



Tackling rare disease forms

Drs Christopher Schaber and **Richard Straube** are working to change the prognosis for patients with rare and poorly treated diseases. They introduce their company Soligenix and its investigational drug, for the treatment of cutaneous T-cell lymphoma

How has Soligenix positioned itself as a biotechnology business?

The company is focused on the late-stage development of products for rare diseases in which there is an unmet medical need. It has expertise in the clinical development of these types of products and looks to partner its development efforts with both the National Organization for Rare Disorders (NORD) and specific patient advocacy groups, such as the Cutaneous Lymphoma Foundation. We have been successful in obtaining non-dilutive funding for these programmes through government contracts and grants as well as through US Food and Drug Administration (FDA) Orphan Drug funding programmes that support rare disease development. In addition, we remain active on the business development front in identifying potential partners for our pipeline programmes.

Soligenix is developing an investigational drug for the treatment of cutaneous T-cell lymphoma (CTCL). What symptoms do patients with CTCL experience?

Although CTCL includes a large number of specific cancers, each with its own natural

history, the majority of patients have a condition known as mycosis fungoides (MF). MF is a disease characterised by skin lesions that can start as

red rash-like patches that may progress to raised plaques or even tumours. For many patients, the disease will have an indolent course with frequent recurrences of their skin involvement over decades. For other patients, the disease can be much more serious with extensive skin involvement and spread of the cancerous cells into the blood and internal organs. This progression can be fatal. It is often difficult to predict which patients will develop severe disease and which will have a more benign course.

Could you discuss the problems with photoactivated drugs in the early stages of CTCL?

The most widely used photoactivated drug for CTCL is psoralen. This requires activation with ultraviolet A in a treatment that is usually referred to as PUVA. Psoralen is a known mutagen and ultraviolet A light (ie. one of the damaging portions of sunlight) is a known carcinogen that promotes skin cancers. PUVA is not FDA approved for treatment of CTCL but has been approved for other skin conditions, such as psoriasis. Unfortunately, because of its negative side effect profile, PUVA carries an FDA 'black box' warning label for heightened

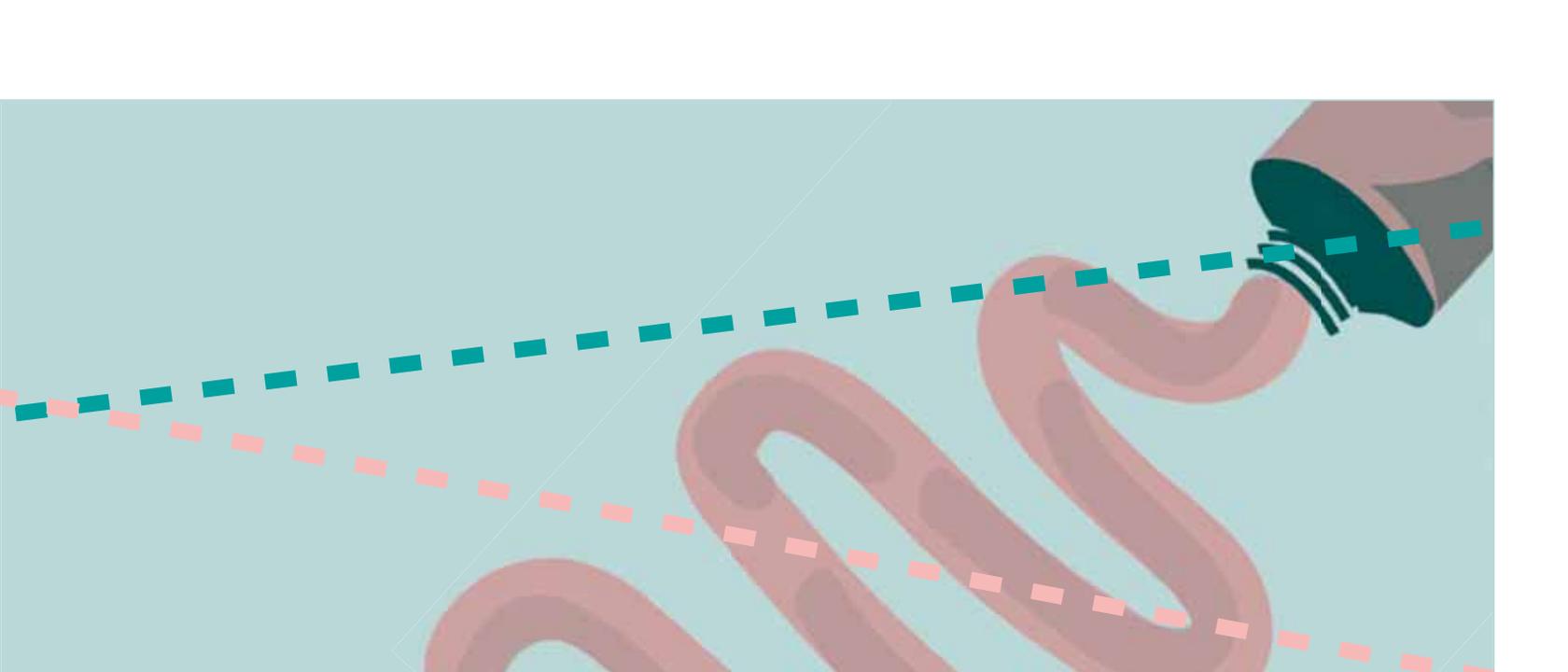
risk of secondary skin cancers such as melanoma, which appear to be increased with increasing doses of the drug and a growing number of treatments received.

What sets Soligenix's novel treatment for CTCL, SGX301, apart?

SGX301 is not mutagenic like most photoactive drugs. In addition, it is activated with safe, visible light that is not carcinogenic. As a result, treatment with SGX301 is anticipated to deliver improved or similar results as PUVA without the long-term cancer risks. This is obviously of critical importance in CTCL, where multiple treatments are required over decades to manage disease reoccurrence.

How do you imagine SGX301 could impact prognosis for CTCL if it became a standard treatment for the disease?

It is generally believed that earlier treatment of CTCL will have a positive impact on progression of the disease, although there are no conclusive data to date. It is important, however, to understand that the emotional and social impact of the disease can be devastating for many patients and a safe alternative to PUVA is likely to allow earlier and more proactive treatment for many of the patients currently receiving no therapy under a 'watch and wait' approach to their disease.



Renewed hope for novel treatments

Soligenix develops novel treatments for rare diseases where there is an unmet medical need. The biotechnology company has recently made strides in the development of a treatment for cutaneous T-cell lymphoma, which will shortly enter phase III clinical trials



CUTANEOUS T-CELL LYMPHOMA (CTCL) is a rare form of non-Hodgkin's lymphoma that affects approximately 30,000 people in the US every year and a comparable number in Europe. CTCL is a disease resulting from mutations and the consequent aberrant function of T-lymphocytes. CTCL includes many different specific types of cancer, but common to most of these patients is a condition called mycosis fungoides – lesions of the skin, which arise as a consequence of malignant T-cells migrating into the skin. These lesions may start as a simple rash, but can eventually form plaques and tumours before spreading to other parts of the body.

CTCL is slow to develop, persistent and relapsing. Current treatments are far from ideal, requiring multiple drug courses, which are administered over several decades. They suppress symptoms but do not cure the disease. For most patients, the disease remains in its early stages, but this is not always the case and many acquire the progressive form of the disease, which can ultimately be fatal. Treatments for patients with the disease are scarce; there are no approved first line treatments for patients with early stage CTCL

PROBLEMS WITH CURRENT CARE

The few treatments currently prescribed for CTCL carry substantial side effects and are potentially harmful with long-term use. Since

the condition lasts for and must be treated over a long time, side effects can be significant and long term. For many, the risks associated with treatment outweigh the potential benefit and this means that patients can remain untreated for a long time after diagnosis. Only once the condition has become severe enough to justify treatment, will patients be given one of three typical treatment options. One option is the photosensitive and mutagenic drug psoralen in combination with ultraviolet A light treatment (PUVA). This treatment potentially leads to an increase in skin carcinomas and melanomas. Steroids are also administered but these are not very successful at treating the condition and their use over long periods of time leads to skin atrophy. Topical chemotherapeutic agents are also prescribed, which are usually mutagenic and therefore also harmful to the patient, especially when administered chronically.

BRIDGING THE GAP

Soligenix is a biopharmaceutical business that aims to bridge the treatment gap for rare diseases such as CTCL: "Soligenix is focused on the late-stage development of products for rare diseases in which there is an unmet medical need," Drs Christopher Schaber and Richard Straube, of Soligenix, explain.

The treatment the researchers have been developing for CTCL, SGX301, is a first-in-class photodynamic therapy that circumvents the

SOLIGENIX

OBJECTIVE

To enhance the late-stage development of products for rare diseases that have an unmet medical need.

KEY COLLABORATORS

Dr Rasappa Arumugham, Vice President, Biopharmaceutical Development; **Dr Oreola Donini**, Senior Vice President and Chief Scientific Officer; **Joseph Warusz**, Vice President, Finance and Acting Chief Financial Officer, Soligenix, Inc., USA

PARTNERS

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DR CHRISTOPHER SCHABER has over 25 years' experience in the pharmaceutical and biotechnology industry. He has been President, Chief Executive Officer and Director

of Soligenix, Inc. since 2006. He was also appointed Chairman of the Board in 2009. From 1998 to 2006, Schaber served as Executive Vice President and Chief Operating Officer of Discovery Laboratories, Inc. From 1996 to 1998, he was a co-founder of Acute Therapeutics, Inc., and served as its Vice President of Regulatory Compliance and Drug Development. Schaber received a BA degree from Western Maryland College, an MS degree in Pharmaceutics from Temple University School of Pharmacy, and a PhD in Pharmaceutical Sciences from the Union Graduate School.



DR RICHARD STRAUBE has over 35 years' experience in both academia and industry. He is a board-certified paediatrician with clinical research experience in host-response

modulation, most notably with Centocor, Ohmeda Pharmaceuticals, INO Therapeutics and Stealth Peptides, Inc. He was the founding Chief Medical Officer for INO Therapeutics. Straube received his medical degree and residency training at the University of Chicago, completed a joint adult and paediatrician infectious diseases fellowship at the University of California, San Diego (UCSD), and completed training in clinical trial design at the London School of Hygiene and Tropical Medicine.

common problems associated with other treatments currently on the market. SGX301 shares its mechanism of action with the leading treatment, psoralen. Both drugs are applied topically to the skin, and kill cancer cells by producing oxygen free radicals in response to stimulation with light. However, SGX301 has a key advantage: it can be activated by stimulation with non-harmful fluorescent visible light. It owes this to its active component, a safe, synthetic version of hypericin, which is a particularly potent photosensitiser that can be activated using harmless fluorescent light bulbs such as those commonplace in offices and homes: "As a result, treatment with SGX301 is anticipated to deliver improved or similar results as PUVA without the long-term cancer risks," Schaber and Straube explain. "This is obviously of critical importance in CTCL, where multiple treatments are required over decades to manage disease reoccurrence."

SGX301 is a first-in-class photodynamic therapy that circumvents the common problems associated with other treatments currently on the market

DRUGS ON TRIAL

So far, high doses of synthetic hypericin have been tested in patients with viral infections and solid tumours. In this study it was found that the only side effects were related to the photosensitisation mechanism of the drug. In healthy volunteers, the topical form of the drug was tested and the only side effect was photosensitivity, which progressed alongside increasing drug dose and light treatment:

"Thus, there is minimal concern that SGX301 will have any unanticipated systemic side effects," Schaber and Straube state.

Phase II trials, which test drug efficacy and further evaluate safety in patient volunteers, consisted of SGX301 drug treatment followed by visible light therapy 24 hours later. A treatment response was defined as a reduction in lesion size of at least 50 per cent, and they found a statistically significant effect of the drug in comparison to placebo. 58 per cent of cases where patients were treated with SGX301 had a treatment response, compared with only 8 per cent in the placebo control group. Soligenix now seeks to push forward into a highly powered, pivotal phase III trial, which has already been designed and accepted by the FDA, with the first patients set to enroll in the next few months. "It is also important to note, that SGX301 has received both orphan drug and fast-track designations from the FDA, which has the potential to accelerate its development," Straube asserts. "We anticipate SGX301 will continue to qualify for comparable designations outside the US in the coming months."

FUTURE GOALS

The team's work is likely to transform treatment quality for patients in two ways. Firstly, those who currently receive treatments such as PUVA will benefit from the removal of side effects associated with UV irradiation. Secondly, the pool of patients who can benefit from any treatment at all will increase. This is because 10 to 20 per cent of patients with CTCL do not receive any treatment as the risks of harm associated with the treatment options outweigh any potential benefit. By reducing potential side effects, more patients can be treated earlier, and overall disease burden can be reduced. This is a dramatic shift in a field where current treatments are thought to do more harm than good, and where the development of drugs for rare conditions is considered to be economically and scientifically challenging.

