RIVERVEST® NEWS

Spring 2008 *Investing in life science innovation* *www.rivervest.com*

RiverVest founds and co-leads Excaliard with $15.5 million investment to fund fibrotic disease treatment

RiverVest Venture Partners, in an oversubscribed syndication with Alta Partners and Pro-Quest Investments, closed in November on a $15.5 million Series A financing of Excaliard Pharmaceuticals.

With a goal of developing antisense oligonucleotide drugs to prevent scarring and fibrosis, the San Diego-based biotech company was co-founded by RiverVest managing director, J. Gordon Foulkes, Ph.D., and Nicholas Dean, Ph.D., a leader in the fields of genomics, antisense and oligonucleotide technology.

"Antisense technology has been in development for 20 years," says Dean, who held key positions for 15 years with Isis Pharmaceuticals, Inc. (Nasdaq: ISIS), the leader in the discovery and development of antisense therapeutics.

"It's only in the last five years that we've had the ability to block disease at the genetic level by means of a drug."

Isis has already successfully commercialized the world's first antisense drug, Vitravene®, demonstrating the ability to meet FDA and European regulatory requirements for safety and efficacy. Isis is currently in mid-stage clinical trials with a cholesterol-lowering application. Excaliard has licensed antisense technology from Isis to treat fibrotic diseases, including scarring. (See accompanying story below.)

Dean met Foulkes and Niall O'Donnell, Ph.D., RiverVest associate and Kauffman Fellow, through a San Diego group called BioBrits, as the three hail from the United Kingdom: England, Scotland and Northern Ireland respectively. Dean approached Foulkes with his anti-scarring concept and "the more we got into it, the more we liked what we saw," says O'Donnell.

The deal was appealing on several levels: "Fibrosis represents a significant and expanding area of unmet medical need. Clinical tests have demonstrated profound efficacy and safety in multiple animal models. There appears to be a clear path to rapid development. Nick had already negotiated the opportunity to license the technology from Isis. And we could see the opportunity to exit within a few years," says Foulkes in a five-point overview.

According to Dean, the Series A funding will sustain Excaliard through proof of concept for drug activity in humans.

EXCALIARD PHARMACEUTICALS, INC.

"… we should very quickly move into proof-of-concept clinical trials in the second quarter of 2009."

Nicholas Dean, Ph.D. Co-Founder and Chief Scientific Officer of Excaliard Pharmaceuticals

"We will be starting toxicology testing in three months and expect to begin a normal Phase I clinical trial in the first quarter of 2009," notes Dean. "From there, we should very quickly move into proof-of-concept clinical trials in the second quarter of 2009."

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RiverVest Venture Partners invests in promising life science companies nationwide, focusing on:

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Technology targets genes that cause scarring

There are more than 30 million surgeries performed annually in the U.S., according to the St. Louis-based Mattson Jack Group. Yet there is no effective method for reducing surgical scarring. Nor is there an effective treatment for injuries, burns, birth defects or diseases that inflict devastating disfigurements or organ-compromising fibrosis (excessive scarring).

"The medical community has been waiting decades for a safe, effective treatment for scarring," says Gregory S. Schultz, Ph.D., professor of OB/GYN and director of the Institute for Wound Research at the University of Florida. "But until now we haven't had the technology to attack it at the molecular level."

According to Schultz, the only current FDA-approved method for reducing scarring is the application of silicone sheeting. "But this is only for surface injuries, and the effects are modest," says Schultz. The other option, which is not approved by the FDA for use in fibrosis, is to inject anti-inflammatory steroids. Again, the results are minimal and frequently include side effects.

Now, with the launch of Excaliard Pharmaceuticals,

"This is kind of the Holy Grail of wound healing…"

Gregory S. Schultz, Ph.D.

Schultz is hopeful that a highly effective anti-fibrosis drug is on the horizon.

"I believe Excaliard's antisense approach has a very high probability of success in multiple clinical conditions," says Schultz. "This is kind of the Holy Grail of wound healing – to be able to conduct surgery and not leave severe scars."

In simple terms, antisense technology works by making short, chemically-modified complementary nucleotide chains that target specific genes. Scientists now know the dominant genes that promote scarring. Therefore, an antisense drug that can intercept and break down the gene products driving fibrosis could reduce scarring.

"It all hinges upon knowing the right genes," says Schultz. "And we do. That's a huge advantage because side effects are minimized."

Schultz has collaborated on papers with Excaliard founder Nick Dean, Ph.D., for 10 years and was influential in pressing Dean to apply antisense research specifically to fibrosis.

"We've seen the effects, and we understand why it works," says Schultz. He and several colleagues, including Tom Mustoe, M.D., chief of plastic surgery at Northwestern University, have employed antisense testing models that have shown dramatic results in the lab.

"There is probably no one who knows antisense technology better than Nick," says Schultz. "Fortunately, RiverVest has superb scientists and business people who really understand technologies like this. The chemistry is sound. RiverVest understands it and had the sense to pursue it."

RiverVest expands interventional cardiology portfolio — founds Lutonix and leads investment in Tryton Medical

RiverVest Venture Partners co-founded Lutonix, a Minneapolis-based medical device start-up with the singular focus of developing a next-generation, drug-eluting angioplasty balloon. The $5 million Series A financing was syndicated with U.S. Venture Partners and closed in June 2007.

Drug-eluting stents have been successfully lowering restenosis rates since 2000, but there are limitations to their application. Lutonix's drug-eluting balloons offer a promising alternative for diseases that have not been well served by stents.

"In-stent restenosis, small vessel and peripheral disease demonstrate unmet clinical needs that open a large market without even considering the theoretical possibility of replacing stents," says co-founder Dennis Wahr, M.D., CEO and RiverVest venture partner. "Drug-eluting balloons are intuitively appealing because they offer the ability to inhibit restenosis without leaving hardware behind."

Exciting clinical proof-of-concept efficacy data from European scientists Ulrich Speck, Ph.D. and Bruno Scheller, M.D., using first-generation technology, demonstrate that drug-eluting balloon treatment results in less late luminal loss, restenosis and target vessel revascularization than conventional balloons or drug-eluting stents.

Lixiao Wang, Ph.D., inventor of revolutionary interventional cardiology products for SciMed, Boston Scientific and ev3 that generate billions of dollars in revenue and still dominate the market today, is co-founder and CTO. He and Dr. Wahr are joined on the Lutonix Board of Directors by Jay Schmelter, RiverVest managing director; Jonathan Root, M.D., USVP managing director; and Michael Berman, former president of Boston Scientific/SciMed.

> "Drug-eluting balloons are intuitively appealing because they offer the ability to inhibit restenosis without leaving hardware behind."
>
> *Dennis Wahr, M.D, Lutonix CEO and RiverVest venture partner*

Also within the interventional cardiology sector, RiverVest Venture Partners co-led a $14 million Series C financing of Tryton Medical, an emerging leader in the development of stents designed to treat coronary artery bifurcation disease, located in Research Triangle Park. Bifurcation lesion treatment accounts for 20% of the more than 2 million angioplasty procedures performed annually.

"After reviewing the landscape of competitive approaches, RiverVest concluded that Tryton's Side-Branch Stent™ is uniquely positioned by its ease of use and ability to marry with a drug-eluting stent of choice for the main branch," says RiverVest managing director Jay Schmelter.

Initial human clinical data shows that after six months, there has been only 3% target lesion revascularization, 0.12 mm side-branch late loss, and no side-branch restenosis. Schmelter and co-lead investor Rick Anderson, managing director of PTV Sciences, have joined Tryton's Board of Directors.

MILESTONES

- **MacroGenics, Inc.** announced a major alliance with Eli Lilly and Company to develop its Phase 3 antibody drug, teplizumab, for type 1 diabetes and other autoimmune diseases. The deal is valued at over $1 billion and includes milestone payments for multiple disease indications as well as royalty payments on product sales.
- **Calypso Medical Technologies, Inc., IDev Technologies, Inc.** and **Xoft, Inc.** launched products in 2007 and are in the early stages of building revenues.
- **Accumetrics, Inc.** closed a Series C round of $29 million that will fund a clinical trial and support revenue growth of its VerifyNow™ system.
- **IDev Technologies, Inc.** closed a $25 million Series C financing that will expand IDev's manufacturing, sales and marketing for the SUPERA™ stent and delivery system.
- **RiverVest Venture Fund II, L.P.** closed with $75 million of committed capital and has made seven medical device and biopharmaceutical investments to date.

Dr. McKearn joins firm as venture partner

RiverVest welcomes John P. McKearn, Ph.D., to the position of venture partner.

Most recently, Dr. McKearn was founding CSO, then CEO of Kalypsys, Inc., a biotech company in San Diego, where as CEO, he raised more than $150 million in private equity and other funding between 2003-2006.

Prior to that, as head of research for Searle and Pharmacia, Dr. McKearn was an important contributor to the discovery, development and launch of eight new prescription drugs, including Celebrex®, one of the leading pharmaceuticals to treat arthritis. At Pharmacia, Dr. McKearn was also responsible for integrating the discovery efforts of more than 1,600 international research scientists with an annual budget of $500 million.

"John's strong scientific training and operational expertise will further our capabilities in sourcing and adding value to our biopharmaceutical portfolio," says Jay Schmelter, RiverVest managing director.

Dr. McKearn completed his Ph.D. in immunology at the University of Chicago and his B.S. in biology at Northern Illinois University. He holds more than 45 patents and numerous patent applications from his 25-year career in immunology, inflammation, and oncology research and development.

Dr. McKearn serves on the Board of Directors for IDM Pharma (formerly Epimmune, Nasdaq: IDMI) and for Keel Pharmaceuticals.

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