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Alnylam party to hot summer

Mad as a hATTR? Akcea, Ionis $1.7B tie-up queried as PDUFA dates approach

By Randy Osborne, Staff Writer

As PDUFA dates near for the antisense drug inotersen and a competing therapy in hereditary transthyretin amyloidosis, or hATTR, Ionis Pharmaceuticals Inc.'s potential $1.7 billion deal with spinout Akcea Therapeutics Inc. was designed to prepare for launch, but not everybody was impressed – at first, anyway.

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Solid's DMD trial halted on adverse event, sending shares into tailspin

By Michael Fitzhugh, Staff Writer

A partial restriction on tests of an experimental and well-financed gene therapy for Duchenne muscular dystrophy (DMD) gave way to a full FDA clinical hold following a serious adverse reaction in the first patient dosed. The boy has since recovered. But shares of Solid Biosciences Inc. (NASDAQ:SLDB), which raised $133.7 million in a January IPO despite a then-partial hold on the candidate, SGT-001, fell 64.6 percent to $9.32 by Thursday's close.

Shares of competing DMD drugmaker Sarepta Therapeutics Inc (NASDAQ:SRPT) tilted lower in their own small decline Thursday, falling $1.05 to close at $81.22. Solid's stumble, however, may turn to Sarepta's advantage, H.C. Wainwright managing director Debjit Chattopadhyay suggested in a research note.

The clinical hold on Solid Bio's IGNITE DMD trial "is likely to make it difficult for Solid to escape the perception

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PARP 2.0

$94M series B funds bright 'Ideaya' in synthetic lethality

By Marie Powers, News Editor

In the two years since Ideaya Biosciences Inc. closed its $40 million series A, the South San Francisco-based company has grown from two to 42 employees, identified lead programs in synthetic lethality and immunotherapy, prepared to file three INDs in the next 12 to 18 months and positioned itself to move multiple candidates into the clinic by the end of 2019. That trajectory was more than sufficient to attract $94 million in a series B financing that will see the company into the second half of 2021, according to CEO Yujiro S. Hata.

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Finger pointing rampant in HELP hearing on 340B drug discount program

By Mari Serebrov, Regulatory Editor

The primary takeaway from Thursday's Senate Health, Education, Labor and Pensions (HELP) Committee hearing on the 340B program is that the committee leadership is serious about crafting legislation to bring more accountability to the prescription drug discount program that helps safety-net hospitals and community health centers provide charity care.

A secondary takeaway is that lawmakers' ire over high drug prices isn't diminishing. Those two threads resulted in the hospital and biopharma industries tangling over transparency and

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Move over, Soliris, for 'new standard of care'

Alexion pins filings on ALXN-1210 phase III win in PNH

By Marie Powers, News Editor

Alexion Pharmaceuticals Inc. is looking to the second half of 2018 as the target for regulatory filings in the U.S., EU and Japan after ALXN-1210, its long-acting C5 complement inhibitor, hit noninferiority to Soliris (eculizumab) across co-primary and the four key secondary endpoints in the pivotal phase III Study 301 in complement

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AACR previews meeting with data on CAR T and HER2

By Brian Orelli, Staff Writer

As 22,000 participants prepare to descend on Chicago next month for the American Association for Cancer Research (AACR) 2018 meeting, the organization released many of the abstracts for presentations. Unfortunately, as Evercore ISI analyst Umer Raffat wrote in a note to clients,

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China government proposes realigning pharma-focused CFDA as part of broader agency

By Cornelia Zou, Staff Writer

HONG KONG – Looking to improve regulatory coordination and supervision of drug and food markets, the Chinese government may merge together several agencies – including the China FDA (CFDA) – into an umbrella State Drug

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"There was a huge amount of enthusiasm in our crossover B round," which was "significantly oversubscribed," Hata told *BioWorld*. "We have a powerful combination of strategics, with Roche coming as a new investor to the syndication. We have four new public crossover investors, helping to set us up for a future IPO. And we have additional venture capital investors."

New investors Nextech Invest Ltd., 6 Dimensions Capital, BVF Partners LP and Perceptive Advisors LLC led the round. In addition to Roche Venture Fund, other new investors included GV (formerly Google Ventures), Boxer Capital of the Tavistock Group and Driehaus Capital Management LLC. Existing investors 5AM Ventures, Canaan Partners, Celgene Corp., Wuxi Healthcare Ventures and Alexandria Venture Investments joined the round.

Growing interest in cancer genetics and personalized medicine – in particular, the potential to use biomarkers to improve patient selection for oncology studies and therapies – lit up investor sentiment, Hata said. Other companies pursuing immunotherapy – he cited Tesaro Inc., Clovis Oncology Inc., Blueprint Medicines Corp. and Ignyta Inc. as examples – already have shown their mettle in the field.

"The catalyst around the financing was the idea that Ideaya represented that next wave of companies in that category," Hata said.

Ideaya is keen to take the concept of synthetic lethality (SL), which became a therapeutic reality with the 2014 approval of Astrazeneca plc's poly ADP-ribose polymerase (PARP) inhibitor Lynparza (olaparib) in BRCA-mutated advanced ovarian cancer, to the next level. (See *BioWorld Today*, Dec. 22, 2014.)

SL describes the phenomenon that occurs when the independent loss-of-function of two unrelated genes that have no significant effect on cell growth and viability on their own results in cell death when the two are combined. Ideaya is examining SL interactions for genetically defined patient populations and assessing how to exploit tumor susceptibilities as a platform to discover and develop small-molecule agents targeting a range of oncology indications.

The SL approach pioneered with Lynparza is now well-validated, Hata pointed out. Since Ideaya closed its series A, the PARP inhibitors Rubraca (rucaparib, Clovis) and Zejula (niraparib, Tesaro) have gained FDA approval while Lynparza continued to accrue label expansions. (See *BioWorld Today*, May 4, 2016, Dec. 20, 2016, and March 28, 2017.)

"Also, since we launched, there's been about $300 million in series A capital raised in the space," he added. "Clearly, there's a lot of enthusiasm."

Indeed, the SL approach has drawn several comers. Last year, Montreal-based Repare Therapeutics Inc. emerged with a $68 million series A and serious ambitions to become a leader in identifying small-molecule drugs that act on targets identified through CRISPR-based induction and screening of mutations that give rise to SL. Repare was jointly founded by Daniel Durocher and Frank Sicheri, both of the Lunenfeld-Tanenbaum Research Institute at Mount Sinai Hospital in Toronto, and Agnel Sfeir, of Skirball Institute of Biomolecular Medicine, NYU Langone Medical Center in New York. Founding investor Versant Ventures incubated the firm and helped conduct some of the early research. (See *BioWorld*, June 23, 2017.)

Ideaya also is using CRISPR, though Hata declined to divulge details.

"All I'll say is that it is differentiated and will give us a competitive edge in this space," he said.

Another organization with designs on SL is Cancer Research UK (CRUK), which this week signed a partnership agreement with Ideaya through its Commercial Partnerships Team and the Drug Discovery Unit at the Cancer Research UK Manchester Institute, part of the University of Manchester, U.K. The collaborators will work to develop small-molecule inhibitors of poly ADP-ribose glycohydrolase (PARG), a cellular enzyme that breaks down PAR through a post-translational modification that modulates protein function required for DNA repair. Inhibition of PARG in cancer cells with highly active PARP results in depletion of cellular nicotinamide adenine dinucleotide, or NAD, an essential co-factor in cellular respiration. Its depletion results in a decrease in cellular adenosine triphosphate, or ATP, and cancer cell death.

'Potential game-changer in breast cancer'

PARG is Ideaya's most advanced SL program, and CRUK "has been one of the key pioneers in the DNA damage repair field and was one of the early contributors to the PARP and BRCA story," Hata said. "The reason we're interested in this new target, PARG, is an emerging synthetic lethality story we believe we've identified with a key gene called XRCC1," which, he explained, emulates the SL relationship between PARP and BRCA. Research conducted in the U.K. and published in 2013 in *Cancer Research* suggested that XRCC1 deficiency in breast cancer results in an aggressive phenotype and that XRCC1 deficiency could be exploited for an SL application using double-strand break repair inhibitors. The researchers reported that, in breast cancer, loss of XRCC1 occurred in about 16 percent of patients – those with high grade, loss of hormone receptors, triple-negative and basal-like phenotypes. Loss of XRCC1 was associated with a twofold increase in risk of death and, independently, with poor outcome.

"If that biomarker is viable and we can deliver a development candidate against that target, this is a potential game-changer in breast cancer," Hata said.

Ideaya's lead immunotherapy program involves small-molecule antagonists of the aryl hydrocarbon receptor (AhR). Hata pointedly noted that company founders came from Flexus Biosciences Inc., which was advancing an indoleamine 2,3-dioxygenase 1 (IDO1)/tryptophan 2,3-dioxygenase (TDO) discovery program, including IDO-selective, IDO/TDO dual and TDO-selective compound libraries, when it was acquired in 2015 by New York-based Bristol-Myers Squibb Co. for up to $1.25 billion. (See *BioWorld Today*, Feb. 24, 2015.)

"One of the reasons people are excited about IDO is its impact on the kynurenine pathway," Hata explained. "We think AhR is

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Financings

Ablynx NV, of Ghent, Belgium, said an additional 179,781 common shares have been issued in exchange for €782,096.92 (US$965,326.59) as the result of the exercise of warrants.

Arcus Biosciences Inc., of Hayward, Calif., said it priced its IPO of 8 million shares at $15 per share, the high point of its pricing range, for gross proceeds of $120 million. An additional $18 million could be generated if the underwriters exercise their 30-day option in full to purchase an additional 1.2 million shares at the IPO price, less the underwriting discount. The company, which was founded in 2015, is working on building a portfolio of small-molecule and antibody product candidates, with an initial focus on the ATP-adenosine pathway, a key driver of immunosuppression in the tumor microenvironment. Its lead product candidate, AB-928, blocks the adenosine receptor in the tumor microenvironment and potently inhibits both the adenosine 2a receptor (A2aR) and the adenosine 2b receptor (A2bR). In addition, the company said in its S-1A filing, it has created a small-molecule inhibitor of CD73, AB-680. The company has also in-licensed two antibody drug candidates: AB-122, an anti-PD-1 antibody, and AB-154, an anti-TIGIT antibody. The company's shares began trading on the New York Stock Exchange on March 15 under the symbol RCUS and closed the first day at $17, up 13.3 percent. (See *BioWorld*, Aug. 18, 2017.)

La Jolla Pharmaceutical Co., of San Diego, said it priced its underwritten public offering of 3.4 million shares of common stock at $29.50 per share, resulting in gross proceeds of approximately $100.3 million. In addition, La Jolla has granted the underwriter an option to purchase up to an additional 510,000 shares. The company intends to use the proceeds for general corporate purposes, which include the continued commercialization of Giapreza (angiotensin II), funding its ongoing and future clinical trials of LJPC-401, and preclinical development work.

Supernus Pharmaceuticals Inc., of Rockville, Md., said it priced a private offering of $350 million aggregate principal amount of 0.625 percent convertible senior notes due 2023 to be sold to qualified institutional investors. It has also granted the initial purchasers of the notes a 30-day option to purchase up to an additional $52.5 million of notes. The company expects to use the net proceeds to acquire or invest in complementary businesses, companies, products and technologies and for working capital and other general corporate purposes.

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a better approach to modulate the kynurenine pathway" and, therefore, a better potential combination strategy with a PD-1 checkpoint inhibitor.

The third program, as-yet undisclosed, is moving into lead optimization and involves "a very compelling synthetic lethality biomarker story and has the potential to go after very significant tumor populations," he said.

Ideaya is looking to extend its SL reach with two additional programs in discovery and a third broad effort in SL target discovery.

With the B round, Ideaya expects to have sufficient capital to a readout in at least two clinical programs.

The company now is looking at partnering, "in a thoughtful manner," Hata said, to diversify its portfolio.

"The fact that we have three strategic investors – in Roche, Celgene and Novartis – is a pretty good reflection of the level of partnering interest in the company," he said. Although "we don't have a specific mandate for partnership at this time, we appreciate the importance of combinations."

In the meantime, the addition of Julie Hambleton, who was named this week as Ideaya's senior vice president and chief medical officer to head development efforts, signaled the next step in Ideaya's build-out. Hambleton, most recently vice president and head of U.S. medical at BMS, also served in key R&D posts at Five Prime Therapeutics Inc., Clovis and Roche Holding AG unit Genentech Inc. Ideaya's head count likely will grow to approximately 50 by year-end as Hambleton assembles a team, Hata predicted.

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> Yujiro S. Hata
> CEO, Ideaya Biosciences

In conjunction with the series B, Thilo Schroeder, Nextech partner, and Edward Hu, founding partner of 6 Dimensions, joined the company's board. Kanishka Pothula, managing director at BVF, Vineeta Agarwala, venture partner at GV, and Nisha Marathe, investment manager at Roche Venture Fund, joined as board observers. ♦