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DRINKING IN PROFITABILITY WITH MULTIPLE AAT BIDS ON TAP

Glassia (more than) half full: Kamada 'pour' no more, to quench market thirst in GVHD?

By Randy Osborne, Staff Writer

"There are many forms of graft vs. host disease [GVHD], many types, so there will not be one solution for all of them," Gil Efron, deputy CEO and chief financial officer of Kamada Ltd., told *BioWorld Today*, but the Ness Ziona, Israel-based firm may have a fix for major unmet need.

The orphan indication-geared company expects to reach profitability this year. Having proven the anti-inflammatory value of its alpha-1 antitrypsin (AAT, purified from human plasma) by way of the marketed product Glassia for AAT-deficient patients

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HIGH FIVE

Targeting innate immune system shrinks pediatric brain tumors

By Anette Breindl, Senior Science Editor

In preclinical experiments, treatment with the experimental antibody Hu5F9-G4 (Forty Seven Inc.), which is designed to block inhibitory interactions between tumor cells and macrophages, shrank several different types of pediatric brain tumors. The study findings,

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BIOASIA 2017

Japan's drug price reforms spark opposing views

By Kohei Kanayasu, Staff Writer

TOKYO – Though Japan's drug sector will maintain a pro-innovation policy with the aim to maximize patient value, discussions between the country's Ministry of Health, Labour and Welfare (MHLW) and the Pharmaceutical Research and Manufacturers of America

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FINANCING

Egenesis' $38M series A to fund early stage work in xenotransplantation

By Jennifer Boggs, Managing Editor

Egenesis Inc., a 2015 startup that has helped put xenotransplantation back on the table as a potentially viable option for organ transplant thanks to its founders' work using CRISPR gene editing technology, closed its first substantial financing, a $38 million series A expected to take development efforts through preclinical proof of concept.

It's a large raise given the early stage nature of Egenesis' work to date. Backers include Biomatics Capital and Arch Ventures Partners, which led the round, with participation from Khosla Ventures, Alta Partners, Alexandria Equities, Heritage Provider Network, Berggruen Holdings North America Ltd., Uprising and Fan Ventures.

"The venture partners put a lot of trust and faith in the team and the

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NEWCO NEWS

After development lull, Briacell presses forward with cancer vaccine

By Marie Powers, News Editor

Briacell Therapeutics Corp. hasn't exactly advanced its only asset, Briavax, with lightning speed. Instead, the cancer vaccine sat on the shelf for much of a decade while its inventor, Charles Wiseman, an oncologist affiliated with St. Vincent Medical Center in Los Angeles, tried to scrape together funding.

Now, following two phase I studies, the FDA cleared the company to begin an open-label phase I/IIa trial of Briavax in patients with advanced breast cancer. The genetically engineered whole-cell vaccine is derived from a human breast tumor cell line. The open-label trial, also designed to help establish the company's companion diagnostic, Briadx, is expected to enroll up to 24 late-stage breast cancer patients with recurrent and/or metastatic disease who will receive Briavax every two weeks for a

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IN THIS ISSUE

OTHER NEWS TO NOTE

Aeolus Pharmaceuticals, Inc., of Mission Viejo, Calif., said a study completed at National Jewish Health showed that AEOL 20415 protects the lungs in a mouse model of cystic fibrosis. The compound has demonstrated potential as both a treatment for cystic fibrosis as well as antibiotic-resistant bacteria. The company's execs believe that AEOL 20415 may have applications as a broad spectrum anti-microbial and in several large medical indications.

DSM Sinochem Pharmaceuticals, of Singapore, executed a definitive agreement providing **Sandoz**, a unit of **Novartis AG**, of Basel, Switzerland, with a nonexclusive global license to certain for the development and commercialization of beta lactam antibiotics. Financial terms were not disclosed.

Endo International plc, of Dublin, responded to the recommendation by the FDA's Drug Safety Risk Management and Anesthetic and Analgesic Drug Products Advisory Committees (adcom), which voted 18-8, with one abstention, that the risks of reformulated Opana ER (oxymorphone hydrochloride extended release) outweighed the benefits of continued use. While several adcom members acknowledged that Opana ER played a role in clinical practice, most suggested its benefits are now overshadowed by public health concerns around the product's misuse, abuse and diversion. During committee discussions following the vote, some panelists suggested the drug remain on the market with additional regulatory restrictions to mitigate risks. The FDA is not bound by the recommendation of the committees. Endo expressed confidence in the body of evidence supporting a favorable risk-benefit profile for the drug, maintaining that Opana ER remains an important choice for appropriate patients and said it will work with the FDA to evaluate the range of available options for maintaining access to the drug. The opioid agonist is approved to manage pain severe enough to require daily, around-the-clock opioid treatment when alternative treatment options are inadequate.

Ferring Pharmaceuticals SA, of Saint-Prex, Switzerland, and Brazil's Instituto de Ciências Farmacêuticas agreed to collaborate on research to develop a mucoadhesive rectal delivery system to treat anal fissures and to improve quality of care for patients with inflammatory bowel disease. Financial terms were not disclosed.

The public-private Dementia Consortium awarded £191,757 (US$205,041) to support a project led by researchers at the University of Manchester to develop therapeutics for Alzheimer's disease (AD) by targeting the immune system. The university team will work in collaboration with drug development experts at MRC Technology's Centre for Therapeutics Discovery to alter inflammatory processes in the effort to reduce the spread of nerve cell damage in AD. The project will seek to develop compounds that target a particular component of inflammasomes called NLRP3, thought to be a primary contributor to the nerve cell damage seen in AD.

Glaxosmithkline plc, of London, said it submitted a supplemental BLA to the FDA for Fluarix quadrivalent influenza vaccine, currently approved for active immunization against influenza A subtype viruses and type B viruses, in persons 3 and older. The submission seeks an expanded indication for children 6 months through 35 months of age.

Glycyx Pharmaventures Ltd., of Douglas, Isle of Man, a biopharma investment and development company, agreed to enter an exclusive license deal with **Valeant Pharmaceuticals International Inc.**, of Laval, Quebec, in which Valeant will grant Glycyx a license or sublicense to develop and commercialize products containing methylnaltrexone bromide for oncology indications in countries outside the U.S. and Canada, with the right to extend the license to the U.S. and Canada if Valeant elects not to exploit the product in such countries. Glycyx would pay sales-based milestones and royalties to Valeant. The arrangement is subject to the negotiation by the parties of a mutually satisfactory license agreement. Specific terms were not disclosed. Valeant currently commercializes methylnaltrexone bromide, known as Relistor, for the treatment of opioid induced constipation in adults with chronic noncancer pain.

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Kamada

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with emphysema, Kamada has begun testing intravenous (I.V.) AAT as an immunomodulator. The compound, partnered with Shire plc, of Dublin, probably has "many therapeutic roles," Efron said. A phase II/III trial is underway in the U.S. in patients with the product called G1-AAT for acute GVHD, which can manifest in the gastrointestinal (GI) system, the liver, or on the skin, and can even affect the lungs. "The most severe patients are those with the gut symptoms, so we are treating GI patients," he said.

A graft-vs.-host reaction refers to the over-activation of a patients' new, modified immune system after an allogeneic hematopoietic stem cell transplantation (HSCT), a procedure that uses the donor's immune system to fight diseases such as acute myeloid leukemia, acute lymphoblastic leukemia and myelodysplastic syndrome. The study with G1-AAT is estimated to enroll as many as 168 adult subjects who've received an HSCT, with the mandating disease in remission at the time and with newly diagnosed, acute GVHD evident, including lower GI involvement; other organ systems may be affected or not. Treatment with methylprednisolone/systemic steroids must have been started within 72 hours prior to the first dose of study treatment after enrollment, the protocol says.

AAT is "naturally occurring in humans so we're using something that should have a very good safety profile" and it does, Efron said. Research began with GVHD patients who were refractory to high-dose steroids, the standard of care (SOC). "Usually these patients are grade 3 and grade 4 of the disease," he said, the worst grades. "We had a proof-of-concept study on these patients, and out of 12 patients in the first two cohorts, eight responded to the treatment – four had partial response and four had complete response." For the phase II/III experiment, Kamada and Shire chose to "engage earlier in the treatment of the disease," so the experiment is "not only in steroid-refractory. It's all patients who have GVHD," with G1-AAT given along with SOC. "It's really a question of how the development will [proceed], but right now we are treating on top of standard of care," he said. Data are due around 2020. "We'll probably have interim data earlier, after we complete the first part of the study," he said. "We expect that toward the end of this year or maybe the beginning of next year."

Shire owns rights to the product in the U.S., Canada, Australia and New Zealand. "We're planning to develop [the compound in] GVHD independently in Europe," Efron said, and the company will ask for a clinical trial authorization, or CTA, there in the second half of the year in order to conduct its own phase II/III experiment. "We had scientific advice from the EMA," he said, as well as "positive feedback."

Phase II/III work also is ongoing with G1-AAT in type 1 diabetes, and results are expected in the first half of this year. A phase II study investigating the compound in the prevention of lung-

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Tumors

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reported in the March 15, 2017, issue of *Science Translational Medicine*, mark the first time that the innate immune system has been targeted in pediatric brain tumors.

The team tested the antibody in models of "five very distinct types of highly malignant brain tumors, which essentially have no standard of care yet," co-corresponding author Siddhartha Mitra told *BioWorld Today*.

In patient-derived xenograft models, treatment with Hu5F9-G4 inhibited the growth of group 3 medulloblastoma, atypical teratoid rhabdoid tumor, primitive neuroectodermal tumor, pediatric glioblastoma and diffuse intrinsic pontine glioma. It was also effective against metastatic medulloblastoma that had spread within the brain.

Pediatric brain tumors, collectively, are challenging to treat. Radiation can be a treatment, but mostly, "there's nothing defined," said Mitra, who is a senior scientist at the Stanford Institute for Stem Cell Biology and Regenerative Medicine.

Like adult brain tumors, their location next to or intertwined with brain structures that are critical for survival often makes them inoperable.

An additional challenge, co-corresponding author Samuel Cheshier told *BioWorld Today*, is that pediatric tumors "seem to have much less mutational burden than adult tumors," whose cells have had a much longer time to accumulate the mutational burden that is an inevitable part of aging. "That limits your ability to do targeted therapies against tumor antigens."

Cheshier is assistant professor of neurosurgery at the Stanford University School of Medicine.

T-cell directed immunotherapy in the form of checkpoint blockade, too, is challenging in brain tumors and more challenging in pediatric brain tumors.

"It's quite a challenge to do immune therapy in the brain, and some of the current immune therapies are running into problems with swelling," Cheshier said. When T cells attack and kill tumor cells, those cells lyse, or burst open, releasing their contents. "That further spurs the immune system," Cheshier said, "but it also causes a very profound inflammatory reaction." One of the byproducts of that inflammatory reaction is swelling, and because brain tumors are confined by the skull, such swelling becomes a problem very quickly, as pressure compromises brain function.

When pediatric brain tumors are treated with checkpoint blockers, though, there is less swelling because there is less of an effect in the first place. T cells are part of the adaptive immune system, which matures relatively late in development.

The antibody tested by the Stanford team targets CD47, a surface protein that is expressed on many different tumor types and interacts with SIRP-alpha. SIRP-alpha is an inhibitors signal on macrophages, innate immune system cells that are a bit like the boa constrictors of the immune system: they swallow their prey whole.

As a result, when the CD47-SIRP-alpha axis is disrupted, "the tumor cells aren't dumping their contents out into the environment, which could cause a very severe [inflammatory] reaction," Cheshier said.

And "because the innate immune system develops much earlier in life, it's actually fairly mature" and better able to respond to disinhibition than T cells, Mitra added.

A January report by the cancer biology reproducibility project that attempted to reproduce an earlier experiment in which disrupting the interaction between CD47 and SIRP-alpha shrank breast tumors in mice was unsuccessful. Mitra, who was a co-author on the original paper, and Cheshier, though, were unconcerned.

Mitra noted that due to resource constraints, the authors attempted to reproduce only one experiment that was part of a much larger five-year study, and that the reviewers of the replication attempt "very clearly" stated in their comments that "the original study was not . . . ambivalent, but the reproducibility study was."

And while there are always multiple reasons for why replication attempts might go awry, Cheshier noted that one distinct possibility is that the replication attempt was done with a mouse version of Hu5F9-G4. "It's essentially a different drug," he said.

Hu5F9-G4 is in multiple phase I trials for both solid and hematological tumors. "We are awaiting the results of the phase I trial," Cheshier said. "Once the phase I trial is done, we plan to lobby the company which has rights to the antibody, Forty Seven Inc., to pursue a trial in pediatric brain tumors."

Stanford University and its Lucile Packard Children's Hospital are part of the Pediatric Brain Tumor Consortium, a cooperative research organization "devoted to the study of correlative tumor biology and new therapies for primary [Central Nervous System] tumors of childhood," according to its web site. The Pediatric Brain Tumor Consortium has "very efficient mechanism to make [trials] happen," Cheshier said. But "that will only happen if the company wants to move in that direction." **//**

Japan

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(PHRMA) showed stark differences in opinions.

Yasuhiro Suzuki, director general at the Health Insurance Bureau and chief global health officer at the MHLW, and Amy Jackson, Japan representative at PHRMA, both spoke during BioAsia International here as part of a session aptly titled "Addressing Shifts in Japanese Reimbursement Policy."

"We are going to be discussing and deciding on the actual reform direction toward the end of this year, but currently we are employing a couple of principle provisions," said Suzuki. "First, I think we have to strike the best balance between innovation and financial sustainability of health insurance in this country. Second, we need transparency and predictability in the pricing policy. Third, we need to maximize patient value and ensure the quality of health care. Fourth, we have to have a pricing system that supports an expedited approval process for pharmaceuticals. Finally, we have to employ the cost-effectiveness analysis to introduce and enforce such pricing revision."

Suzuki added that the MHLW would hold discussions with industry professionals, patient associations and medical associations, with the aim to resolve some issues by the end of summer 2018.

PHRMA, however, has been critical of changes in pricing policy and published a joint statement together with six other organizations in December to oppose it. The issue came to the forefront at the end of last year when regulators in Japan cut the reimbursement price for anticancer drug Opdivo (nivolumab) by as much as 50 percent. In Japan, Opdivo is distributed by Ono Pharmaceutical Ltd. (See *BioWorld Today*, Dec. 7, 2016.)

The cuts last year were not done as part of the biannual price revisions.

"For repricing of new indications, I think there is a strong agreement among all stakeholders in this system that this is something that needs to be addressed. It is a flaw in the current Japanese system, and Opdivo unfortunately highlighted that flaw. It is something we all believe needs to be corrected," said Jackson.

"In terms of the annual price survey, we would be very concerned if Japan were to implement full-scale annual price cuts on all drugs including innovative new drugs. If there is an overhaul of this system and it is severely curtailed or even completely rescinded or overturned, this will be a significant concern and a really anti-innovative measure that could discourage further innovation in this market and turn around some of the progress that Japan has made," she added.

During the discussion, when asked about opportunities for stakeholders to provide their input, Suzuki answered that aside from unofficial communication, the MHLW is providing opportunities for the industry to join discussions with the Central Social Insurance Medical Council (Chuikyo) to have their input considered as much as possible. For the annual price review, most stakeholders are going to be concerned with generics, since brand names would not have discounts.

Jackson said that when the reform process kicked off in November, it took the government four weeks to set its parameters despite the magnitude of the effort, and that they did not want to have conversations with relevant stakeholders, including industry as well as patient groups and pharmaceutical wholesalers. She added that any country seeking such changes should employ a strict and transparent process to get the best outcome and avoid unintended consequences.

Despite the fact that the MHLW told *BioWorld Today* that the emergency price review of Opdivo was "an exceptional case," the discussion to change price revisions away from a biennial basis has been ongoing. On Dec. 20, Chuikyo published a policy paper proposing ideas to annually review and reprice drugs with considerable price differences on the market, while maintaining the major review at the biennial level, quarterly review of drugs with new indications, and fundamental review of premium prices for innovative drugs.

The policy paper further emphasized the need to address the accuracy and transparency of drug price calculation, its influence on business stakeholders, and improvement of logistics. This leaves little room for agreement between the government and the industry, industry analysts have said. //

REGULATORY FRONT

U.S. lawmakers are once again pressing the **FDA** for answers about the adulterated heparin sourced from China in 2007-2008 that caused 149 deaths worldwide, including more than 80 in the U.S. Wednesday, Republican leadership of the House Energy and Commerce Committee and two of its subcommittees wrote to Stephen Ostroff, FDA acting commissioner, requesting all documents related to the agency's two criminal investigations into the matter. The FDA has consistently rejected the committee's past efforts to get the documents, claiming the matter was still under investigation. But last month, the committee was informed that the agency had closed its final investigation in November, according to the letter. Meanwhile, the committee is continuing its investigation into the incident as part of its efforts to help improve the FDA's strategy to combat economically motivated adulteration of medical and food products imported to the U.S. In the past, Congress has been critical of how the FDA responded to the contamination, noting that no enforcement action had been taken against at least two companies allegedly involved in the adulteration. (See *BioWorld Today*, Oct. 31, 2011, and Nov. 30, 2016.)

Egenesis

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technology," said Luhan Yang, co-founder and chief scientific officer.

The team boasts an impressive pedigree. Yang co-authored, along with famed geneticist – and Egenesis co-founder – George Church, one of the seminal papers published in *Science* in early 2013 detailing work using CRISPRs, or clustered regularly interspaced short palindromic repeats, to precisely edit mammalian cells. (See *BioWorld Today*, Jan. 4, 2013.)

Other members of the founding team include managing director Geoff Mackay, who previously helmed cell therapy firm Organogenesis Inc., and Harvard Medical School's Marc Güell, who invented the CRISPR-GA software for large-scale gene editing assessment.

"Right now we have a team of eight people at Cambridge, working to deliver human transplantable organs from genetically engineered pigs," Yang said.

The need is enormous. According to the FDA, 10 patients currently die every day in the U.S. while on the waiting list for organ transplant. In end-stage renal disease, for example, patient estimates are about 650,000 in the U.S.; yet, only about 100,000 are put on the list.

"But because of the limited supply, it's highly selective," Yang said. "Only about 20 to 30 percent" of people on the list end up receiving a transplant. "So human life is at stake."

And in Asia, where the culture does not encourage organ donation, the need is even greater. "In China, for example, there are 3 million people waiting but only a couple thousand donations per year," Yang said.

The Egenesis team is "really motivated . . . to create a world where there is no shortage of organs" for transplant, she told *BioWorld Today*.

Xenotransplantation – the process of transplanting organs or tissues across species, pigs to humans, for example – emerged as a potential method of dealing with the organ shortage. And work conducted during the 1990s generated interest but not success. "The technical hurdles were insurmountable," Yang said. "People were under the assumption that knocking out the antigen with an immunosuppressant" would be sufficient to prevent organ rejection, "but they underestimated how many modifications they would have to do, and there was no tool for doing them."

There was another problem. Given that pig organs are roughly the same at human organs in terms of size and physiology, they became the obvious alternative for human organ transplants. But pig DNA contains PERVs, or porcine endogenous retroviruses. "Once you co-culture the pig cell with the human cell, the virus will jump from pig genome to human genome," Yang explained.

In vitro evidence of that transmission prompted the FDA in 1997 to place a clinical hold on xenotransplantation, while subsequent efforts launched to find ways to monitor PERV transmission or block the viruses' ability to replicate. (See *BioWorld Today*, Jan. 23, 1998.)

But it was the advent of CRISPR that has proved a potential game-changer for xenotransplantation.

"The beauty of CRISPR is its ability to hit multiple parts in the genome at the same time," Yang said.

In an October 2015 issue of *Science*, Church, Yang and the team at the Wyss Institute for Biologically Inspired Engineering at Harvard Medical School, described using the CRISPR/Cas9 tool to make 62 simultaneous edits to the pig DNA, aimed at inactivating all the PERVs found in the pig genome.

"That broke the record of the number of modifications you can do in a mammalian system," Yang said. "We had a parallel program in the meantime, [in which] we were trying to do dozens of modifications to address the immunology issue." That work included modifying antigens known to trigger a human immune response.

Modifications to both PERVs and antigens are needed for eventual transplant into humans.

GETTING TO PROOF OF CONCEPT

For Cambridge, Mass.-based Egenesis, human testing is still a ways down the road. With the recently closed series A, the firm will start with genomic engineering of pig cells and will clone a pig to use a bioreactor for organ maturation.

"We've entered the pig production phase now," Yang said, with the goal of "trying to produce pig 2.0 by the end of this year." After that comes preclinical proof-of-concept testing, in which it will test transplantation in a human immune system to evaluate compatibility and ensure there is no virus transmission.

The $38 million should carry the firm through "demonstration of proof of concept at the preclinical level," Yang said.

Concurrent with the financing, Egenesis added members to its board, including Boris Nikolic, whose firm, Biomatics Capital, announced the close of its initiatory fund Wednesday, bringing in $200 million, ahead of its $150 million target. Biomatics will dedicate the fund to genomics, digital health and data-driven health care technologies and anticipates investing in 15 to 20 companies with the latest fund, acting as series A lead investors in a majority of the deals. Biomatics said initial investments typically range from $5 million to $10 million, with up to $20 million over the life of the investment.

Other additions to Egenesis' board include Steven Gillis, of Arch Ventures, and Daniel Lynch, who is taking on the role of executive chairman. Lynch previously served as CEO of Imclone Systems Inc. and as executive chairman of Avila Therapeutics Inc. and Stromedix Inc.

Close of the financing fell roughly a month after the U.S. Patent and Trademark Office issued a decision of "no interference-in-fact" in CRISPR/Cas9 interference motion phase, a judgment

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Briacell

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month, then monthly for up to one year.

Safety data from the first nine patients are expected by year-end.

Although the trial is designed primarily to evaluate safety, a principal secondary objective is to evaluate tumor size reduction. Briacell, based in Vancouver, British Columbia, with R&D in Berkeley, Calif., also will monitor tumor response and evaluate progression-free survival and overall survival.

Findings, if positive, could "give new life to the field of whole-cell cancer vaccines," observed Bill Williams, who joined Briacell last year as president and CEO.

Williams explained that Wiseman, who co-founded Briacell and remains on its board of directors, experimented with a number of cancer vaccines while a researcher and clinician at St. Vincent and, before that, at the University of Texas MD Anderson Cancer Center. Wiseman's approach was to isolate a tumor from a patient, growing out a cell line and then using the irradiated cell line to vaccinate other patients with similar cancers.

When an initial treatment regimen in 14 patients using a breast cancer cell line named SV-BR-1 didn't yield any responders, Wiseman took the cell line and transfected in the gene encoding Granulocyte-macrophage colony-stimulating factor (GM-CSF), using the so-called Gvax strategy. He then treated three additional breast cancer patients and one with ovarian cancer, with the thought that the two cancers sometimes shared antigens. Median survival for the four patients was nearly three years.

One metastatic breast cancer patient had a particularly "remarkable" response, Williams said, resulting in shrinkage of the primary tumor and metastatic sites following three months of treatment. Although the patient was in nearly complete remission, the protocol at the time only allowed for six treatments over approximately five months. When she came off therapy, the cancer recurred, including new metastases in the brain.

Wiseman then received permission to repeat the treatment, administering 10 doses across a schedule of alternating weeks. Initially, the patient again enjoyed another nearly complete remission until the cancer recurred and she came off the study.

Still, to have a patient respond twice to the cancer vaccine "was very intriguing," Williams told *BioWorld Today*.

'SCIENTIFICALLY, WE KNOW WHERE WE WANT TO GO'

When Wiseman couldn't get additional funding through academic channels, he placed the asset and its intellectual property into Briacell. Development remained nearly at a standstill until 2014, when Wiseman connected with Saeid Babaei, a serial entrepreneur and current co-founder, president and CEO of Abcelex Technologies, a vaccine development firm. Babaei, who chairs Briacell's board of directors, engineered Briacell's reverse merger with a Canadian mining shell that resulted in a listing on the Toronto Stock Exchange's Venture Exchange, a concurrent financing with Ansell Capital Corp. and a brokered private placement with Sunel Securities Inc. and M Partners Inc. for gross proceeds of approximately C$2.2 million (US$1.93 million).

"Since that time, [Wiseman] has been busily trying to get this back into the clinic," Williams said.

In the meantime, Briacell hired Markus Lacher as senior director of R&D. Lacher previously served as senior clinical scientist of R&D at Cesca Therapeutics Inc., an autologous cell therapy company where he helped oversee the bone marrow transplantation program, and scientist at Biotime Inc. and subsidiary, Oncocyte Corp., where he developed key components of the company's therapeutic and diagnostic technology.

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Kamada

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transplant rejection. Kamada and Shire hope the treatment can do the job across the board. For type 1 diabetes, the benefit could be in G1-AAT's "ability to halt the progression of the autoimmune attack on the beta cells," Efron said. "In GVHD, it's [the capacity] to have an impact on the immune system of the graft that attacks the host following the bone-marrow transplant." In preventing lung-transplant rejection, "the idea is similar to GVHD. In GVHD, it's the graft immune system that attacks the host. In lung transplant, it's the host that attacks the new solid organ. We're trying to reduce the level of rejection." Lung transplant represents a strong market because about "33 percent of lung transplants do not survive after one year, and 50 percent after five years," he said. "We started the clinical study in a very large lung-transplantation center in Israel last year. It should take us a few years to complete, because the treatment period is about two years," so the readout will likely come in late 2019.

'TRANSFORMATIVE' YEAR: ANALYST

There's also an inhaled version of AAT for people who are deficient in the protein. A would-be pivotal phase II/III clinical trial was completed in Europe and Canada. Though the primary endpoint of the study (time to first exacerbation) was not met, updated results showed clinically and statistically significant improvements in lung function and complementary efficacy in the severity of the first exacerbation, Kamada said, with safety data remaining supportive and consistent with the firm's previous inhaled AAT studies. Better news came in August, when a phase II trial in the U.S. with the inhaled version using the Eflow device from Pari Gmbh, of Starnberg, Germany, hit its endpoint. The product, tested at two dose levels (80 mg/day or 160 mg/day) vs. placebo, turned up a significant increase in endothelial lining fluid (ELF) AAT antigenic level compared to the placebo group [median increase 4551 nM, p-value<0.0005 (80 mg/day, n=12), and 13454 nM, p-value<0.002 (160mg/day, n=12)]. These results are more than twice the increase of ELF antigenic AAT level (+2600 nM) that appeared in Kamada's I.V. AAT pivotal study (60mg/kg/week). Antigenic AAT represents the total amount of AAT in the lung, both active and inactive. The company submitted a marketing authorization application to the EMA, and gatekeepers are due to decide around mid-year. In the second half of this year, an IND for the inhaled version will go to regulators in the U.S., where Kamada's recently completed "day 120" responses to European regulators will help steer talks with the FDA. (See *BioWorld Today*, May 19, 2014.)

Kamada recorded positive cash flow last year, when (in October) the company extended the contract with Shire for manufacturing Glassia supply for the fourth time since the deal was signed in 2010. Minimum revenue for Glassia in the lengthened pact for the years 2017 to 2020 will reach about $237 million during the period and may be expanded to $288 million. Kamada will now continue to produce Glassia through 2020 for Shire, after which Shire may produce the product at its facility and pay Kamada established royalty rates. "We are already generating a significant amount of revenue," Efron said, and the company is on track to record $100 million in sales this year. "We are in a good position to execute [our] plans," he said. (See *BioWorld Today*, Aug. 25, 2010.)

Jefferies analyst Raj Denhoy said the $100 million Glassia sales mark "looks achievable," as does profitability. Fourth-quarter 2016 sales landed "directly in line with the $24.3 million we modeled," he added in a research report in February, predicting this year could be "transformative from a regulatory standpoint" for Kamada. "Shire's $237 million in guaranteed U.S. revenue provides a solid base to the story with the only question lingering of if and when Shire will bring manufacturing capabilities in-house," he said. H.C. Wainwright analyst Andrew Fein was optimistic, too. "This steady uptrend of Glassia revenue should provide investors a relatively de-risked entry point with eyes towards the numerous pipeline programs with catalysts on tap for the year," he said in a Feb. 7 research report.

Earlier this month, Lifesci Capital analysts attended a key opinion leader event focused on GVHD, which featured talks by Joachim Deeg of the Fred Hutchinson Cancer Research Center and David Gelmont, who recently served as senior medical director at Shire and acts as clinical advisor for Kamada's GVHD program. Deeg pointed out that about half of patients who undergo HSCT will develop acute GVHD and need treatment, and about 70 percent of these will respond to high-dose steroids. "This leaves approximately 15 percent of the patients undergoing allogenic HSCT with persistent GVHD, and Deeg noted that there is no standard treatment for second-line therapy," Lifesci analyst Jerry Isaacson wrote. "About 13,100 individuals worldwide develop acute GVHD and will require therapy with steroids. We note that this is the population being targeted in Kamada's phase II/III studies with G1-AAT. The company has also mentioned the potential of G1-AAT as a prophylactic therapy, which could expand the market opportunity to include a greater number of allogenic HSCT procedures."

Also in the GVHD game with AAT is Melbourne, Australia-based CSL Ltd. unit CSL Behring. A pilot phase II study sponsored by the University of Michigan Cancer Center with CSL collaborating, along with The Leukemia and Lymphoma Society, is testing Zemaira – approved by the FDA in 2003 for AAT-deficient people with emphysema – in steroid-refractory GVHD. The trial is expected to enroll about 40 patients and end in June 2019. **//**

OTHER NEWS TO NOTE

Immunocellular Therapeutics Ltd., of Los Angeles, said, as disclosed on its annual report on form 10-K for the year ending Dec. 31, 2016, the audited financial statements contained an audit opinion from its independent registered public accounting firm that included a going concern emphasis of matter paragraph. Immunocellular, which is developing dendritic cell-based immunotherapy ICT-107, in a phase III study in glioblastoma, previously reported cash and equivalents totaling $11.4 million as of Dec. 31.

Merck & Co. Inc., of Kenilworth, N.J., said the FDA approved PD-1 inhibitor Keytruda (pembrolizumab) for the treatment of adult and pediatric patients with refractory classical Hodgkin lymphoma, or who have relapsed after three or more prior lines of therapy. Under the FDA's accelerated approval regulations, that indication is approved based on tumor response rate and durability of response. Continued approval may be contingent upon verification and description of clinical benefit in the confirmatory trials. In separate news, Merck said the FDA extended the action date for the supplemental BLA for Keytruda in previously treated patients with advanced microsatellite instability-high cancer. The company recently submitted additional data and analyses to the FDA related to the pending application. The new PDUFA date is June 9, 2017.

Ocular Therapeutix Inc., of Bedford, Mass., reported results of a patient experience study of Dextenza (dexamethasone insert) 0.4 mg for intracanalicular use, published in Patient Preference and Adherence. The retrospective trial was conducted with 25 patients who received Dextenza for the treatment of post-surgical ocular pain and inflammation in the phase III studies. Results showed all patients reported that the intracanalicular insert was comfortable, and 96 percent felt the insert was extremely or very convenient vs. topical eye drops on a tapered schedule. Ninety-two percent reported the highest level of overall product satisfaction, with 88 percent saying they would request the insert if they were to undergo cataract surgery again. An NDA for Dextenza is under FDA review, with a PDUFA date of July 19, 2017.

Synthon Biopharmaceuticals BV, of Nijmegen, the Netherlands, reported that the Patent Trial and Appeal Board of the U.S. Patent and Trademark Office (USPTO) denied institution of Menlo Park, Calif.-based **Forty Seven Inc.**'s petitions for inter partes review of the U.S. 9,352,037 patent which was issued in May 2016. The board determined that Forty Seven has not shown a reasonable likelihood that it would prevail in establishing the unpatentability of claim one or claim two of the patent. Forty Seven has submitted requests for the rehearing of the USPTO decisions. The patent, exclusively licensed to Synthon, relate to the use of antibodies that block the CD47-SIRpalpha interaction in combination with therapeutic antibodies for treating cancer. //

Egenesis

Continued from page 6

that favored the Broad Institute at the Massachusetts Institute of Technology, which is aligned with Editas Medicine Inc., of Cambridge, Mass. – Church is listed as one of the founders of Editas over in the IP battle with the University of California at Berkeley. (See *BioWorld Today*, Feb. 16, 2017.)

Egenesis' news is only the latest in a string of CRISPR-based transactions. On Tuesday, Editas disclosed a research alliance with Allergan plc including its lead drug, LCA10, for Leber congenital amaurosis type 10, a genetic form of progressive blindness. Crispr Therapeutics AG, meanwhile, inked a deal through its Bayer-partnered joint venture, Casebia Therapeutics, gaining nonexclusive commercial-use rights to Maxcyte Inc.'s cell engineering platform to develop CRISPR/Cas9-based therapies for hemoglobin-related diseases and severe combined immunodeficiency. (See *BioWorld Today*, March 15, 2017.) //

REGULATORY FRONT

Companies marketing prescription drugs in Canada must now report shortages, anticipated shortages and planned discontinuations on DrugshortagesCanada.ca. Reporting had been voluntary, but under new **Health Canada** regulations that went into effect Tuesday, reporting is now mandatory for many types of drugs. According to the new rules, shortages must be reported within five days of a company becoming aware of a problem, and plans to discontinue a drug are to be reported at least six months before the discontinuation. Having timely access to reliable industry information is expected to help Canada's health system respond to drug shortages and discontinuances more quickly and minimize the impact on patients, according to Health Canada.

A bipartisan push is on in the **U.S. House of Representatives** to get full funding for the NIH's Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative. Reps. Tim Murphy (R-Pa.), Earl Blumenauer (D-Ore.), Cathy McMorris Rodgers (R-Wash.) and Bill Pascrell (D-N.J.) are asking the leadership of the Labor, Health and Human Services, and Education Appropriations Subcommittee to include robust funding for the initiative in its spending proposals. The BRAIN Initiative is intended to discover the underlying pathology of an array of brain disorders and provide new therapeutic avenues to treat, cure or prevent a variety of neurological and psychiatric conditions, including addiction, schizophrenia and suicide. "We need more neuroscience research. This shouldn't be controversial," Blumenauer said.

IN THE CLINIC

Advaxis Inc., of Princeton, N.J., presented data from the GOG-0265 study at the Society of Gynecologic Oncology's Annual Meeting on Women's Cancer in National Harbor, Md. The single arm, phase II trial evaluated axalimogene filolisbac for the treatment of persistent or recurrent metastatic (squamous or non-squamous cell) carcinoma of the cervix (PRmCC). The primary endpoints of the study were to assess the safety and efficacy of the compound. The primary efficacy endpoint was overall survival at 12 months from initial treatment with axalimogene filolisbac. The primary safety endpoints were to evaluate the number of patients with dose-limiting toxicities and the frequency and severity of adverse effects. The final efficacy results of GOG-0265 demonstrated that 38 percent of patients (n = 19/50) with heavily pretreated PRmCC were alive 12 months following treatment with the drug. The study protocol used a logistic model-based calculation to establish the expected 12-month survival rate. The model identified the key prognostic factors of age, race and performance status significantly related to survival from a database of about 500 patients with PRmCC who participated in 17 previous phase II studies conducted by the Gynecologic Oncology Group (GOG), now part of NRG Oncology. Using this model, the expected 12-month survival rate of patients enrolled in the study was calculated to be 24.5 percent, which means drug-treated patients showed a 52 percent improvement over the expected survival rate and is the highest 12-month survival rate achieved to date in this setting. The probability of this survival improvement being detected by chance vs. a true treatment effect was calculated to be 0.02. An ongoing complete response of 18.5 months was observed and the longest ongoing survival is 40.6 months, the company said. The drug is derived from Advaxis' Lm-based Antigen Delivery System, which uses live, attenuated bioengineered Listeria monocytogenes bacteria to stimulate the immune system to view tumor cells as potentially bacterial-infected cells and target them for elimination.

Amarin Corp. plc, of Dublin, disclosed the publication of the rationale and design for the company's REDUCE-IT phase III cardiovascular outcomes study in *Clinical Cardiology*. REDUCE-IT is a global study of about 8,000 patients to evaluate whether treatment with prescription pure EPA Vascepa (icosapent ethyl) at 4 gm per day reduces cardiovascular events in patients, who despite having their LDL-cholesterol (LDL-C) controlled with statin therapy, have elevated triglyceride levels and demonstrate other risk factors, such as diabetes and previous cardiovascular events. The study is being conducted under a special protocol assessment agreement with the FDA. Ethyl- eicosapentaenoic acid (EPA), the drug's active ingredient, is converted to free EPA by esterases, and then incorporated into phospholipids, cholesteryl esters and triglycerides in the blood and other tissues. Data suggest that EPA reduces hepatic very low-density lipoprotein triglyceride (VLDL-TG) synthesis or secretion and enhances TG clearance from circulating VLDL particles.

Amgen Inc., of Thousand Oaks, Calif., said four-year follow-up results from the Repatha (evolocumab) OSLER-1 study, the longest proprotein convertase subtilisin kexin type 9 inhibitor trial to date, were published in *JAMA Cardiology*. Repatha, when added to standard of care, achieved median low-density lipoprotein cholesterol reductions of 57 percent at four years, with no new safety concerns identified and no neutralizing antibodies observed with cumulative exposure. An open-label extension study, it enrolled 1,324 of the 1,650 (80.2 percent) eligible patients who completed a phase II parent study. OSLER-1 evaluated the durability of LDL-C reduction and incidence of adverse events with long-term therapy with Repatha. Once therapy was initiated, 79 percent of patients persisted with Repatha treatment with average exposure duration of 44 months. Patients who reached four years of follow-up achieved a median LDL-C of 60 mg/dL.1

REGULATORY FRONT

The **FDA** revised its draft guidance on the design of bioequivalence studies to be used in developing generic versions of rifaximin tablets (Xifaxan), an anti-diarrhea drug marketed by **Salix Pharmaceuticals Inc.**, which became part of **Valeant Pharmaceuticals International Inc.** in 2015. The revision consolidates two draft guidances released in 2011 and 2012 that separately addressed bioequivalence for the 200 mg and 550 mg tablets, according to a notice slated for publication in Thursday's *Federal Register*. In addition to the revised draft guidance, the FDA said it would respond to two citizen petitions Salix filed in 2008 and 2016 requesting that the agency not approve generics referencing Xifaxan unless they met certain conditions, including bioequivalence. As of Wednesday, the FDA had not yet posted those responses. Salix, through its attorneys, submitted a supplement this week to the 2016 petition. Comments on the revised draft are due by May 15.

The **FDA** issued a safety alert Wednesday warning doctors that Viberzi (eluxadoline) shouldn't be used in patients with no gallbladder, as they have an increased risk of developing serious pancreatitis that could result in hospitalization or death. The agency said it is addressing the safety concerns with **Allergan plc**, the Dublin-based manufacturer of Viberzi, which is used to treat irritable bowel syndrome with diarrhea. //

IN THE CLINIC

Catalyst Pharmaceuticals Inc., of Coral Gables, Fla., disclosed positive topline results from the investigator-sponsored trial evaluating the potassium channel blocker Firdapse (amifampridine phosphate) as a treatment for myasthenia gravis (MG) patients with anti-MuSK antibodies, an ultra-rare sub-population of MG patients which is a debilitating neuromuscular disease, and there are no FDA approved therapies for this specific form of MG. Both of the co-primary efficacy endpoints of change from baseline (CFB) in total Quantitative Myasthenia Gravis score (p=0.0003) and CFB in total Myasthenia Gravis Activities of Daily Living score (p=0.0006) were statistically and clinically significant in this seven-patient trial. Several secondary efficacy measures also achieved statistical significance. The drug was well tolerated, Catalyst said.

Cesca Therapeutics Inc., of Rancho Cordova, Calif., disclosed what the company said are encouraging data from a study evaluating the use of autologous platelet-rich plasma (PRP) for the treatment of chronic non-healing ulcers. Results from the 24-patient patient study were published in the peer-reviewed *Journal of Biomedical Science*. In the study, patients with one wound/ulcer of varying etiology were treated with a single dose of PRP injections around the wound alongside a topical administration of autologous platelet gel. The process was completed at the patient's bedside in a single session within 30 minutes. Healing of the wound/ulcer was observed in patients as early as four weeks after the PRP treatment with a mean healing time of 8.2 weeks ±1.9. All patients demonstrated healing of the wound/ulcer, with 17 (70.8 percent) showing a 90 percent reduction in wound size and three (12.5 percent) showing an 80 percent to 90 percent reduction over the course of the 24-week follow-up. The study also reported that there were no adverse events on the day of treatment or during the patient's 24-week follow-up, demonstrating a good safety profile for the treatment of chronic non-healing wounds/ulcers, Cesca said. PRP is composed of thrombocytes, cytokines and various growth factors which are secreted by α-granules of platelets help wounds heal.

Greenovation Biotech GmbH, of Freiburg, Germany, said it dosed the first patient in a phase Ib study of lead candidate, moss-agal, in adults with Fabry disease. The recombinant form of human alpha-galactosidase was developed by the company as an enzyme replacement therapy for patients with the genetic lysosomal storage disorder. The multicenter, open-label, single-dose trial is assessing the safety, pharmacokinetics and efficacy of moss-agal on lyso-Gb3 levels in plasma and urine.

Immunomedics Inc., of Morris Plains, N.J., reported that sacituzumab govitecan (IMMU-132), the company's lead antibody-drug conjugate, was "highly active" in heavily-pretreated patients with metastatic triple-negative breast cancer (TNBC) who received a median of five lines of therapy since diagnosis. Among the 69 enrolled patients reported in the article, the overall confirmed objective response rate, with a cutoff as of Aug. 2, 2016, was 30 percent, with two patients having complete remissions and 19 patients achieving partial responses (95 percent confidence interval [CI], 20 to 43 percent). Median progression-free survival was six months (95 percent CI, 5 to 7.3 months) vs. the 3.5 month generally attributed to standard agents, including cisplatin, capecitabine, nab-paclitaxel, and eribulin, as reported in earlier metastatic TNBC trials. The median overall survival during the trial was 16.6 months (95 percent CI, 11.1 to 20.6 months). Grade 3 or higher adverse events included neutropenia (39 percent), leukopenia (16 percent), anemia (14 percent) and diarrhea (13 percent). Notably, the company said, few patients had febrile neutropenia (7 percent) or severe diarrhea (13 percent). Results from the single-arm phase II study were published online in the *Journal of Clinical Oncology*. The company has signed an exclusive and high-profile global licensing agreement with Seattle Genetics Inc. (See *BioWorld Today*, Feb. 13, 2017.)

EARNINGS

Arena Pharmaceuticals Inc., of San Diego, reported that its revenues for the fourth quarter ending Dec. 31, 2016 totaled $85.4 million, including $15.2 million in net product sales of Belviq, $1.3 million in milestone payments earned from Tokyo-based **Eisai Co. Ltd.**, and **Ildong Pharmaceutical Co. Ltd.**, of Seoul, South Korea, and $66.1 million of revenue associated with up-front Belviq payments. Net income was $38.3 million or $0.16 per share. For the year revenues totaled $124 million, including $26.3 million in Belviq net product sales, $12.3 million of milestone payments earned from Eisai and Ildong for Belviq, and $72.1 million of revenue associated with up-front Belviq payments. The company reported a net loss for 2016 of $22.9 million, or $0.09 per share. At Dec. 31, 2016, cash and cash equivalents totaled $90.7 million. //

IN THE CLINIC

Ixaltis SA, of Toulouse, France, is launching its first phase II study of litoxetine (IXA-001), a drug exclusively licensed from Sanofi SA. Preclinical trials, conducted by private and academic institutes, have yielded positive results in treating urinary incontinence, the company said. The study will include 240 women aged 18 to 75 years suffering from mixed urinary incontinence. Efficacy of the treatment will be assessed by reduction in numbers of urinary incontinence episodes, the change in Patient Perception of Bladder Condition and the Patient Global Impression of Improvement questionnaires, as well as other. Safety and tolerance vs. a placebo will also be measured.

Kite Pharma Inc. highlighted the online publication of results in the *Journal of Clinical Oncology* from a National Cancer Institute study of anti-CD19 chimeric antigen receptor (CAR) T-cell therapy in patients with relapsed/refractory non-Hodgkin lymphoma (NHL). The 22 NHL patients enrolled in the study received a single dose of anti-CD19 CAR T-cell therapy after a low-dose chemotherapy conditioning regimen. Objective responses (OR) were seen in 73 percent of patients, and complete remissions (CR) were observed in 55 percent of patients. Among patients with aggressive B-cell NHL, OR and CR were 68 percent and 47 percent, respectively. Duration of responses ranged from more than seven months to more than 24 months, and 11 of the 12 CRs were ongoing. Reversible grade 3 or 4 neurotoxicity including confusion, dysphasia, encephalopathy and gait disturbances was observed in 55 percent of treated patients. The study showed the low-dose conditioning regimen led to the depletion of lymphocytes and increase in serum interleukin-15, the company said. A similar conditioning regimen is used in Kite's ZUMA-1 study of axicabtagene ciloleucel, the Santa Monica, Calif.-based company's lead candidate.

Mateon Therapeutics Inc., of South San Francisco, reported preliminary data from the third dose cohort of its ongoing phase Ib study of the vascular targeting agent OXi4503, combined with cytarabine, in patients with relapsed/refractory acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS). The cohort enrolled four patients who received a dose of 6.25 mg/m2 of OXi4503 in combination with an intermediate dose (1g/m2/day x 5 days) of cytarabine. One patient with a high risk TP53 gene mutation had a complete remission. Two other patients demonstrated evidence of AML blast reduction after one cycle, one of which is receiving additional cycles of OXi4503 plus cytarabine therapy, the other of which has since progressed. The fourth patient did not show a response and experienced progressive disease. Seeing no dose-limiting toxicities, the trial's safety review committee has recommended that Mateon proceed to the fourth cohort, which is now enrolling patients at an OXi4503 dose of 7.81 mg/m2.

Prima Biomed Ltd., of Sydney, said that a second cohort has been fully recruited for its TACTI-mel (Two ACTive Immunotherapeutics in melanoma) trial being conducted in Australia. Six patients with unresectable or metastatic melanoma that have had a suboptimal response to Keytruda (pembrolizumab, Merck & Co. Inc.) were dosed with the higher 6 mg dose of IMP321, the company's antigen presenting cell activator, in combination with Keytruda.

Vtesse Inc., of Gaithersburg, Md., said that its ongoing phase IIb/III registrational study of the investigational drug VTS-270 in Niemann-Pick Type C1 disease is fully enrolled, having exceeded its goal of reaching 51 participants. Additionally, the company said that it has initiated a device development program to eliminate the need for lumbar punctures for administration of VTS-270. The randomized portion of the trial will conclude in about a year. //

FINANCINGS

Autifony Therapeutics Ltd., of Stevenage, U.K., said it received a new funding award of £895,000 (US$1.09 million) from the Biomedical Catalyst for initiation of a dementia research program. An investment of £400,000 from the Dementia Discovery Fund (DDF) will also be used to support the research. The company will use its expertise in the voltage-gated ion channel field to tackle a different subtype of potassium channel, which has been implicated in Alzheimer's disease (AD) and potentially other dementias, through regulation of synapse function.

Peptimimesis SAS, Strasbourg, France, said that Cap Innov'Est, a regional seed fund, has released €0.7 million (US$0.74 million), the second tranche of its investment secured in 2016. This new investment will be complemented with non-dilutive funding to reach more than €1 million (US$1.05 million) to support its next development phase. The company is advancing a pipeline toward an HER2-candidate nomination for breast cancer-derived brain metastasis. //

Briacell

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Lacher characterized SV-BR-1 molecularly and then conducted human leukocyte antigen (HLA) typing on patients who had received the vaccine.

"He found that the one patient with the remarkable response had a double match, at HLA-A and HLA-DR-beta-3," Williams said. "That gave us a clue that, perhaps by doing HLA typing on patients, we may be able to predict who's going to be most likely to respond."

For now, the company isn't limiting trial participants based on their HLA profile, "but we are going to look at that going forward and try to develop the companion diagnostic in parallel with clinical development," he added.

Briacell isn't oblivious to the numerous trial failures in cancer vaccines, such as Curevac AG's mRNA-based prostate cancer vaccine, CV9104; HS-410 (vesigenurtacel-L) from Heat Biologics Inc.; and Galena Biopharma Inc.'s Neuvax (nelipepimut-S). (See *BioWorld Today*, June 30, 2016, Dec. 2, 2016, and Jan. 13, 2017.)

Briavax is believed to activate the immune system to recognize and eliminate cancerous cells by inducing tumor-directed T cell and, potentially, antibody responses. Wiseman's early findings may have been completely serendipitous, Williams acknowledged. But, he added, Briavax is differentiated from cancer vaccines developed from single antigens or even a single peptide from a cancer antigen.

"That's an interesting approach, but we're using the whole-cell vaccine so there are numerous antigens that are being expressed by our vaccine," he pointed out. "That gives us a distinct advantage."

To date, the targeted vaccine candidate also has been well tolerated with a favorable safety profile – a notable difference from broader checkpoint inhibitors, which can provoke autoimmune responses, Williams said.

"We're very encouraged, but obviously we have a long way to go," he said.

Still, Briacell's premise and early data on Briavax were sufficiently compelling to attract Williams from Incyte Corp., where he served for more than a decade as vice president of exploratory development. Earlier, Williams served as head of experimental medicine and vice president of clinical pharmacology at Glaxosmithkline plc and had an academic career at the University of Pennsylvania, where he ran a research program in receptor biology, including developing bioactive peptides that mimicked GM-CSF.

The virtual company, with just four full-time employees, has approximately C$2.5 million (US$1.88 million) in the bank and plans another capital raise this year. Although the company isn't looking for suitors, it's discussing combination trials with several big pharmas where Briavax could boost response rates of existing cancer therapies without provoking a safety signal.

Briacell also has a second-generation cancer vaccine in development.

"If our current thinking is correct about matching for HLA, probably about 20 percent of patients would have a double match with our current vaccine," Williams said. "But we want to develop it further so we can swap out different HLA molecules in the vaccine" to treat different types of cancer.

"Scientifically, we know where we want to go," he added. "From a business perspective, we're open to different possibilities." //