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J.P. Morgan Notebook Day 4: US Generics Steady, UroGen, REGENXBIO, Dr. Reddy's In China, And Investor Sentiment Shifts

by Emily Hayes

Daily round-up of news and notes from the 2019 J.P. Morgan Healthcare Conference in San Francisco: US generics see gains, researcher calls for more tech transfer, and biotech investor sentiment rises as big deals bring optimism – among other items from the last day of this year's JPM.

US Generics: Shaky, But Steadier Ground

Generic drug manufacturers presenting at the J.P. Morgan Healthcare Conference were cautiously optimistic that US drug pricing pressure is resolving. US generic drug prices have been under pressure for several years, driven by buyer consolidation and increased generic drug approvals from the FDA.

Teva Pharmaceutical Industries Ltd. CEO Kare Schultz referred to the trend as a "death spiral," while *Mylan NV* CEO Heather Bresch likened the situation to an earthquake.

But the worst of the drug pricing pressure appears to be abating, according to both executives. "There has been a dramatic change, and we no longer have this death spiral of price declines," Schultz told investors. "We have a much more stable situation." Schultz made the decision, shortly after taking over as CEO in 2017, that Teva would raise prices on unprofitable products, about 10% of the company's portfolio, or discontinue them. (Also see "*Schultz Swings The Cleaver At Teva, Cutting 25% Of The Workforce*" -

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Scrip, 14 Dec, 2017.) But the chief exec cautioned the improvement doesn't mean the market will go back to where it was several years before the persistent price declines. "It just means that this constant reduction of the marketplace has stopped," he added.

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Mylan's Bresch echoed the sentiment, though she sounded more cautious. "When you have an earthquake and you say is the ground solid and steady again, you're measuring the Richter scale," she said. "I think there is no question this industry has gone through an earthquake."

"I think the word stability is relative," she added, noting the generic drug industry is still grappling with the fallout and trying to get back on steady footing.

Pharma Needs To Reward Academia More Appropriately

While pharma's movers and shakers were celebrating a record year for new drug approvals in 2018, it is not clear that the success will be sustainable. Speaking at the 2019 Wuxi Global Forum, one of the meetings running adjacent to the J.P. Morgan jamboree, Laurie Glimcher, president and CEO of the Dana-Farber Cancer Institute, expressed concerns that pharma's own focus is too narrow and its engagement with external research resources too parsimonious.

"We have seen some great advances with immunotherapies but we are only treating 20% of patients with immunotherapy and only eight to nine tumors are sensitive to that approach. I find it a little disturbing that the major pharma companies are focusing on the same things – we want more checkpoint blockers and only have two. Developing more molecules against PD-1 is an enormous waste of time," she noted.

Arguing that industry needs to be exploring other spaces, she said academia and small biotechs are more likely than big pharma to achieve that. However, that will only happen if big pharma provides appropriate resources and support similar to the $80m investment that Deerfield Management made to create the Center for Protein Degradation at Dana-Farber, announced November 2018.

"Most of the discoveries of new targets are going to take place in academia but we can only get them to a certain point. At Dana Farber we can derisk quite intensively because we have models and new technologies that can help us predict who is going to respond to what. We can increase the probability of success moving it from industry's 1 in 10 INDs to 1 in 4," she noted.

The problem, Glimcher added, is that academic centers are not being fairly rewarded for their contributions to industry. “When we work with venture capitalist firms or pharma we only get 2% royalties because we are partnering early stage. If we want to exponentially increase the number of new drug targets, pharma is going to have to work more with academic institutes and reward them appropriately for the brilliant work irrespective the stage of development,” she said.

Glimcher believes the relationship between Dana-Farber and Deerfield is one that pharma should look at. “Deerfield has a unique approach to funding science at academic institutions. They are generous about who gets compensated for what. They are providing up to $80m to fund a series of basic and translational science projects in the protein degradation field. More importantly, Deerfield recognises that they have to share the benefits with academia so we have 50% equity stake in the results,” she added.

Regenxbio Is Readjusting Its Partnering Focus

REGENXBIO Inc.'s adeno-associated virus (AAV) platform for delivering gene therapies has been licensed to more than a dozen partners to use in treatments for a range of diseases. And 2019 will be a big milestone year for one of the company's partners as well as for Regenxbio's own portfolio of four clinical and one preclinical gene therapy candidates.

"The biggest milestone for us as a company is transitioning to a later-stage company," founder and CEO Ken Mills told *Scrip* in an interview at J.P. Morgan.

REGENXBIO has reported positive Phase I/IIa results in wet age-related macular degeneration (AMD) for lead program RGX-314 and plans to take the gene therapy into Phase IIb later this year. The program is big for the company in many ways, including the pivot to late-stage development and the size of the wet AMD market, with millions of patients and growing numbers as the population ages.

Mills noted that a "mainstream" indication like wet AMD is not the norm for gene therapies, which tend to focus on rare diseases, such as partner *Novartis AG*'s AVXS-101. That gene therapy for spinal muscular atrophy (SMA), which Novartis bought in its $8.7bn acquisition of *AveXis Inc.* last April, is under US FDA review with approval expected this year.

Mills noted that he launched REGENXBIO at a time when gene therapies were considered unsafe and not innovative,

Novartis Goes Big On Gene Therapy With $8.7bn AveXis Acquisition

By Kevin Grogan

09 Apr 2018

The Swiss major has made a larger-than-expected bolt-on buy, using a large chunk of its $13bn windfall from GSK to get hold of a potential cure for spinal muscular atrophy and

because of safety concerns that arose in a previous era of gene therapy development. Now, 10 years later, "seeing a product approved is really satisfying," he said. "But the mainstream aspect of wet AMD is exciting too."

an additional gene therapy platform, as well as manufacturing capabilities.

Read the full article here

REGENXBIO has three other programs in or entering Phase I/II: RGX-501 for homozygous familial hypercholesterolemia with interim data expected in the second half of 2019, RGX-111 for Mucopolysaccharidosis Type I (MPS I) with trial enrollment expected to begin mid-year and RGX-121 for MPS II also with interim data in the second half of this year. An investigational new drug (IND) application is planned for the second half of 2019 for the company's preclinical candidate RGX-181. That program is designed to treat late-infantile neuronal ceroid lipofuscinosis Type 2 (CLN2), a form of Batten disease.

REGENXBIO is focusing less on partnerships and more on its own pipeline these days, but Mills said the company continues to license out its NAV Technology Platform to partners with the right product candidates and technical strength, because it doesn't want a reputation for not enabling gene therapies that could help patients in need.

Dr. Reddy's 'Going Big' In China

Dr. Reddy's Laboratories Ltd. stuck it out in China when things were tough, but with evolving regulations opening up opportunities in the world's second largest pharma market, the Indian firm believes that its long-standing base could now bring payback.

"Being there for the last 20 years, selling about $100m, about 10 products, we never left China even when it was hard and hopefully now we can reap the benefit of it," Dr. Reddy's COO Erez Israeli said Jan. 8 at the J.P. Morgan meeting .

Israeli shared some more specifics on the firm's game-plan in China, building on the basics outlined at the time of the firm's second quarter earnings in October last year. Dr. Reddy's believes that 70 products from its US portfolio can meet China's new regulatory requirements and registration is already underway for some of the products. "Some of it [is]even going to be launched soon, because we started registration further than that," Israeli, a former Teva executive, said. No product specifics were provided, however. China has, over the recent past, introduced a string of regulatory changes aimed at encouraging innovation and speeding up drug approvals; it has set out norms for accepting foreign clinical trial data towards new drug approvals in the country. (Also see "*Cancer, Orphan, Pediatric Drug Developers Join China Foreign Data Acceptance Party*" - Pink Sheet, 17 Jul, 2018.) (Also see "*Drug Price Waterloo: China's New Bidding Process Hits MNCs Hard*" - Scrip, 11 Dec, 2018.)

Dr. Reddy's JPM presentation also referred to scale-up plans in local manufacturing and partnerships in specific areas in China. Israeli said that Dr. Reddy's would choose "whether to walk within the JV that we have in China or outside of it." Dr. Reddy's existing China subsidiary, Kunshan Rotam Reddy Pharmaceutical Co. Limited (KRRP), is a joint venture with the Rotam Group of Canada. In 2017, Dr. Reddy's incorporated another subsidiary, Dr. Reddy's (Wuxi) Pharmaceutical Co. Limited in China. (Also see "*India Pharma Firms Eye China, Dr Reddy's Sees 'Great Opportunity' There*" - Scrip, 29 Oct, 2018.)

Established credentials with Chinese regulatory agencies and familiarity with commercialization in all Chinese provinces are other strengths that Dr. Reddy's expects will hold it in good stead as it expands in the market. "It's about going big into China by introducing more products – 70 instead of 10 that we have right now and to do it within the changes of the landscape in China," Israeli added. (Also see "*Duet Or Duel: Will 2019 See More India Pharma Linkages In China?*" - Scrip, 4 Jan, 2019.)

A renewed thrust on the India market is another key cog of Dr. Reddy's strategy, with management recognizing that the firm may not have been as focused as it perhaps ought to have been. "We used to be an important player in India and we are coming back with a new management, with new brands, with a renewed brand into India and we actually [are]now growing faster than the market in India," Israeli said, adding that about 70% of the firm's management had been changed in the last 18 months.

UroGen's Barrett Wants 'Significant' Price For UGN-101

New York-based biotech *UroGen Pharma Ltd.* hasn't decided on pricing yet for UGN-101 (mitomycin gel, 0.4%), which is in Phase III for low-grade upper tract urothelial cancer, but based on value, the product will command a "significant" price, new CEO Liz Barrett said during a Q&A at the J.P. Morgan meeting Jan. 10.

The product is a sustained-release formulation of mitomycin C, a DNA cross-linking chemotherapy that is liquid when chilled but then becomes solid in the body. It was developed with UroGen's platform *RTGel* technology.

Barrett is a very recent addition to UroGen; the biotech announced on Jan. 3 that Barrett – formerly the head of Novartis Oncology – was coming on board to oversee the approval and launch of UGN-101. (Also see "*Oncology Leader Liz Barrett Joins UroGen As CEO As It Heads Towards Commercial Stage*" - Scrip, 3 Jan, 2019.)

Then on Jan. 8, the company released additional data from an intent-to-treat analysis of its Phase III OLYMPUS study, showing that 57% of 61 evaluable patients treated with UGN-101 with low-grade upper tract urothelial cancer (LG UTUC) achieved a complete response at their primary disease evaluation time point, the primary endpoint of the study. (Also see "*UroGen's Lead*

Product Data Back Barrett's Interest" - Scrip, 9 Jan, 2019.)

Barrett said that UroGen is planning to launch UGN-101 in 2020.

The company has done a lot of work to prepare, although it has not yet decided pricing. Current treatment involves multiple comorbidities and surgeries, so the value proposition from the pharmacoeconomic standpoint is strong, Barrett said. "We feel very confident that we will be able to demand a fairly significant price," she said.

The company has another uro-oncology formulation in Phase II called UGN-102 (0.18% mitomycin), but the exec said that they are keen to expand beyond this disease space.

UroGen already has a partnership with *Allergan PLC* to develop a *Botox* product for overactive bladder, using its RTGel technology platform.

"What's important in this patient population is, today, the treatment for Botox is they really have to inject Botox about 40 to 60 times into the bladder. And you can potentially have one installation of Botox with our RTGel and be able to deliver the same efficacy that you have with those. So you can imagine the significant advance that this would be for patients," Barrett said during the company's main JPM presentation.

The botulinum toxin product is in Phase IIa and data are expected in 2019.

Biopharma Investors Sentiment Turns On A Dime

After a tough second half of 2018 for biotech stocks and a brutal December for the market overall, investors were less enthusiastic about boarding a plane to go to J.P. Morgan this year, commented Brad Loncar, CEO of Loncar Investments, which manages a couple of biopharma-focused exchange-traded funds.

"People could not have been coming in to 2019 with lower expectations for biotech – nobody wanted anything to do with any biotech companies," Loncar told *Scrip*. Two major M&A deals around the start of the meeting changed all that.

Bristol-Myers Squibb Co. announced plans to acquire *Celgene Corp.* in a deal worth $74bn on Jan. 3. (Also see "*Bristol Values Celgene's Hematology, Immunology Portfolio At $74bn, But Does It Price In Risk?*" - Scrip, 3 Jan, 2019.) Close on the heels of that deal, *Eli Lilly & Co.* swooped in on Jan. 7 with an agreement to buy

Bristol/Celgene Made Perfect Sense, But Doesn't Promise Big M&A Year, EY Says

By Joseph Haas

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Loxo Oncology Inc. for $8bn. (Also see "*Lift-Off For Lilly In Cancer Genetics With Loxo Buy*" - Scrip, 7 Jan, 2019.)

08 Jan 2019
The conditions that produced a sluggish biopharma M&A environment in 2018 persist, with bolt-on deals like Lilly/Loxo more likely than another mega-merger.

Read the full article here

The Bristol/Celgene tie-up makes sense when one considers that each of the companies was suffering from significant late-stage R&D setbacks. "Both were limping into 2019," Loncar said. Bristol and Celgene needed to do something to appease frustrated investors and they may be stronger together than alone, he added, noting that the companies expect to realize $2.5bn in synergies after their businesses are combined.

This isn't going to be the only major M&A deal of the year though, Loncar predicted, citing drug pricing pressures that are giving payers the upper hand in negotiations. Already, biotech and pharma companies are forecasting lower operating margins as revenues get squeezed by declining net drug prices. He said drug makers will be pressured to combine forces, adding bulk and bargaining power while finding ways to run their businesses more efficiently to cut costs.

Lilly stepping up to pay so much for Loxo also is catching a lot of investors' attention. "Things can turn on a dime and that's exactly what's happened," Loncar said.