

NANOMEDICINE

Kala Pharmaceuticals Inc.

Nanoformulations to treat eye disease

135 BEAVER STREET
SUITE 309
WALTHAM, MA 02452
Phone: (781) 810-4748
Web Site: WWW.KALARX.COM

Contact: Guillaume Pfefer, PhD, President & CEO

Business: Nanomedicines for transmucosal drug delivery

Founded: July 2009

Founders: Robert Langer, ScD (Massachusetts Institute of Technology); Justin Hanes, PhD (Johns Hopkins University School of Medicine); Colin R. Gardner, PhD (formerly Transform/Johnson & Johnson)

Employees: 13

Financing To Date: \$22.7 million

Investors: Lux Capital; Polaris Venture Partners; Third Rock Ventures; Crown Venture Fund

Board Of Directors: Kevin Bitterman, PhD (Polaris Venture Partners); Robert Langer (MIT); Bernard Gilly, PhD (formerly Fovea/Sanofi); Robert Paull (Lux Capital); Robert Tepper, MD (Third Rock Ventures)

Scientific Advisory Board: Colin R. Gardner; Justin Hanes; Peter Hutt, LLM (formerly FDA); Howie Rosen (formerly Alza Corp.); Richard Lindstrom, MD (Minnesota Eye Consultants); Ed Holland, MD (Cincinnati Eye Institute); Eric Donnenfeld, MD (Ophthalmology Consultants of Long Island); Peter Campochiaro, MD (Wilmer Eye Institute); Jeff Heier, MD (Tufts Medical School)

most recently served as general manager of Sanofi Pasteur Mexico. Pfefer's previous positions include VP, global head of the Sanofi Pasteur's influenza and pneumococcal franchise, by far the company's largest by sales.

Why the eye? Pfefer says, "It's an organ that represents a unique challenge. The barrier and clearance of the eye make it difficult to effectively deliver drugs. We have an opportunity to fundamentally transform the way drugs are administered to the eye." This opens up several commercial pathways, both for in-house drug development and for partnering with companies seeking improved formulations of their products. "We can add value to existing products by reducing dosing concentrations and/or frequency of dosing and yet achieve higher efficacy," he says. Pfefer notes that companies

Every 10 waking seconds the human eye blinks, keeping its protective mucosal coating fresh. That's a good thing for trapping and removing foreign matter that comes in contact with the eye; but it's not so good for medications struggling to penetrate into the eye. **Kala Pharmaceuticals Inc.** possesses a nanoparticle technology engineered to enable drugs to penetrate mucosal barriers. Kala intends to open the eye – and other organs protected by mucosal barriers such as the vaginal tract, intestine, and lung – to a range of new or improved treatments. The company is initially pursuing topical ophthalmic products for both front and back of eye diseases. Breakthrough mucosal penetrating formulations would dramatically transform care for ocular diseases, with blockbuster product potential.

The eye is exceptionally effective at protecting itself. Each blink exposes the corneal surface to a fresh layer of sticky, tear mucin that acts like natural "fly paper" to trap, hold, and, in the next blink, sweep away would-be invaders. But that protective mucosal barrier also hinders topical medications from penetrating the eye and reduces their active agents' effectiveness.

To treat conditions of the anterior segment of the eye, such as allergy, inflammation, blepharitis, and dry eye, topical drug formulations must deliver dosages sufficient to suffuse the eye's surface, penetrate the mucosal barrier, and have a therapeutic effect before the medication gets blinked away. This is difficult to achieve with traditional eyedrop formulations. For posterior segment diseases, such as wet age-related macular degeneration (AMD), posterior uveitis, and macular edema, current products must be injected directly into the eye, often at frequent intervals. Kala's proprietary delivery technology offers the possibility of simpler, less painful, and better controlled delivery of drugs to the eye, reducing the amount and frequency of drug administration and bypassing injections.

According to Kala president and CEO Guillaume Pfefer, the company's technology originated about a decade ago

when Justin Hanes, while training in Bob Langer's lab, Kala's co-founder and now a professor at the Johns Hopkins University School of Medicine, grew curious about viral infections and the ease with which some viruses penetrate mucosal surfaces and infect cells. How, he wondered, did they manage to get past the mucosal barrier? Hanes decided to develop mimics of a virus able to coat and penetrate mucosal barriers. He and his team explored the bio-inertness of low-molecular-weight polymers formed of polyethylene glycol (PEG). Hanes eventually engineered a proprietary PEG-coated nanoparticle technology able to slip through mucosal barrier in the same fashion as viral particles. He termed the technology Mucosal Penetrating Products (MPPs) and teamed up to launch Kala with Colin Gardner, who had been chief scientific officer of an earlier, successful, Langer start-up formulation company, TransForm Pharmaceuticals, which **Johnson & Johnson** acquired in 2005 for \$230 million.

Since its inception in late 2009, Kala's team, under the direction of Hongming Chen, PhD, another MIT chemical engineer trained in the Langer lab and the first employee at Kala, has developed the MPP technology into a multifaceted platform capable of working with drugs with various properties. These MPPs have been shown in various animal models to have significantly improved pharmacokinetics and efficacy compared with conventional "naked" nanoparticle forms of drugs.

According to Pfefer, Kala's first three years following its start-up in late 2009 – drawing on \$11.2 million in seed funding from Lux Capital, Polaris Venture Partners, and Third Rock Ventures – were focused on optimizing MPPs and exploring their commercial potential in various therapeutic areas. This culminated in the recent decision to focus the company's efforts on ophthalmology.

A chemical engineer by training with a PhD in material sciences and a Wharton MBA, Pfefer joined the company in July 2012 after spending the previous nine years in leadership positions at Sanofi Pasteur. He

often reformulate insoluble ocular agents into ointments or gels, which can provide some incremental improvement in efficacy but can also cause patient discomfort and difficulty in application. In contrast, MPP suspensions behave like solutions, he says. “MPPs are a much more elegant and more effective formulation than traditional suspensions, gels, and ointments.”

The company is pursuing two ocular product tracks at present, an anti-inflammatory agent for use after surgery and a topical treatment for AMD. Following cataract surgery, surgeons typically have patients apply steroids to the eye for two weeks to reduce inflammation. Kala is working to improve the delivery and effectiveness of a commonly used corticosteroid eyedrop, loteprednol, which is marketed by **Bausch & Lomb Inc.** as *Lotemax*. Early next year, Kala expects to be ready to begin clinical testing of its MPP version of loteprednol. “It’s an easy readout for a clinical study with relatively high probability of success,” says Pfefer. He expects to have a 505(b)(2) pathway to FDA approval, with an anticipated NDA filing in 2015. “With loteprednol-MPP, we have not only the opportunity to rapidly establish key advan-

tages of our technology in the front of the eye, but also to create the foundation of a billion dollar franchise,” he says. Pfefer believes Kala’s MPP version of loteprednol should allow for an increase in potency of the product while reducing the frequency of dosing. There is also potential beyond surgery to expand into posterior uveitis, blepharitis, allergy, dry eye, and perhaps macular edema, according to Pfefer.

Kala is also pursuing a topical treatment for wet AMD, a \$4 billion market that is currently served by products that are administered by intraocular injection only. The company is developing a topically applied MPP formulation of a receptor tyrosine kinase inhibitor (RTKI) for the treatment of AMD and other retinal diseases. Bringing to market a topical treatment for AMD would be a significant advance in the treatment of the disease that would transform the standard of care.

The company recently completed a Series A financing of \$11.5 million with all the original investors but led by new investor Crown Venture Fund. The money, according to Pfefer, will carry Kala through to the IND FDA filing for the MPP corticosteroid drug and selection of an RTKI as an MPP can-

didate for development in wet AMD. “We are also in discussion with several organizations interested in the Kala loteprednol-MPP program and also in our delivery platform, which they see as potentially enabling their own molecules,” he says.

Kim Brazzell, PhD, recently joined the firm as chief medical officer. He has long experience in ophthalmic drug development, most recently at Inspire Pharmaceuticals Inc., where he was EVP, medical and scientific affairs, until it was acquired by Merck in 2011 for \$416 million. At Inspire, he also oversaw a cystic fibrosis R&D program. Before that he was global head of clinical R&D and SVP of US R&D for Novartis Ophthalmics.

Last month Kala announced receipt of a grant from the Cystic Fibrosis Foundation to study the use of MPP for antibiotic penetration of CF sputum. “We have the possibility to leverage the platform in several ways beyond the ocular pipeline,” says Pfefer, envisioning multiple indications for in-house programs and external partnerships ahead for Kala.

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— MARC WORTMAN