BioWorld
The news source of record covering the development of innovative human therapies
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Clarivate Analytics

January 8, 2018
Volume 29, No. 5
Special Reprint

36th Annual J.P. Morgan Healthcare Conference

‘Spirit’ of JPM lives on as other meetings muscle in on biopharma playground

By Marie Powers, News Editor

Two weeks before the start of the 36th annual J.P. Morgan (JPM) Healthcare Conference, the annual gauge of life sciences investor sentiment, organizers caused a firestorm with their decision to bar media from the breakout sessions that follow canned presentations by 480 public and private companies over the four-day meeting. They relented 24 hours later, after media outlets took to Twitter to complain and stories in consumer press riled up retail investors, who publicly charged the forum with giving preferential treatment to institutional customers.

JPM’s initial stance on the breakout rooms – allegedly a newly established policy “due to capacity issues” – was just the latest in a code of conduct that has slowly choked much of the spontaneity out of the event. Over the years, organizers have limited the number of press, banned reporters from one-on-one meetings, forbidden the use of photos during sessions and taken keynote speeches officially “off the record.”

But not to worry. Many of the thousands braving the early January trip to San Francisco never step inside the venerable Westin St. Francis, where JPM is said to be filled to the brim, as usual, with more than 9,000 attendees. A lively cadre of alternative events attracts bigger crowds every year. And let’s be real: Most investors and partnering hopefuls come to town mainly for individual meetings across dozens of venues surrounding Union Square. If recent events are any indication, this year’s conversations about drug development and medical devices will sound an upbeat tone.

“I haven’t gone to the J.P. Morgan conference in at least a decade, maybe even longer,” confessed Chen Yu, managing partner at Vivo Capital, “but it’s still the overall event of the year, and I think it’s going to be the bellwether for 2018.”

Earnings pre-announcements are traditional fodder at JPM, and crossover investors like Vivo will be watching carefully this year.

“If you look at the back of 2017, the biotech market was pretty weak,” Yu told *BioWorld*, attributing that sluggishness to profit-taking more than fundamentals. “If J.P. Morgan starts off tough for our sector, I’m definitely going to be a little more cautious through the end of the year, but if it turns out with a nice kick, we’re in for a good year.”

Yu is betting on the latter. Big picture, the life sciences are enjoying a strong tailwind. Yu cited the U.S. tax plan and its incentives for repatriation, which could potentially drive M&A in the sector; the business tax cut, which could improve bottom lines for small to mid-cap firms and maintain the stock market at record levels; and an overall deregulatory approach by the federal government in clear illustration at the FDA, suggesting the near-record approval of new molecular entities (NMEs) in 2017 – at 46, second only to the 1996 total of 53 new medicines – won’t hit pause anytime soon. (See *BioWorld Insight*, Jan. 2, 2018.)

“The positives out there will probably drive a fairly robust first half in 2018,” Yu said. “If you look back over the last two or three years, classic crossover rounds have been a fruitful area, particularly for funds like ours that are a little bit larger and have the ability to anchor larger rounds and also play the private to public. For us, biopharma was a very attractive space over the last cycle. The question is, as the market approaches the back end of a positive three-year cycle, will that momentum continue? If it changes, it will have a pretty big impact in terms of how private companies are valued. That could have a ripple effect if the crossover round story plays itself through.”

Targeted therapeutics with companion diagnostics ‘a big theme’

Although some investors bemoaned big pharma’s relatively small appetite for large M&As in 2017, that posture – coupled with a strong IPO spigot – benefited the crossover story, according to Yu.

“For now, we can afford to be a little bit indifferent to big pharma, because we’re being well-rewarded with public companies getting high valuations,” he said. “If the crossover piece goes away over the next year, private companies will be forced to look for M&As, which will compel people to be a little more conservative on valuations.”

“One of the underlying drivers for our industry is always M&A,” agreed Christiana Bardon, partner of the MPM Oncology Impact Fund and founder and managing member at Burrage Capital. Although 2017 wasn’t a standout year for biopharma M&A and, in fact, was skewed by a very few large deals, big pharma – which has

downsized, closed or outsourced its research capabilities – has no choice but to stay in the hunt.

Bardon characterized the year-end bid by Roche Holding AG to acquire Ignyta Inc. for $1.7 billion, or $27 per share in cash, as a smart deal and a harbinger for M&A activity heading into 2018. Through the transaction, Basel, Switzerland-based Roche gained entrectinib, Ignyta's tyrosine kinase inhibitor that is in the pivotal phase II STARTRK-2 trial in patients with fusions of the ROS1 and NTRK genes. (See *BioWorld*, Dec. 27, 2017.)

"In general, pharmaceutical companies want to buy drugs which are going to be successful in terms of their regulatory approval and their commercial impact," she pointed out. "Ignyta was a great example of a company that was a low-risk winner because it was working in a targeted patient population and it had a companion diagnostic, so you knew which patients were going to benefit. Targeted therapeutics with companion diagnostics is a big theme in oncology and one that will continue to play out."

Bardon also agreed that changes in tax law that put more cash in company coffers also will boost M&A, even if most biopharmas choose to use their money elsewhere. But changing M&A dynamics also could affect, for better or worse, the ability of mid-size biopharmas to access funding. Backing by crossover investors enabled many early stage companies to move to the public markets on the back of preclinical data alone. In all, 41 biopharma IPOs were completed in the U.S. in 2017 – 12 in the last quarter of the year – easily supplanting the previous year's crop of 31 U.S. biotech IPOs.

Europe also saw something of a fundraising renaissance. The European biotechnology sector tapped the global equity markets to the tune of $6.85 billion in disclosed transactions in 2017 – a tally that was 81 percent ahead of $3.789 billion in investment in 2016 and comfortably ahead of $4.913 billion secured by the sector in 2015. (See story in this issue.)

Still, biopharma is subject to what Yu called the "barbell" effect. Early stage efforts in cell and gene therapy, immuno-oncology (I-O) and emerging neuroscience discoveries have been richly rewarded, along with late-stage development on the cusp of regulatory approval. Rising valuations driven by exciting science and preliminary data, in fact, have forced crossover investors to move upstream, Yu said. The challenge occurs in the large middle ground, where companies need to fund phase II programs but may struggle more with valuations in comparison to shiny new startups. Long term, midstage biopharmas will see a return to value as some early stage deals burn up, but predicting the flash point isn't a simple matter.

"We're looking at this phenomenon with a watchful eye, because it's very market cycle-dependent," he said. If the market stays hot, as it has over the past year, "we're going to be forced to keep moving upstream."

'We're in a remarkable period of discovery'

The funding environment has been a boon for Flagship Pioneering, according to founder and CEO Noubar Afeyan. In December, the firm hauled in $618 million in a new round of capital commitments from long-time investors and additional institutional investors, bringing its total raise to more than $2.3 billion. Its Venturelab operation experiments with 50 to 100 projects each year, leading to 10 to 15 early stage proto-companies and six to eight startups. Portfolio firms Rubius Therapeutics Inc., Torque Therapeutics Inc., Codiak Biosciences Inc. and Denali Therapeutics Inc. were among those making headlines with their 2017 fundraisings. (See *BioWorld*, June 21, 2017, Nov. 15, 2017, Nov. 30, 2017, and Dec. 8, 2018.)

Predicting winners and losers in biopharma is a thankless job, Afeyan said, "so we try to start with neither a problem nor a solution," instead beginning with "white space that we populate with what could be problems and what could be solutions, and then see which ones match." At the time Rubius was getting underway, for instance, chimeric antigen receptor T cell (CAR T) was a technology with no patient data, he said.

The one common denominator for Flagship is to identify potentially "disruptive" technologies overlooked by investors focused on "adjacency-based" innovation. Although he didn't tip his hat on internal technologies that might move toward the clinic in three to four years, Afeyan expressed optimism at progress in understanding the interface between immunology and other body systems by studying mechanisms in the gut and in unraveling mysteries of the central nervous system.

"We have a lot more molecular techniques to identify how cells operate from a circuitry standpoint, how they respond to different stimuli and how to grow and culture them to simulate in vivo conditions," Afeyan told *BioWorld*. "There are an immense number of new biological insights in important unmet medical need areas coupled with new tools across the board – cell therapy, gene therapy, RNA, small RNAs, protein conjugates. There are many more things to paint and many more colors to paint with. We're in a remarkable period of discovery."

Limited partners and institutional Investors, alike, understand the potential opportunities.

"In the limited partner investor market, we've seen a significant increase in the appreciation for how science and biotechnology can create substantial value," Afeyan said. "JPM is a good place and time to assess investor sentiment vis-à-vis the mid- to large-cap biotechs as it portends to IPOs for newer companies. We have nine or 10 companies presenting there, so we'll get a pretty good read across therapeutic areas. I generally expect more of an upbeat attitude than over the last two years."

Looking for 'the proof of the pudding'

Certainly, the expanding breadth of technologies seeking investment will garner discussion in San Francisco. The 2017 NME total doesn't even include the three groundbreaking cell and gene therapies – Kymriah (tisagenlecleucel, Novartis AG), Yescarta (axicabtagene ciloleucel, Gilead Sciences Inc.) and Luxturna (voretigene neparvovec-rzyl, Spark Therapeutics Inc.) – green-lighted by the FDA's Center for Biologics Evaluation and Research, adding to the industry's impressive output in 2017. (See *BioWorld*, Aug. 31, 2017, Oct. 20, 2017, Dec. 20, 2017, and Dec. 27, 2017.)

Investors expect gene therapy and I-O, in particular, to continue their upward trajectories.

"What's exciting about gene therapy is that we now have proof of concept that it can work to cure patients of diseases in multiple organs," Bardon told *BioWorld*. In addition to the Luxturna, approved by the FDA to treat children and adults with confirmed biallelic RPE65 mutation-associated retinal dystrophy, an ultra-rare progressive disease, Bardon labeled as "remarkable" early findings from the Avexis Inc. gene therapy candidate, AVXS-101, in infants and children with spinal muscular atrophy type 1, now being assessed in a pivotal trial.

Although such therapies target an inherited disease, caused by mutations in a specific gene, the CAR T therapies Kymriah and Yescarta, which modify the genetic material of living cells, are no less impressive, she said.

On the heels of Luxturna's pricing at $850,000 – $425,000 for each eye, largely in line with analyst expectations – Bardon also downplayed the outcry by some consumer and patient groups over the cost of breakthrough therapies, especially gene therapies that represent one-time treatments for patients who might otherwise incur significant life-long disability or death.

"These aren't chemotherapy drugs which kind of make you better and these aren't drugs that you have to take year in and year out for the rest of your life," she said. "These are therapies that can potentially cure. In some ways, these drugs come from a position of strength because they are transforming people's lives."

Bardon also sees room to grow for checkpoint inhibitors – "one of the largest drug classes, not just in oncology but across biotherapeutics," she said. And with the growing movement toward combination therapies, "if everything has to be evaluated in a study with checkpoint inhibitors, you always need a pharma partner. If you're a small biopharma, you can't pay for these checkpoint inhibitors to run trials."

That reality also is prompting early partnering in the checkpoint space, where big pharmas continue to run the show for now, and to fuel competitive M&A activity.

But smoke and mirrors will no longer suffice, a lesson ruefully learned last year in the dust-up over Astrazeneca plc's phase III blowup with the MYSTIC trial in non-small-cell lung cancer, which came just as the Cambridge, U.K.-based giant made public its $8.5 billion deal with Merck & Co. Inc. around the oral poly ADP ribose polymerase, or PARP, inhibitor Lynparza (olaparib). (See *BioWorld*, July 28, 2017, and July 31, 2017.)

Similarly, for new I-O entrants, "we're moving into the phase where clinical data is going to begin to trump," Yu observed. "Over the last three years, you could get away with a great story, a great management team and a great syndicate of investors, and that fueled these massive series A and series B rounds into pretty robust public offerings. The next cycle will be the proof of the pudding. You'll have to show data to differentiate yourself. There's no other way to predict which of these companies will be the winners."

Cross-border dealmaking 'one of the most exciting things'

This year also could see an acceleration of cross-border deals between the U.S. and Asia in both biotech and med tech, Yu said. China's domestic life sciences companies are exerting their muscle, he noted, pointing to the $172.5 million U.S. IPO by Zai Labs Ltd. as one of the year's largest – second only to Ablynx among ex-U.S. biopharmas to list on Nasdaq in 2017 and No. 4 overall, according to BioWorld Snapshots. At year-end, Shanghai-based Zai also nabbed greater China rights for FPA-144, a fibroblast growth factor, or FGF, monoclonal antibody for gastric and gastroesophageal junction cancer in development by Five Prime Therapeutics Inc., of San Francisco. (See *BioWorld*, Dec. 28, 2017.)

Another cross-border deal that attracted attention was the broad alliance bonding Celgene Corp., of Summit. N.J., which paid $263 million up front and made a $150 million investment in Beijing-based Beigene Ltd. to in-license ex-Asia rights to Beigene's PD-1 inhibitor, BGB-A317. Celgene pledged to collaborate on up to eight registrational studies for the candidate in solid tumors, including studies already in the planning stages. In turn, Beigene, which stands to collect up to $980 million in milestone payments from the deal, takes charge of selling Celgene's top products in China and advancing new candidates. (See *BioWorld*, July 7, 2017.)

Cross-border dealmaking "is one of the most exciting things that's happening" in the industry, Yu maintained. "We're actively involved in buying U.S. companies that we think may ultimately be attractive to Chinese acquirers."

"Biopharma is definitely the forerunner in terms of cross-border dealmaking," agreed Janet Xiao, co-chair of the global life sciences group at Morrison & Foerster LLP and a moderator at this week's Chinese American Biopharmaceutical Society (CABS) Investor Forum. Last year set a record for U.S.-China cross-border transactions in biopharma, she said, with assets in oncology and I-O, cell therapy and cardiovascular disease at the top of their prospect list, along with drug and device treatments for diabetes.

Investors in China have grown more sophisticated about evaluating technologies that fill gaps in their internal development, Xiao added, "so the deals they're looking for have become more tailored to their specific needs."

Medical device deal flow is growing, although deal sizes fall far below those in biopharma.

"Going forward, I expect more interest in medical devices, especially in the cardiovascular area and in digital health," Xiao told *BioWorld*. "Chinese companies have a good appetite for mid-size firms with interesting technology."

On the flip side, China is emerging as a source of technology, she pointed out, citing the year-end partnership inked between Nanjing-based Legend Biotechnology Corp. and Janssen Biotech Inc., a subsidiary of Johnson & Johnson, to develop CAR-B38M, a CAR T therapy for multiple myeloma that targets B-cell maturation antigen. (See *BioWorld*, Jan. 2, 2018.)

All eyes will be on China this year, Xiao acknowledged, as several critical CAR T trials read out.

"If the data are good, that will provide a significant boost to the industry," she said. "On the other hand, if there are safety or toxicity issues, that will give people pause. People are very, very excited about cell therapy and CAR T, but it remains to be seen whether the players in China have paid sufficient attention to safety and related issues. There is a learning curve."

'The capital markets have incredible enthusiasm for biotech'

Enthusiasm for such transactions isn't limited to U.S.-China deals. At the close of 2017, a consortium of Chinese investors acquired a 90 percent stake in oncology therapy developer Group NMS Co. Ltd., of Milan, Italy, in a deal valued at approximately €300 million (US$361.25 million). (See *BioWorld*, Jan. 5, 2018.)

For now, pharmaceuticals remain more interesting to Chinese investors than medical devices, in part because of the M&A environment and a large crop of big pharmas buoyed by a "very healthy" mid-cap sector with the ability to manage "reasonably sized" deals.

"In med tech, you basically have five big guys and no middle ground," Yu said. "The emergence of Chinese investors represents a new mid-cap buyer," bringing fresh energy to the space and changing its M&A dynamics.

"Ten years ago, we never talked about a China strategy," Yu said. "Nowadays, every board is asking itself, 'What should we be doing with our assets with anything in China?' I would expect to see a whole slew of these deals in 2018, and I think it's going to be an exciting area for the next five or 10 years."

Fundamentals remain important, and concern over the 2017 pipeline shakeouts at Eli Lilly and Co. and Glaxosmithkline plc, not to mention staff rollbacks at Teva Pharmaceutical Industries Ltd. and Allergan plc, will likely generate chatter. (See *BioWorld*, July 27, 2017, and Dec. 15, 2017.)

But many panels at the confabs that surround JPM – Biotech Showcase, Redesigning Early Stage Investments (RESI), CABS and the Wuxi Global Forum, among them – will focus on more productive industry themes. Agendas are packed with discussions on cell-based immunotherapies, gene therapy, the microbiome, infectious disease, diabetes and the growing incidence of nonalcoholic steatohepatitis, or NASH, not to mention regulatory reform, digital health, artificial intelligence, deep learning and the ubiquitous dumping ground known as precision medicine.

Some participants will no doubt leave San Francisco wondering if the buzzwords will ever change, but most will come away energized, as they always do, to jumpstart 2018.

Bolstered by continued scientific innovation and near-record regulatory approvals, "the capital markets have incredible enthusiasm for biotech, and from that perspective JPM is a very important conference for our industry," said Bardon, a panelist at this week's Market Trends in Biotech event, co-sponsored by Bloomberg Intelligence and Women in Bio.

That's true no matter what your mission in San Francisco.

"We've transitioned to the spirit of J.P. Morgan," Xiao observed. "It's all about establishing contacts and connections, whether through the J.P. Morgan conference, through CABS or through any other venue. It's still the leading event in the industry."