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Financings Roundup

Clinical Data Pads Coffers, Adds \$25M in Private Financing Round

By Jennifer Boggs
Assistant Managing Editor

Clinical Data Inc., which last month pumped up its development pipeline with the acquisition of Adenosine Therapeutics LLC, pulled in \$25 million through a private placement to support general working capital purposes.

The Newton, Mass.-based firm agreed to offer 1.5 million shares priced at \$16.44 each, plus 6 cents per share, and warrants to buy an additional 757,461 shares, to certain affiliates of Randal J. Kirk, the company's chairman. The financing comes a little more than a year since Kirk and his affiliates helped Clinical Data obtain about \$66 million in exchange for 3 million shares priced at \$22 each to fund further work on depression drug Vilazodone. At that time, Kirk held about a 48 percent stake in the firm. (See *See Financings Roundup, Page 3*)

Drug Regulators Mark First Anniversary of FDAAA

By Donna Young
Washington Editor

WASHINGTON – The new authorities granted by Congress last year under the FDA Amendments Act (FDAAA) has allowed the FDA to avoid the often drawn out bargaining process, which sometimes took some “arm-twisting,” involved in seeking new safety warnings on drug labeling, regulators said Friday.

FDAAA, which marked its first anniversary this past Saturday, gave regulators the ability to require, rather than negotiate, safety labeling changes.

The agency four times has invoked its new safety labeling powers since they took effect in March, said Janet Woodcock, director of the FDA's Center for Drug Evaluation and Research. All four of those orders involved classes of drugs rather than a single medication, Woodcock noted Fri-
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Nitec Pharma Gets \$22M to Fund Lodotra Launch

By Cormac Sheridan
BioWorld Today Correspondent

With a first European approval for its rheumatoid arthritis drug Lodotra imminent, Nitec Pharma AG raised CHF24 million (US\$22 million) in a private equity round led by Munich, Germany-based TVM Capital.

The funding, which takes the company's total investment to CHF64 million, is primarily earmarked for the commercialization of Lodotra, a night-time release formulation of the corticosteroid prednisone.

The drug, which is based on GeoClock technology from London-based SkyePharma plc, reduces morning stiffness and pain caused by the night-time release of inflammatory cytokines, such as interleukin-6. Nitec CEO Anders Härfstrand told *BioWorld Today* he is confident the company will obtain a first approval before year-end.

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NEW CO NEWS

Taking the Long View, Inverseon Develops Beta-Blocker for Asthma

By Anette Breindl
Science Editor

Asthma is one of the most common chronic diseases in the U.S., but one that, as *The Lancet* puts it in an editorial in a recent issue, is still “a genuine medical mystery.”

In that light, it is perhaps a bit less surprising that one approach to asthma drug development involves the use of drugs that are contraindicated for the disease: San Francisco-based Inverseon Inc. is developing the beta-blocker nadolol for chronic use in asthmatics.

Inverseon, which was founded in 2004, has so far been what co-founder and Chairman William Garner termed a

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Inverseon

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“bootstrap operation.” The company has approximately 50 angel investors and option holders, and has had several Small Business Technology Transfer grants, but has raised less than \$1 million to date. But, Garner said, that will change when an ongoing open-label Phase II trial is done in early 2009. “Then we’ll take it up a notch and seek more significant funding,” he said.

With that funding, the company plans to conduct placebo-controlled Phase II trials to make the program attractive to a mid- and large pharma partners for Phase III trials. Inverseon co-founder Amie Franklin told *BioWorld Today* that the company estimated it will take “two to three years and about \$10 million” to finish the Phase II studies.

The usual acute treatment for asthma is exactly the opposite of Inverseon’s approach. Drugs like albuterol are beta-agonists, which make it easier to breathe by relaxing the airways. And by the same token, beta-blockers, which constrict the airways, are contraindicated for asthmatics because they can cause so-called airway hyperreactivity or bronchospasms.

But beta-blockers have gone from contraindicated to front-line therapy in another area: chronic heart failure.

The trick, Garner told *BioWorld Today*, is to “separate acute from chronic effects of drugs in chronic diseases.” And Franklin added that in chronic heart failure “the acute effect of beta-blockers was detrimental. But chronically it was the best therapy.”

Inverseon scientific co-founder Richard Bond, professor at the University of Houston, thought the same rationale might make beta-blockers worth investigating for the treatment of asthma. Bond and his colleagues have published both human and animal data in support of their ideas.

In a Phase IIa trial, results of which were reported in *Pulmonary Pharmacology and Therapeutics* earlier this year, 10 mild asthmatics were chronically treated with nadolol for 11 weeks. All subjects tolerated the drug well, and eight of them showed what Inverseon, in a press release announcing the findings, termed “clinically meaningful, dose-related reduction in airway hyperresponsiveness.”

The possible mechanisms are elucidated in an animal study published in the *American Journal of Respiratory Cell and Molecular Biology*. In that study, the authors showed that chronic dosing of certain beta-blockers induced what Garner termed “profound airway remodeling and anti-inflammatory effects.”

In that study, nadolol or another beta-blocker were chronically given to mice that had been sensitized by the repeated administration of asthma-inducing stimuli. Treated animals were able to cope much better with asthma-inducing stimuli than controls that were not on beta-blockers.

Asthmatic animals on chronic beta-blockers have

lower levels of eosinophils, which are immune system cells and asthma drug targets, as well as lower levels of cytokines and less mucin, which is overexpressed in asthma as well as some other lung diseases.

By comparing several different experimental protocols, the authors were able to demonstrate that beta-blockers specifically affect the response to an asthma challenge, similar to an asthma attack, rather than affecting the so-called sensitization phase where asthma is induced in the animals by repeatedly exposing them to asthma-causing stimuli.

An editorial published along with the animal data cautioned that “It is likely that in the heterogeneous environment of human asthma, the benefit will be small, difficult to detect, and may not significantly affect standard clinical outcomes. While the [Phase IIa] trial demonstrated that nadolol was relatively safe in individuals with mild asthma, the niche for beta-blockers will likely be in patients with moderate to severe disease, a subset of patients that may be significantly more susceptible to the deleterious effects of acute bronchospasm.”

But its author nevertheless concluded that low-dose chronic beta-blocker treatment may prove useful to reduce inflammation and mucus in a subset of individuals with asthma.

Even if that turns out to be correct, there is, of course, not exactly a dearth of beta-blockers on the market. But Garner said that “historically, for small companies based on university technologies, more value has been created with other approaches than the development of new chemical entities.”

And Franklin added that Inverseon, which is developing a controlled-release version of nadolol, an already marketed beta-blocker, would capture a significant market share by getting an approval specifically for asthma. “This is not a class effect . . . only a subset of beta-blockers would work. And physicians would be reluctant to use a nonapproved drug, given that it is contraindicated,” she told *BioWorld Today*. “There’s contraindication labels on every other beta-blocker.” ■

OTHER NEWS TO NOTE

- **ImClone Systems Inc.**, of New York, said the unnamed large pharmaceutical company that offered to acquire the biotech for \$70 per share has extended its due diligence period. The suitor was expected either to make a proposal or withdraw by Sunday; ImClone now says the decision will be made by 11:59 p.m., Oct. 1. The offer arose in the wake of New York-based **Bristol-Myers Squibb Co.**’s \$60-per-share bid, which last week was raised to \$62-per-share and taken directly to shareholders. (See *BioWorld Today*, Aug. 1, 2008, Sept. 11, 2008, and Sept. 24, 2008.)