RIVERVEST® News

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Investing in Life Science Innovation

RiverVest startup brings proven drug back to clinic for promising new application

What if you could create a biotech startup focused on treating rare diseases, with clinical-stage drug candidates already in hand, and high odds of success in clinical trials?

That was the compelling opportunity RiverVest has helped build at Lumena Pharmaceuticals.

The story begins when Ted Greene, CEO of Satiogen Pharmaceuticals, reached out to John McKearn, Ph.D., RiverVest managing director, and to Mike Grey, venture partner at Pappas Ventures to discuss a clinical-stage compound Dr. McKearn had worked on as head of discovery research at Searle/Pharmacia in St. Louis. Greene was interested in developing the drug to treat type 2 diabetes.

Grey formed a new company, Lumena, with seed funding from Pappas, to work with Greene and to license technologies from Satiogen.

RiverVest joined forces with Pappas to add additional seed capital. Grey worked with Dr. McKearn and Niall O'Donnell, Ph.D., RiverVest principal, to further develop the company, license the clinical-stage Searle molecule from Pfizer and build a compelling clinical proposal.

"We've been working in stealth mode during these early years," says Grey, now CEO of Lumena. "While diabetes was and is an exciting opportunity for Lumena, we decided it was not the place to start. We needed to look at diseases that provide a lower regulatory hurdle."

In developing the new clinical strategy, Grey and Dr. O'Donnell, now in an operating role, focused on cholestatic diseases, in which bile acids build up in the liver. There are several rare, orphan diseases (see below) that may benefit from Lumena's compound, LUM001. "If we can get this compound through regulatory approval quickly, we can have a profound impact on the health of these patients," says Grey.

This new clinical strategy drew in Alta Partners who led a $23 million Series A financing in June 2012. Dr. McKearn became chairman of the board.

Dr. O'Donnell and Grey led the Lumena team's negotiations with U.S. and U.K. regulators. "We obtained encouraging and favorable guidance on both sides of the Atlantic," says Dr. O'Donnell. "We were able to map out a very achievable route to approval."

"LUM001 has a long safety history with over 1,400 patients of clinical exposure," says Grey. "It is not absorbed into the body, which increases its safety, and its mechanism of action suggests it could bring a significant benefit to liver disease patients. This is why Pappas, RiverVest and Alta invested."

Mike Grey, Ted Greene and John McKearn

Clinical programs in pediatric and adult liver diseases will begin later in 2013 in the U.S. and U.K.

LUM001 takes aim at cholestasis, may relieve debilitating itch in children and adults

An itch sounds like an annoying but benign symptom. But for children with Alagille syndrome or progressive familial intrahepatic cholestasis (PFIC), the itch—called pruritus—is so severe that it drives them to scratch right down to the bone.

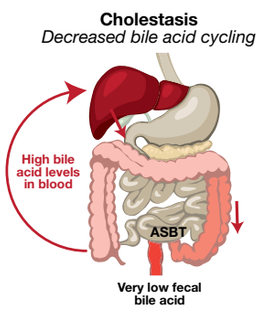
"Pruritus destroys these children's lives," says Richard Thompson, M.D., Ph.D., senior lecturer in paediatric hepatology at King's College London, which houses perhaps the largest Alagille and PFIC clinical practice in the world. "They can't sleep at night because of the itching, they can't concentrate or stay awake at school. They don't develop properly. It's miserable."

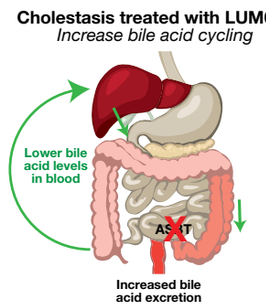
Alagille and PFIC are rare disorders, affecting 4,500 children in the U.S. and U.K. Patients suffer from a buildup of bile acids in liver cells that leads to liver disease and in many cases, liver transplant.

"The primary role of bile acids is to act as a detergent, breaking down fats in the digestive system," says John McKearn Ph.D., RiverVest managing director. "In the right place at the right time, they are a life saver. But we are convinced that a buildup of bile acids in these children is a disaster."

The physiology works like this: "Bile acids enter the small intestine and drop down into the ileum. Here, apical sodium dependent bile acid transporter (ASBT) sucks the bile acids back into the body, straight to the liver," explains Dr. Thompson. "The cycle goes round and round five to eight times a day with very few bile acids released in the feces."

Lumena believes their compound, LUM001, can block the reuptake of bile acids in the ileum, pushing them down into the large intestine and out into the feces, eliminating them from the liver. This may be achieved through a safe, effective, minimally absorbed, once-daily pill that would alleviate pruritus and potentially improve liver function.





"We don't have cast iron proof of what causes itch in liver disease, but there is a definite correlation between elevated bile acids and pruritus, which has been proven through a surgical procedure that diverts bile acids from the liver," says Dr. Thompson. The surgery is effective in relieving pruritus, but it is disfiguring and requires an ostomy bag, which negatively affects quality of life.

"Lumena's objective is to achieve the same benefits without surgery," says Niall O'Donnell, Ph.D., RiverVest principal.

"We hope that the medication may also be efficacious in slowing down the progression of the disease itself," says Ben Shneider, M.D, director of pediatric hepatology at Children's Hospital of Pittsburgh of UPMC and professor of pediatrics. "It certainly is a reasonable expectation."

"Lumena is a collaborative effort between academics, clinical work and drug development," says Dr. Shneider. "Together we are working to tackle a significant unmet need."

In addition to clinical trials treating children with Alagille and PFIC, Lumena will target a cholestatic disease known as primary biliary cirrhosis, which affects some 150,000 adults.

MILESTONES

- **Pfizer Inc.,** reports that PF-06473871 (formerly EXC001) is progressing into Phase IIB clinical studies in hypertrophic skin scarring. EXC001 was the lead asset of **Excaliard Pharmaceuticals,** founded by RiverVest and acquired by Pfizer in 2011. Initiation of the study triggered a milestone payment to former Excaliard shareholders.

- **Aptalis Pharma** has completed two Phase III clinical studies testing Aeroquin in patients with cystic fibrosis. Aeroquin was the lead asset in **Mpex Pharmaceuticals,** a RiverVest portfolio company acquired by Aptalis in 2011. Approval of Aeroquin in Europe and the U.S. would trigger further milestone payments to former Mpex shareholders.

- **Otonomy** and **ZS Pharma Inc.**, report the initiation of clinical studies. Otonomy's study, titled "Middle Ear Effusion in Pediatric Subjects Requiring Tympanostomy Tube Placement," commenced on December 18, 2012 and will complete middle of 2013. ZS Pharma's, titled "Safety & Efficacy of Zirconium Silicate in Mild to Moderate Hyperkalemia" started in 2013 and is projected to complete in June 2014.

- **Tryton Medical, Inc.** completed enrollment in its Pivotal IDE trial evaluating the Tryton Side Branch Stent™. The study is a multi-national randomized trial that compares a Tryton stent to the use of balloon angioplasty in the side branch.

Positive clinical outcomes put IDEV's SUPERA stent on path to PMA approval

IDEV Technologies, Inc. is targeting an approved premarket approval application (PMA) from the FDA by the end of 2013. The application was filed in November 2012 as a result of positive clinical outcomes of the SUPERA® Peripheral Stent System in the SUPERB pivotal U.S. clinical trial.

"This FDA Investigational Device Exemption (IDE) trial demonstrated the highest patency rates in peripheral stent trials for superficial femoral and proximal popliteal artery disease that have been publicly reported," says Christopher M. Owens, president and CEO of IDEV. "In addition, this is the first and only femoral-popliteal artery IDE trial to record zero stent fractures for bare or drug-coated nitinol-based technologies."

Of 42 physicians surveyed following initial presentation of SUPERB IDE data, 88 percent believed the results were excellent or very good and said their use of SUPERA would increase as a result.

"All the hard work and dedication by Chris and the IDEV team is coming to fruition," says Jay Schmelter, managing director of RiverVest and member of IDEV's board of directors. "SUPERA is clearly positioned in the doctors' minds as best-in-class."

The SUPERA stent is a highly differentiated and disruptive interwoven nitinol wire technology platform that offers significantly improved radial strength, flexibility and kink resistance, which is designed to adapt to the anatomy.

SUPERB™ STUDY

"SUPERA is clearly positioned in the doctors' minds as best-in-class."

Jay Schmelter
Managing Director of RiverVest

SUPERA is currently CE marked for biliary and peripheral vascular use in Europe and 510(k) cleared for biliary use in the U.S. PMA approval would allow vascular labeling in the U.S.

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Niall O'Donnell named to experts advisory panel at Stevenage Bioscience Catalyst

RiverVest Principal Niall O'Donnell, Ph.D., has been invited to serve on the Experts Panel at Stevenage Bioscience Catalyst, the U.K.'s first open innovation bioscience campus focused on driving early-stage biotech, pharma and medtech developments.

Dr. O'Donnell joins a panel of commercial, financial and technical experts advising Bioscience Catalyst and its tenants on all aspects of business development.

Funded by partners including GlaxoSmithKline and the Wellcome Trust, and located just outside of London, Stevenage Bioscience Catalyst's goal is to stimulate the growth of the U.K. life sciences sector.

"I'm looking forward to this opportunity to advise the bioincubator and its promising entrepreneurs," says Dr. O'Donnell. "At the same time, we at RiverVest will get an early look at some potential opportunities, which we think will enhance our deal flow."

Niall O'Donnell, Ph.D.