

## PULMONARY DRUG DELIVERY

### Savara Inc.

*Using nanoparticles for effective drug delivery*

While there are many effective inhaled drugs on the market, the existing techniques for pulmonary delivery result in much of the drug being deposited at the back of the throat where it can potentially enter the systemic circulation. In most products, only 15 to 30% of the drug actually reaches the lung, with just 20% of that reaching the deep lung.

To resolve this drug delivery challenge, Cory Berkland and George Laurence co-founded **Savara Inc.** in March 2007. The company is developing respiratory therapeutics using its proprietary *NanoCluster* dry powder aerosol drug delivery platform, which is based on Berkland's research.

Berkland designed and developed the *NanoCluster* technology at the **University of Kansas** to improve the aerosol properties of drugs delivered into the lung. The *NanoCluster* technology has potential for local or systemic delivery of a wide variety of drugs, including poorly soluble and highly soluble drugs, small molecules, peptides and biological therapeutics. The *NanoCluster* manufacturing process can create microparticles to specific sizes and incorporate two or more different therapeutics to make a combination product.

"We typically create nanoparticles and assemble these into low-density microparticles that can be delivered using an oral or nasal inhaler," explains

Berkland. "The technology allows us to create defined particle sizes, which 'fly' in different ways—for example, larger particles are deposited in the upper airways and smaller particles travel further, into the deep lung."

The *NanoCluster* technology can be used for life cycle management and line extensions, increasing the patent life of existing marketed drugs. It also has potential for improving the efficiency of delivery of drugs, thereby increasing the therapeutic efficacy or reducing the required dose of drugs to reduce side effects. Due to the powder performance, the microparticles can be delivered using older off-patent dry powder inhaler devices, which would reduce the cost of entry to market.

Savara's business operations are based at the Austin Technology Incubator (ATI) in Texas, where it moved in late 2008, and its labs and technical operations remain at KU, from which it obtained exclusive rights to the *NanoCluster* technology. The company applied for the first *NanoCluster* patent in 2005, and expects approval during 2009.

Savara regards **Nektar Therapeutics Inc.**'s pulmonary assets (now owned by **Novartis AG**) and **Alkermes Inc.** as its nearest rivals. "While our competitors generally use spray drying to produce the particles and excipients to provide the 'flight' properties, we are able to do this sim-

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**Contact:** Rob Neville, Executive Chairman  
**Business:** Dry powder pulmonary drug delivery

**Founded:** March 2007

**Founders:** Cory Berkland, PhD (University of Kansas); George Laurence, President & CTO

**Employees:** 5 full-time, 10 part-time

**Financing:** \$1.83 million

**Investors:** Private investors

**Board of Directors:** Curt Bilby, PhD (Terapio, BioAustin); Matt Dennis (Invesco AIM); Nevan Elam; Rob Neville; George Laurence  
**Scientific Advisory Board:** Cory Berkland Chair; Chet Leach, PhD, DABT (Lovelace Respiratory Research Institute); Stephen R. Byrn, PhD (Purdue University); Robert Lee, PhD (Particle Sciences)

**Clinical Advisory Board:** James L Mulshine, MD (Rush University Medical Center)

**Board of Advisors:** Jessica Hanover, PhD (ATI-Bioscience); Thomas W. Fredrick (Life Science Legal)

ply using our nanoparticle technology, without the need for non-active ingredients, which increases the drug loading," says Rob Neville, Savara's executive chairman.

"A key differentiator between us and our competitors is our ability to manufacture fine particles of one to three microns, leading to improved aerosol performance," explains Berkland. "We are not aware of anyone else tailoring microparticle size using nanoparticle building blocks as we do. Improvements in aerosol efficiency and elimination of unwanted excipients will allow us to deliver

at least two to three times more drug to the lung than our competitors.”

Savara’s business model is based on out-licensing, and the company has a number of agreements ongoing, with further discussions under way with a number of top-10 pharmaceutical companies as potential partners.

Potential partners pay Savara for a feasibility study with the partner’s drug and Savara’s technology. If the study is successful, the partner has the option to license the technology. Savara can provide pharmaceutical companies with preclinical- and clinical-scale batches of material.

“We allow the industry to drive the development of our technology, based on the formulation issues presented by our clients,” explains Neville.

He says that Savara’s *NanoCluster* technology is broadly applicable across a number of therapeutic areas. The company has successfully formulated products for asthma, COPD and pulmonary infections, cancer diagnosis and treatment, tuberculosis and hypertension. Savara is in the process of publishing some of its preclinical data that demonstrate effective deposition in the peripheral lung.

In July 2008, Savara closed a seed round providing \$1 million, and in June 2009, the company received an \$833,000 first tranche of its Series A funding. The second tranche will close in the second half of 2009, providing a total of \$1.4 million, and involves most of the company’s existing investors. Savara has earmarked the Series A funding for expansion of the *NanoCluster* platform into new areas, such as combining it with nebulizers, or propellant-based inhalers.

“As we out-license the technology, and receive fees from service agreements, we do not need to seek as much funding as a typical drug development company would,” says Neville. “We also have some grant applications underway and should be able to run for two years without seeking any additional money. We feel that this financial strength is an achievement for a young company.”

Rob Neville has been with Savara since the beginning, and he saw the opportunities presented by Berkland and Laurence, and by the *NanoCluster* technology. “Not only did this present financial potential, but I also saw an opportunity to have an impact on marginalized people—people without a voice, such as those in South Africa, where I was born, for example. We are currently working with leading researchers and organizations to create pulmonary based tuberculosis and vaccine treatments,” says Neville. “I had a real desire to see my ideas translated into products that could better lives,” adds Berkland.

Neville was previously the founder and CEO of a software company, Evity Inc., which was acquired by BMC Software Inc. in 2000. He also founded

the management consulting company Clockwise Consulting, which has partnerships with a number of Texas biotech companies. Neville was a finalist for the Ernst & Young Entrepreneur of the Year award.

Over the next 12 to 24 months, Savara hopes to see some of its partner products move into clinical trials. “I think the major challenge that we face is skepticism from the pharmaceutical industry. They see the performance as too good to be true for such a simple and integratable particle engineering concept,” says Berkland. “We need people to appreciate the clinical benefits of this unique approach.”

Despite the current economic climate, Savara is still expanding. “We took on three new people in June 2009, taking our staff up to five full-time people and 10 part-time people. We would expect to have recruited another three or four people by mid-2010,” says Neville.

Like all start-ups, Savara will face the trials of the economic slowdown, but it appears to be riding it. “We seem to have

done well. Our reach must exceed our grasp,” says Neville.

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—SUZANNE ELVIDGE

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