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2017 partnering analysis

Biopharmaceutical industry has strong appetite for deal making

By Peter Winter, BioWorld Insight Editor and Karen Carey, Analyst

Last year, there were 1,015 biopharmaceutical deals recorded by Cortellis Deals Intelligence, with projected values at signing of $80.89 billion. This total represented a slight 3 percent drop on the deal totals calculated in 2016, and a 24 percent decline over 2015, despite the fact that the deal volume was 24 percent and 12 percent higher than the 2016 and 2015 volumes, respectively. (See Biopharma Deals:

See Deals, page 3

Celgene scheme yet to be seen

Agios, amigo: Hello $475M as rumors swirl re partner's would-be takeover of Juno

By Randy Osborne, Staff Writer

While Agios Pharmaceuticals Inc. waits to hear from the FDA about its acute myeloid leukemia (AML) therapy's NDA, the company is mulling the prospect of an eventual label "in newly diagnosed patients unfit for any therapy," CEO David Schenkein said, and it's ambitions of that caliber that helped the company raise $475 million in a public offering set to close Tuesday.

In December, Cambridge, Mass.-based Agios submitted the NDA for oral ivosidenib to treat relapsed or refractory (r/r) acute AML and an isocitrate dehydrogenase-1 (IDH1) mutation, asking for priority review. Schenkein's remarks came during the recent meeting of the American Society of Hematology (ASH) in Atlanta, where he and other company officials outlined the latest outcomes with the IDH1 inhibitor. The NDA package included all results available so far, and broadening the

See Agios, page 6

Shutdown showdown revs up fed contingency planning

By Michael Fitzhugh, Staff Writer

With the prospect of a U.S. federal government shutdown appearing ever more likely Friday, the potential tolls that action might take on the FDA, NIH and other federal elements crucial to industry's forward momentum became clearer in some respects, but not others.

The U.S. Department of Health and Human Services rolled out a contingency plan that appeared drawn in large part from the last time it faced a potential government shutdown. That plan outlined expectations that the FDA would furlough 42 percent of its staff and

See Shutdown, page 7

Newco news

Aussie biotech Imugene leads pack in HER2-targeting B-cell immunotherapies

By Tamra Sami, Staff Writer

PERTH, Australia – Australia's Imugene Ltd. could be the first biotech out of the gate in developing B-cell peptide vaccines in the immune-oncology space.

"Although everyone else is doing a me-too attitude toward this platform, we are the forerunners in the B-cell space," CEO Leslie Chong told *BioWorld*. "I think we're light years ahead of everyone else."

Created in partnership with the Medical University

See Imugene, page 9

The BioWorld Biome

Less is more

SEEK, and ye shall find multiple types of cancer

By Anette Breindl, Senior Science Editor

By looking for a combination of DNA and protein biomarkers, a single experimental blood test could detect eight different cancers, and identify the anatomical location of the majority of tumors it detected.

The sensitivity of the test, which its creators have dubbed CancerSEEK, varied widely between tumor types. It was able to detect 98 percent of ovarian and liver tumors, but only 33 percent of breast cancers. And the test, which was developed using samples from diagnosed cancer patients, will need to be validated "in a more real-world setting, where we will be screening healthy individuals," Joshua Cohen told *BioWorld*.

But in principle, CancerSEEK offers a way to simultaneously screen for multiple early stage tumors.

Cohen is a student at Johns Hopkins University School of Medicine, and the first author of the paper describing the CancerSEEK test, which appeared in the Jan. 19, 2018, issue of *Science*.

See CancerSEEK, page 8

Bench Press

BioWorld Senior Science Editor Anette Breindl takes a closer look at translational medicine

Read this week's edition

Imugene

Continued from page 1

of Vienna, Austria, lead candidate B-cell peptide vaccine HER-Vaxx (IMU-131) stimulated a polyclonal antibody response to HER2, the same biomarker targeted by Herceptin (trastuzumab, Roche Holding AG). The vaccine was designed to treat tumors that overexpress HER2 such as gastric, breast, ovarian, lung and pancreatic cancers.

HER-Vaxx aims to combine the basic mechanism of action of Roche's Herceptin and Perjeta (pertuzumab) in one vaccine construct. The two drugs are used in combination because of their synergistic effect. Combined sales of the two drugs in 2015 were $8.2 billion.

But instead of infusing patients with antibodies synthesized in a factory, Imugene plans on inducing a patient's own B cells to make similar cancer-fighting antibodies using its mimotope technology.

> *"The idea of the B-cell vaccine is to combine two to three drugs in one peptide fusion vaccine.*
>
> Leslie Chong
> CEO, Imugene

Chong was previously senior clinical program leader for Genentech, and was familiar with the Herceptin technology. She left the San Francisco area and moved to Sydney in September 2015 to lead the fledgling company.

A leading European immunologist, Imugene's chief scientific officer, Ursula Wiedermann, is a founding inventor of the HER-Vaxx along with Christoph Zielinski, who is director of the Clinical Division of Oncology and chairman of the Department of Medicine at the Medical University of Vienna. Wiedermann said she and Zielinski identified peptides on the outer membrane of the HER2 molecule and developed the vaccine against the HER2 molecule.

"At the time, it was a different paradigm," she said, "and it still is really because most are going for the T-cell vaccine, not the B cell."

Chong said Wiedermann and Zielinski were the perfect partners in immune-oncology since Wiedermann is an immunologist and Zielinski an oncologist.

"The B cells are woken up toward the cancer target, and they've done an eloquent job of marrying that," Chong said.

Wiedermann and Zielinski met Axel Hoos, senior vice president and therapeutic area head, oncology R&D, at Glaxosmithkline plc, and he introduced them to Paul Hopper, who is now Imugene's executive chairman. Hopper has been involved in a number of biotech startups in Australia, including Prescient Therapeutics Ltd., Viralytics Ltd. and other ventures when he headed up the Australia Life Sciences Practice for the Cappello Group.

Best known for his clinical lead role in developing CTLA-4 checkpoint inhibitor Yervoy (ipilimumab, Bristol-Myers Squibb Co.) for melanoma, Hoos helped forge the partnership with the medical university, and the group founded Imugene. Hoos remains a nonexecutive director, and has permission from GSK to participate in the project.

Why a B-cell approach?

Imugene is developing a pipeline of mimotope-based B-cell peptide vaccines against novel oncology targets that could replace or be used in combination with monoclonal antibodies.

Until now, the B-cell approach has largely been ignored in immune-oncology, but Imugene said it could have certain advantages and work with the body's immune system to produce natural antibodies that are potentially safer.

Early studies suggest that B-cell epitopes have less restrictions than T-cell epitopes and have the potential to replace or augment monoclonal antibodies (MAbs). B-cell vaccines create a polyclonal antibody response, which could provide the same anticancer effects but at a much lower cost.

Peptide vaccines – consisting of one or more amino acid sequences representing tumor antigens – allow the immune response to focus on the relevant epitopes. Even so, a peptide vaccine has not yet been approved for human use.

Imugene's vaccine stimulated a potent polyclonal antibody response in an earlier phase I study in HER2-positive breast cancer, and the company is now recruiting for a phase Ib/phase II study in HER2-positive gastric cancer.

Conducted at the Medical University in Vienna, the phase I trials showed patients' immune systems created target-specific antibodies with antitumor activity, reduced Treg cells and induced cytokines. The primary endpoint in the phase I study was safety and immunogenicity.

Wiedermann said there were no side effects and the vaccine was well tolerated. "It showed that you could have antibodies and a cellular response at the same time to help boost the immune system."

Gastric cancer was chosen as the target population for the phase II trial, largely because the breast cancer space is crowded. Gastric cancer also is quite prevalent in Asia, and there are numerous countries in which Herceptin is approved but not reimbursed, so Imugene plans to run duel studies comparing the standard of care against HER-Vaxx.

Eight sites in Thailand, Taiwan and Hong Kong will enroll up to 18 patients in three cohorts with three different designs for the phase Ia trial. The phase II study will enroll up to 70 patients in combination with chemotherapy. Data are expected in the first half of 2018.

Zielinski said the group is developing a pipeline directed against PD-1 and PD-L1 and is working on combining the HER-Vaxx vaccine with one of those compounds.

"The idea of the B-cell vaccine is to combine two to three drugs in one peptide fusion vaccine," said Chong.

Imugene plans to conduct combination studies in breast cancer with HER-Vaxx and Herceptin. Other indications could include

See Imugene, page 10

Deals

Continued from page 5

for all immuno-oncology indications. It included $150 million up front and $750 million in milestones. A royalty rate rising in tiered amounts from 15 percent to 24 percent for a single early clinical-stage product sets this particular deal apart from other high-dollar valued deals.

Other hot areas

Neurology/psychiatric deals ranked second behind cancer with 100 signed (13 percent) and infection-related deals ranked third at 72 (about 10 percent).

An interesting deal in the neurology space saw South San Francisco-based Alector LLC partnering with North Chicago-based Abbvie Inc. to focus on the emerging field of immuno-neurology, involving $205 million in option rights to two candidates for Alzheimer's disease and other neurodegenerative disorders. Alector stimulates the innate immune system (as opposed to the adaptive immune system as typically done with immuno-oncology agents), targeting multiple pathologies, not just amyloid beta or tau.

By value, cancer still led with deals worth $28.6 billion followed by immune-focused deals worth $8.5 billion and gastrointestinal deals worth nearly $5 billion, ahead of both neurology/psychiatric ($4.8 billion) and infection ($4.7 billion). (See Value of Biopharma 2017 Deals by Therapeutic Focus, p. 5.)

A major deal in the infectious diseases space involved privately held Vir Biotechnology Inc. and Alnylam Pharmaceuticals Inc. It will focus on developing and commercializing RNAi therapeutics targeting chronic hepatitis B virus (HBV) infection and other infectious diseases. As part of the agreement, the companies plan to advance Alnylam's HBV program and initiate a research collaboration to develop and advance up to four additional RNAi therapeutic programs for undisclosed infectious disease targets.

Alnylam received an up-front payment, comprising cash and Vir's shares under the deal terms, and will be eligible for more than $1 billion in potential milestone payments. ♦

Imugene

Continued from page 9

bladder, ovarian and non-small-cell lung cancers.

Each individual mimotope has its own patent and IP around it. Down the road, the company envisions designing a vaccine or drug with a range of targets, Chong said.

Imugene listed on Australia's Securities Exchange (ASX:IMU) as Imugene in December 2013 via a reverse merger into a listed shell, Imugene Ltd. Hoos joined the board in 2014.

In November 2017, Imugene raised A$8.7 million (US$7 million) via a A$6.7 million institutional placement and A$2.03 million fully underwritten entitlement offer. The funds will allow the company to complete its phase Ib/phase II HER-Vaxx trial.

The company's market cap is A$52.1 million (US$39.8 million). ♦

In the clinic

Bavarian Nordic A/S, of Copenhagen, started a phase I trial testing MVA-BN Brachyury vaccine, followed by a Brachyury encoded fowlpox booster in up to 10 patients with metastatic or unresectable, locally advanced malignant solid tumors. The primary purpose of the study is to assess safety and tolerability, but the trial will also measure immunologic responses through changes in brachyury-specific T cells and other tumor-associated antigens, as well as evidence of clinical benefit through progression-free survival and objective response. The priming vaccine, MVA-BN Brachyury, was previously tested as a monotherapy in a phase I trial in 38 patients with chordoma or metastatic solid cancers, where it induced brachyury-specific T-cell immune responses in the vast majority of patients.

Merck & Co. Inc., of Kenilworth, N.J., reported results of the phase II KEYNOTE-224 trial testing its anti-PD-1 therapy Keytruda (pembrolizumab) in patients with advanced hepatocellular carcinoma who were previously treated with Nexavar (sorafenib, Bayer AG) at the ASCO Gastrointestinal Cancers Symposium in San Francisco. Keytruda produced an overall response rate of 16.3 percent with a disease control rate of 61.5 percent in 104 evaluable patients. The median progression-free survival (PFS) was 4.8 months with a six-month PFS rate of 43.1 percent. While the median overall survival (OS) hadn't been reached yet, the six-month OS rate was 77.9 percent.

Nucana plc, of Edinburgh, U.K., reported interim results from the ABC-08 study at the ASCO Gastrointestinal Cancer Symposium in San Francisco, with the analysis of the phase Ib study showing that Acelarin, its nucleotide analogue, when combined with cisplatin, achieved high response rates and was well-tolerated in front-line advanced biliary tract cancer. Eight patients were treated. A complete radiological response was achieved in one patient, a partial response was achieved in three patients and one patient achieved stable disease, for an objective response rate (ORR) of 50 percent and a disease control rate of 63 percent on an intent-to-treat basis. One patient with stable disease, whose cancer initially had been considered unsuitable for surgical resection, went on to have surgery to remove the tumor completely. Two of the eight patients received only one cycle or less of therapy due to complications unrelated to either Acelarin or cisplatin, so the ORR in those patients who received adequate treatment was 67 percent. Shares of Nucana (NASDAQA:NCNA) gained $6.02, or 41.6 percent, to close Friday at $20.51.

Regulatory front

Pfizer Canada, a unit of New York-based **Pfizer Inc.**, advised Health Canada that there is a shortage of Epipen auto-injectors in the 0.3-mg format, reported due to a manufacturing disruption currently anticipated to be resolved by March 2. According to Pfizer, the shortage does not impact Epipen Jr (0.15 mg) products, which remain available. Epipen is used to deliver an emergency treatment of adrenaline (epinephrine) to patients who are at risk or have a history of life-threatening allergic reactions. There are currently no alternative auto-injectors available on the market in Canada.