergan Executive Vice President and Chief R&D Officer David Nicholson told *Scrip* in an interview at J.P. Morgan that rapastinel is an easy-to-administer I.V. drug, with a rapid injection rather than a lengthy infusion. And while psychiatrists generally don't administer medicines to patients, he said several have indicated to Allergan that they are comfortable having nurses in their offices administer the drug.

Nicholson also noted that the intravenous administration does not seem to be a barrier for patients who have participated in an ongoing open-label trial for rapastinel. About half are still going back every week for their injections.

Rapastinel was notable in Phase IIb, when still owned by Naurex and known as GLYX-13, for its

rapid onset and significant efficacy in data reported at the end of 2014. (Also see "*Naurex presents 'compelling' data for depression drug GLYX-13*" - Scrip, 11 Dec, 2014.) Allergan announced that it would pay $560m to acquire Naurex – and allow for the spin out the NMDA modulator platform in an independent company – seven months later. (Also see "*Allergan paying $560m for Naurex; stays quiet on rumored generics sale to Teva*" - Scrip, 27 Jul, 2015.)

The resulting company Aptinyx raised $65m in Series A venture capital in May 2016 and a $70m Series B round at the end of 2017. (Also see "*Aptinyx Reaches Milestones, Raises $70m To Develop NMDA Modulators*" - Scrip, 18 Dec, 2017.) It launched an initial public offering in July grossing $117.8m to develop its pipeline of NMDA modulators, including three in the clinic. (Also see "*Finance Watch: Is The IPO Boom Making Anyone Nervous Yet?*" - Scrip, 27 Jun, 2018.) Since all of those candidates come from the same technology used to discover and develop rapastinel, success with Allergan's program will be an important validating event for Aptinyx. (Also see "*Naurex Spinout Aptinyx Launches After Allergan Deal*" - Scrip, 16 Sep, 2015.)

Aptinyx CEO Norbert Riedel told *Scrip* in a separate J.P. Morgan interview that the company had $165m as a result of its venture capital and IPO financings as of the third quarter of 2018.

The company will report Phase II data for NYX-2925 in diabetic peripheral neuropathy (DPN) in the first half of the first quarter of 2019 and in fibromyalgia in the first half of this year as well as Phase I results for NYX-458 in Parkinson's disease with cognitive impairment in the first half of 2019 and Phase II data for NYX-783 in post-traumatic stress disorder in the second half of 2019.

"Our plan is that when we unblind the [300-patient DPN] study hopefully we get positive results and then we will talk to the FDA about how to proceed from there," Riedel said.

He indicated that Aptinyx has the capacity to run two or three Phase III trials for NYX-2925 in DPN on its own and likely would wait until closer to commercialization to seek a partners for the asset.

"I would like to remain in charge of my destiny as long as I can until it no longer makes sense," Riedel said. "I do not think we can commercialize a chronic pain therapy. I think you would be best to partner with a large pharma for that."

The intent of Aptinyx's IPO was to give the company the financial wherewithal to do a deal from a position of strength based on positive late-stage trial results.

Sangamo CEO Outlines Partnering Strategy

Sangamo Therapeutics Inc. CEO Sandy Macrae told *Scrip* in an interview during the J.P. Morgan meeting that "partnering is important, because there's some things you can't do unless you're able to do it with a bigger company." That's where, Macrae said, his past experience working at

GlaxoSmithKline PLC and *Takeda Pharmaceutical Co. Ltd.* comes in handy.

"It makes a difference to have someone at a company like ours who's worked at a big company, because we understand what they need and we understand the quirkiness of the committee structure and the decision-making at a big company," he noted.

Sangamo has five programs in the clinic and four that are expected to move into clinical trials this year. The company's Phase I/II gene therapy SB-525 for hemophilia A is partnered with *Pfizer Inc.* and ST-400, its Phase I/II beta-thalassemia cell therapy, is partnered with *Sanofi*, but its other Phase I/II programs – the gene editing therapies SB-318 mucopolysaccharidosis type I (MPS I), SB-913 for MPS II, and SB-FIX for hemophilia B – are unencumbered. (Also see "*Sangamo Data Is A Moment For Gene Editing, But Leaves Questions* " - Scrip, 5 Sep, 2018.)

Two of its programs moving into the clinic in 2019 are partnered – BIVV-003 for sickle cell disease with Sanofi and a CD19-targeting chimeric antigen receptor T-cell (CAR-T) therapy with *Gilead Sciences Inc.*/*Kite Pharma Inc.* (Also see "*Gilead Partners With Sangamo For Gene Editing As It Builds Up Kite's Cell Therapy Platform*" - Scrip, 22 Feb, 2018.) The other two are wholly owned – the gene therapy ST-920 for Fabry disease and a chimeric antigen receptor-modified regulatory T-cell (CAR-Treg) candidate designed to induce immunologic tolerance in solid organ transplant, which was acquired in the recently closed purchase of *TxCell SA*.

Sangamo Buys TxCell To Get In Early on CAR-Tregs In Immunology

By Eleanor Malone

23 Jul 2018

Sangamo is to pay €72m to acquire France's TxCell, a specialist in chimeric antigen receptor-modified regulatory T-cells. It hopes ultimately to apply its zinc finger nuclease gene editing technology to develop next-generation allogeneic CAR-Treg therapies for immunological conditions.

Read the full article here

"We choose to partner things where it's a competitive commercial space or a trial program that is just too big for a company of our size," Macrae said. "I came from GSK and Takeda, and I've realized there are some things that big companies are good at and some things that small companies are really good at. It's a matter of finding the right solution for each program."

For instance, Sangamo has a tau-reducing program that could be developed in Alzheimer's disease or in smaller indications, like frontotemporal dementia. The latter would require a clinical trial program and commercial strategy manageable for a small company like Sangamo, but a $1bn Alzheimer's program and the disease's large market would require a big pharma partner, Macrae explained.

He noted that Sangamo has built good relationships with Sanofi, Pfizer and Gilead, but *Shire PLC* – newly acquired by Takeda – licensed in Sangamo's Huntington's disease program and was going it alone with that asset.

"I know a lot of people at Takeda, so hopefully that relationship will improve," he said, but noted that it will take a few more months for Takeda to review Shire's assets. However, there's a chance the Japanese big pharma could pass on Sangamo's Huntington's disease program because Takeda already has a Huntington's candidate.

"We would love to have it back and many other companies have come to us and said, 'If you do get it back, we'd like to talk to you about it,'" Macrae added.

Scrip spoke with the CEO on Jan. 7, prior to his presentation at J.P. Morgan. Sangamo saw its stock close down 14.2% at $10.99 on Jan. 9 following the review of its pipeline progress at the meeting after Macrae disclosed that the company is not likely to report data regarding enzyme replacement therapy withdrawal for MPS II patients treated with SB-913 at the WORLD Symposium in February. The exec said the data are not likely to be ready for presentation at that time, but should be available later this year.