Hong Kong stock exchange opens to biotechs

On April 30, the Hong Kong Stock Exchange officially laid out the welcome mat for innovative companies with a special focus on biotechs. The newly established biotech chapter has relaxed listing rules to allow prerevenue biotechs with a market cap of at least HKD1.5 billion ($190 million) to go public. China's biotech sector has been enjoying explosive growth thanks to regulatory reforms made in 2017, but Chinese biotechs had few options for raising capital on a market close to home. Leading biotechs such as BeiGene of Beijing, Zai Labs and Hutchison Medipharma, both of Shanghai, listed on the NASDAQ instead. This looks set to change with HKEX, and all eyes are on Hong Kong to see how investors respond to the emerging Chinese biotech story. The HKEX admits that assessing biotech companies requires unique knowledge that they currently lack. To deepen its expertise and protect investors from poor-quality companies, the HKEX has established an advisory panel with 13 industry experts to provide advice to investors as needed. The exchange is also hiring experts while a professional ecosystem of bankers, analysts, lawyers and accountants is also coalescing. Currently, the HKEX is vetting companies that have decided to file for listing under the biotech chapter. Anti-viral developer Ascletis Pharma of Hangzhou was the first and, as of May 15, the only biotech to file an application to list. But reports suggest others intend to follow such as Ascentage Pharma of Suzhou, Tianjin-based China Tasly Pharma Group and Innovent Biologics of Suzhou. Foreign biotechs have also shown a strong interest in going public in Hong Kong according to Jeffrey H.W. Ng, senior vice president corporate communications, HKEX. So far none have filed an application to list but Grail, a cancer detection company backed by Bill Gates and Jeff Bezos, plans to take advantage of the new rules in Hong Kong. According to Ng, the first IPO could occur as early as late June or early July.

Shannon Ellis

"All of Us is one of the most ambitious research efforts that our nation has ever undertaken. More than almost anything we've ever done, this program has the potential to shed new light on how to manage disease + keep people healthy." Francis Collins kicks off the million person project with a tweet. (*@NIHDirector*, May 2017)

"It's safe to say that the average patient does not have the time or expertise to keep up with the actual biomedical literature, and thus relies on headlines and advertisements for an impression of the field, and that impression is pretty far off of reality." Derek Lowe blog entry on the hype and reality of cancer sequencing. (*In the Pipeline*, 2 May 2018)

tal health tools have been published—a quarter of those in 2017 alone, according to IQVIA.

Novartis' interest in digital therapeutics was piqued when its leaders noticed efficacy papers being published "left and right," says Joris Van Dam, executive director of digital therapeutics at Novartis Institutes for BioMedical Research. Although, the Basel-based company already had programs such as Elevate MS, which collects sensor-based data on people with MS, and a collaboration with Propeller Health to develop a sensor to track usage of Novartis' Breezhaler inhaler for chronic obstructive pulmonary disease. In the partnership, Novartis and Pear will further develop THRIVE for schizophrenia, and also design and develop the software to treat mental health symptoms related to MS, such as depression, anxiety and cognitive impairment. In Pear's collaboration with Sandoz, a division of Novartis in Holzkirchen, Germany, the companies aim to commercialize reSET and, if approved, reSET-O.

Elsewhere, Roche's French pharma unit in March announced the expansion of a partnership with Voluntis, both in Paris, to develop a digital therapeutic that makes personalized recommendations to people with cancer to help them manage symptoms. Voluntis' long-running collaboration with Paris-based Sanofi has boosted its development of software for diabetes management.

Such partnerships will help software start-ups break into the therapeutics market, says St. Claire. "Something digital health companies are really struggling with is getting market traction," she says. "The physician market is super-fragmented and difficult to tackle. If you want to [market a prescription-only app], I think the most successful route is going to be through a pharma company."

But Akili's Martucci says he's not ruling out the go-it-alone approach. "We don't know what the full commercialization models for digital therapeutics will be," he says. "I think it would be a mistake to hinge that entirely on pharma." Akili partnered early, in 2014, with Pfizer, to test its video game platform as a potential biomarker in early Alzheimer's disease.

Something pharma companies want to see in a medical software developer is a clear plan for regulatory approval. Novartis chose to partner with Pear partly because "they had FDA approval squarely in their path," says van Dam at Novartis. "It's much more of a natural fit to our current business" to work on a product that will be vetted by regulatory agencies, rather than wellness apps that don't require such reviews, he says.

Right now, that pathway in the US looks promising. The FDA has created what it calls the "pre-cert" program, in which digital health companies can get pre-certified by the agency. Once they have, their software products go through a streamlined review, or no review, depending on the risk of the product.

The FDA selected nine companies, including Pear, to participate in a pre-cert pilot program. Companies will be examined using several metrics, including cyber security, user safety, customer service, product quality and clinical responsibility, says Caccomo. The agency plans to announce the expansion of the pre-cert program by the end of 2018, she says.

"What we're trying to do is something similar to a TSA precheck," says Stephanie Caccomo, a spokesperson for the agency, alluding to the US government's expedited security screening system for low-risk travelers. "The FDA recognizes that our traditional regulatory paradigm for traditional hardware medical devices doesn't necessarily correlate with the design, development, and execution phases that software developers use," she says.

For a software company, one of the things that is initially really intimidating about the FDA is not so much the clinical trials and data but the fact that changes are hard to make.

Medical app developers say the program will allow them to be nimble, continually improving their software, without having to stop and wait for the FDA. "In the software world, changes are critical to staying relevant, because data is so much faster than traditional modalities," says Jo Masterson, COO at 2Morrow, a smoking cessation and behavioral app developer. "For a software company, one of the things that is initially really intimidating about the FDA is not so much the clinical trials and data but the fact that changes are hard to make," she says.

Of course, if digital therapeutics makers successfully ingratiate themselves into the pharma world, complete with FDA approvals and prescription-only marketing, they could, in some respects, lose one of the hallmarks of the digital world: accessibility. "I'd hate to see everything go prescription," says Masterson. "The real promise of digital health is to remove some of the barriers to health care," she says. If app developers all make their products prescription-only, "you have to have health care before you can get health care."

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