

# Topica Pharmaceuticals

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**Summary:** Topica began its life with a promising novel anti-fungal called luliconazole (Lulicon) in hand. The compound was developed by Nihon Nohyaku and is already approved in Japan for tinea infections. Topica's initial focus will be on advancing ongoing clinical trials of the drug in athlete's foot, but even as it begins studies in athlete's foot, a market IMS estimates to be approximately \$400 million in the US alone, the end goal is a topical treatment for onychomycosis.

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## Topica Pharmaceuticals

### Potent topical medicines for skin and nail diseases

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**Contact:** Greg Vontz, President and CEO

**Industry Segment:** Pharmaceuticals

**Business:** Topical medicines for onychomycosis and other dermatological conditions

**Founded:** August 2008

**Founders:** Norifumi Nakamura, PhD, SVP Corporate Development; Rick Anthony, PhD, CEO Catalyst Pharmaceutical Research LLC

**Employees:** 4

**Financing to Date:** \$6.5 million

**Investors:** Alex Barkas, PhD (Prospect Venture Partners)

**Board of Directors:** Greg Vontz; Norifumi Nakamura; Alex Barkas; Dave Markland (Prospect Venture Partners); Rick Anthony

**Scientific Advisors:** Howard Maibach, MD (University of California, San Francisco School of Medicine); David Cohen, MPH, MD (New York University School of Medicine); William Cunningham, MD (Columbia University); Jay Birnbaum, PhD (Co-founder, Kythera Biopharmaceuticals Inc.)

Greg Vontz, president and CEO of dermatology start-up **Topica Pharmaceuticals Inc.**, is no stranger to the potential ups and downs of drug development. In 1999, Vontz, the former director of new markets and health policy at Genentech Inc., joined Connetics Corp. to help commercialize the biotech's connective tissue disorder treatment *Relaxin*. One year later, the unthinkable happened: when Phase III data of a critical *Relaxin* trial were unblinded, scientists discovered the naturally occurring hormone failed to show efficacy. Connetics' share price tanked on the news, plunging 80% almost overnight. Vontz helped reorient the company in a safer direction, developing a pipeline of dermatology products around the company's *VersaFoam* drug delivery technology. Fast forward five years to 2005: Connetics was profitable and Vontz had donned the mantles of president and chief operating officer. Because of the company's success, privately held Stiefel Laboratories Inc. (itself recently acquired by **GlaxoSmithKline PLC** [W#200910044]) purchased the company in a deal worth \$640 million in 2006. [W#200610178]

The Connetics experience taught Vontz important lessons about drug development, how to best interface with US regulatory officials, and the appropriate positioning of dermatology products in the marketplace. That's a unique skill-set, according to Alex Barkas, managing director at Prospect Venture Partners, and Connetics

founding CEO. "There have only been a handful of successful dermatology companies, so the pool of experienced managers is limited," he says. In early 2008, Barkas recruited Vontz to work with Prospect evaluating potential dermatology opportunities.

Vontz spent five months researching a promising novel anti-fungal called luliconazole (*Lulicon*) developed by **Nihon Nohyaku Co. Ltd.** and already approved in Japan for tinea infections. Back in 2007, Norifumi Nakamura had in-licensed North American, South American, and European rights to the drug during a stint as CEO of Janus Pharmaceuticals Inc., a specialty pharma company predicated on the strategy of bringing approved Japanese medicines to the US market. On the basis of early data showing luliconazole's potency and broad-spectrum activity, as well as a robust safety profile, Vontz believed the compound could serve as the linchpin of a dermatology-focused start-up.

In August 2008 Topica launched with early financing from Prospect Venture Partners. The company operated in stealth mode until late March, announcing its structured \$19 million Series A at the 2nd Annual BIO National Ventures Conference in Boston, MA. To date, the company has pulled in \$6.5 million from Prospect. It hopes to bring in a new investor and an additional \$4.5 million by June 30, 2009, and another \$8 million in 2010.

Vontz says the \$19 million Series A will finance Topica's ongoing work with luliconazole, which the start-up is studying as a possible treatment for both tinea pedis and onychomycosis. Initially, the focus will be on advancing ongoing clinical trials of the drug in the athlete's foot indication. To that end, the company recently announced the start of a Phase II, 120-patient multi-center trial testing the safety and optimal duration of a 1% luliconazole cream dosed once daily for two or four weeks. The ultimate goal: complete resolution of the fungal infection two weeks after treatment finishes. If a two-week course with luliconazole ultimately proves safe and effective, that would be a significant dosing advantage relative to the currently approved topical products for tinea pedis, which include **Sanofi-Aventis/Medicis Pharmaceutical Corp.**'s ciclopirox (*Loprox*) and **Schering-Plough Corp.**'s clotrimazole (*Lotriderm*).

But even as it begins studies in athlete's foot, a market IMS estimates to be approximately \$400 million in the US alone, the end goal is a topical treatment for onychomycosis. Largely benign medically, patients' anxiety over the toenail disfiguration it causes has helped **Novartis AG** and **Johnson & Johnson** sell a combined \$2.5 billion for their oral drugs, terbinafine (*Lamisil*) and itraconazole (*Sporanox*). Both of these medicines, however, are far from universally efficacious, and come with the potential for liver toxicity, which means regular monitoring via blood tests. Because the drugs' benefits don't necessarily outweigh the risks, some experts believe roughly 50% of the estimated 35 million US patients with onychomycosis opt not to receive treatment.

Sanofi has also developed a version of ciclopirox called *Penlac* for onychomycosis, but the topical nail lacquer, while safe, is much less effective than oral *Lamisil* or *Sporanox*. Indeed, that's been the problem with topical anti-fungal formulations generally. There are plenty of medicines that kill the fungus in the petri dish; finding a compound that is potent enough to sufficiently penetrate the toe nail, which can be up to 1 mm thick, has proved another story. So great is the need that **Anacor Pharmaceuticals Inc.**, a start-up founded in 2002 with backing from Care Capital, Venrock Associates, and Rho Ventures, was able to ink a lucrative partnership with Schering-Plough in 2007 around its Phase II boron chemistry-based onychomycosis drug, AN2690, despite the fact that composition-of-matter and original use patents for the compound expired in 2003. [W#200720100] In early 2009, Anacor attracted an additional \$50 million in investor money, with GlaxoSmithKline and Schering-Plough joining the private company's existing syndicate of backers. [W#200930021]

The interest of Big Pharmas such as GSK and Schering shows why Barkas, Vontz, and Nakamura were so keen to develop luliconazole, which in *in vitro* models developed by scientific advisory board member Howard Maibach, MD, penetrated finger nails 42 times better than Anacor's AN2690. But the drug hadn't been studied in a toe nail model, where the increased thickness of the nail might impede drug penetration,

trimming its potential. So Vontz and Nakamura worked with the UK-based contract research firm **MedPharm Ltd.** to develop a system to assess luliconazole's potential as an onychomycosis medicine. MedPharm procured human toenails and inoculated them with dermatophytes from onychomycotic patients and allowed the fungus to grow for two weeks before administering a solution containing 5% luliconazole. After seven days, researchers discovered the compound had completely penetrated into the nail bed and had achieved a 53% reduction in total fungal load; by day 21, 93% of the fungus had been eradicated. According to Vontz, Topica has created new formulations of the medicine that contain concentrations of luliconazole above 10%. "At these concentrations, the medicine is powerful enough to statistically eradicate the fungal load by day 21 in the *in vitro* model. That should translate very well into a treatment for patients with onychomycosis," he says.

But those data would be less impressive if they were accompanied by adverse side effects. Onychomycosis is hardly a life-threatening condition, so unless the medicine has a pristine side-effect profile it's likely to face stiff opposition from regulators and an uphill battle in the marketplace. That's where Vontz and his team can take comfort in the fact that luliconazole is already on the market in Japan. "More than four million people have been treated with the 1% luliconazole and there have been no reports of serious adverse events," he says. Indeed, in the controlled clinical studies in Japan, adverse drug reactions were reported in just 2.5% of the 1,035 patients, and the reported side effects were minor, with 0.7% of the patients reporting itching, 0.6% reporting redness, 0.5% reporting skin irritation, 0.4% pain, and 0.2% eczema.

Topica's intellectual property is robust, says Vontz. Three patent applications for new formulations of luliconazole have been internationally filed and if issued will expire in 2026. Earlier this year the start-up also filed a new provisional patent application for additional formulations that include a higher concentration of drug and method-of-use claims for the treatment of onychomycosis. If awarded, those patents should provide broad protection from generic competition until 2029.

Vontz's immediate goal is to bring in a new investor and announce the second close of the first tranche of its Series A financing. Once the money is in hand, work will shift to first-in-man studies of luliconazole in onychomycosis, while Topica also looks for a potential partner for the tinea pedis indication. (For the moment Topica plans to retain luliconazole rights for onychomycosis.)

Importantly, Topica is already trying to diversify beyond luliconazole. Because of Vontz's background and therapeutic area expertise, he is looking to in-license another topical agent, potentially for atopic dermatitis, in the coming months. More than likely he will go back to Nakamura's extensive contacts within the Japanese pharmaceutical industry to identify another potentially exciting asset for development. **Ellen Foster Licking.**