IN brief

Otsuka snaps up cancer drugmaker Astex

Otsuka Pharmaceutical Group of Tokyo completed a \$886-million merger with Astex Pharmaceuticals, Dublin, California, on October 11. Taro Iwamoto, Otsuka Pharmaceutical's president and representative director cited Pyramid, Astex's fragment-based drug discovery technology, as a driving factor for the acquisition. Although the fragment-based discovery platform is still unproven, eight of Astex's nine pipeline drugs were developed using the platform. The deal is a vote of confidence for the biotech's platform, says Brean Capital analyst Gene Mack in New York, adding that Otsuka's primary aim was to shore up its own drug development capabilities. "Otsuka has said the Pyramid platform can be used to look into central nervous system diseases, an area that is more of a traditional strength," says Robert McTiernan of IHS in Englewood, Colorado. Otsuka's portfolio contains the blockbuster schizophrenia drug Abilify (aripiprazole), with a patent expiring in 2015 in the US; marketing rights for two oncology drugs; and compounds under development for Alzheimer's and other disease areas. "Otsuka does seem to have some oncology compounds [under development], but mostly in phase 1, so the acquisition allows them to jump a few steps with minimum work," McTiernan adds. Astex's most successful commercial product, in partnership with Tokyo-based Eisai and New Brunswick, New Jersey-based Johnson & Johnson, is the epigenome-targeted drug Dacogen (decitabine), approved in 2006 for treating myelodysplastic syndrome. Dacogen (not developed with the Pyramid technology) is a cytidine antimetabolite analog that is incorporated into DNA and inhibits DNA methyltransferase, resulting in hypomethylation and cell cycle arrest. Also promising is a small molecule follow-up agent to Dacogen—SGI-110. At the end of August, Astex announced early results from a phase 2 trial reporting a complete remission rate of 25% in elderly acute myeloid leukemia patients. Full trial results are expected in December 2013. Otsuka must be banking on the success of the phase 2 trial of SG-110, says Mack, but pointed out that the same investors who initially objected to the merger think Astex should have waited for the full trial results before agreeing to a sale price.

Alli Proffitt

IN their words

"We needed to retrain peoples' receptors from not running to the [other] side of the room when you heard the words gene therapy to, 'just hold on, let us tell you the data.' So it really became gene therapy at the intersection of orphan diseases very quickly." Nick Leschly, CEO of bluebird of Cambridge, Massachusetts, explaining how they managed a successful IPO in a historically unpopular field. (*Xconomy*, 4 October 2013)

Table 1 FDA's expedited programs

	Breakthrough therapy	Fast track	Accelerated approval	Priority review
Qualifying criteria	Designation for drugs intended to treat a serious condition and which have preliminary clinical evidence indicating substantial improvement on a clinically significant endpoint over available therapies	Designation for drugs intended to treat a serious condition, where nonclinical or clinical data show potential to address unmet need	Approval pathway for drugs treating a serious condition and which show meaningful advantage over existing drugs and have an effect on a surrogate endpoint that is likely to predict clinical benefit, or on an intermediate clinical endpoint	Designation for a drug treating a serious condition, which could provide a significant improvement in safety or effectiveness
When to submit	With IND or after; ideally not later than end of phase 2 meeting	With IND or after; ideally no later than pre-BLA or pre-NDA meeting	To be discussed with FDA review division during development	With original BLA or NDA
Features	All fast track features plus intensive guidance on efficient development, even phase 1 Organizational commitment from senior managers	Actions to expedite development and review Rolling review/submission	Approval based on effect on surrogate or intermediate endpoint	Shorter review of marketing application (6 months vs. 10 months)

IND, investigational new drug application; NDA, new drug application; BLA, biologics license application. SOURCE: US Food and Drug Administration

companies don't reveal when they've applied for breakthrough. So, too, could the hit to a company whose candidate's breakthrough designation is withdrawn, if subsequent data mean it no longer meets the criteria. "At the moment, the focus is totally on being a breakthrough, not on what happens if not, if you apply and fail, or if you apply and fail later on," says Brenda Huneycutt, senior manager at Washington, DC-based consultancy Avalere Health.

So does the breakthrough designation actually lead to faster development and regulatory review times? Yes, according to Urte Gayko, vice president, regulatory affairs at Sunnyvale, California-based Pharmacyclics. "Things were accelerated by two- to three-quarters, relative to our previous plans," she says. Pharmacyclics' oral ibrutinib, an inhibitor of Bruton tyrosine kinase, is being developed in partnership with Johnson & Johnson. It was the first cancer drug to receive breakthrough designation, in February 2013, for patients with relapsed or refractory mantle cell lymphoma, and for Waldenstrom's macroglobulinemia. In April, the compound received a further designation for B-cell malignancies.

Pharmacyclics, which leads development of the drug for specific indications, with Johnson & Johnson funding 60% of the costs, was proactive in outlining what it wanted breakthrough to mean. "We made the case for submitting a data package earlier," explains Gayko. Instead of

completing a second phase 2, the company went to FDA with data from one phase 2 trial only—albeit one that showed a good, and durable, overall response rate. Gayko claims the company talked more often with FDA, got meetings set up "in weeks, rather than months," and got full attention from a cross-functional team, rather than a single reviewer, as is usually the case. That meant clinical, chemistry, manufacturing, and controls (CMC), and preclinical issues could be addressed in concert.

It also meant a lot more work for Pharmacyclics across most functions, in preparation for an early filing—and in responding promptly to FDA's requests. "We hired more people, and worked late nights. Don't go down this path if you're not prepared," warns Gayko.

For other biotechs, breakthrough designation has had a less noticeable impact. For Catalyst, our "clinical timeline won't change," notes McEnany. That's mostly because its phase 3 candidate received the mark later than the ideal submission stage, which comes before the end-of-phase-2 meeting at the latest. McEnany's hoping the breakthrough label will improve review time, but won't know until the company meets with FDA later this quarter. Six months after Scioderm's designation for SD-101, not much has changed there either, notes Coull. The company hasn't had any additional FDA meetings yet; its next, due in November 2013, was planned as part of the regular review process. Like many of