



TopiVert announces positive results from the Phase 1 study with its oral formulation of TOP1288 for the treatment of ulcerative colitis

London, UK, 8 January 2018: TopiVert Pharma Ltd (“TopiVert” or the “Company”), a clinical-stage biotechnology company developing Narrow Spectrum Kinase Inhibitors (NSKIs) as novel, locally-acting medicines for the treatment of chronic inflammatory gastrointestinal and ocular diseases, today announces positive data from its Phase 1 study (TV03) with its oral formulation of TOP1288 for the treatment of ulcerative colitis (UC).

UC is a form of inflammatory bowel disease (IBD) affecting the colon. As many as 40% of patients fail to respond to current drug therapy, which is also often poorly tolerated, and around 15% of patients may still require surgical removal of the colon to manage the disease. TOP1288 is a NSKI developed by TopiVert that targets several important kinases in inflammatory cells, leading to synergistic inhibition of key signalling pathways involved in innate and adaptive immunity. TOP1288 also has very low systemic bioavailability such that its activity is confined to the site of active disease in UC patients and thus provides an improved safety and tolerability profile.

TV03 was a randomised, double-blind, placebo-controlled Phase 1 study to assess safety, tolerability, pharmacokinetics and pharmacodynamic responses to single and multiple oral doses of TOP1288. Employing an innovative trial design, individual subjects received serial sigmoidoscopies so that multiple colon biopsies could be obtained to allow the direct measurement of tissue drug concentrations, as well as markers of target engagement and pharmacodynamic responses, from colon tissue.

The results demonstrated that TOP1288 was being delivered to the colon with drug detected in tissue biopsies up to 36 hours after last dose. In addition, dose-dependent positive effects on markers of target engagement and biomarker responses were seen (in cells taken from colon tissue), indicating that the measured concentrations were pharmacologically relevant. TOP1288 was also found to be safe and well tolerated when administered orally with minimal systemic absorption being noted, confirming results from prior studies.

In parallel, a proof of mechanism study in UC patients comparing TOP1288 and placebo, both delivered as a liquid enema, has also reported. Clinically relevant changes from baseline were seen in the TOP1288 arm for all endpoints but due to a large response in the placebo arm, including for centrally read endoscopic endpoints, the efficacy assessment was uninterpretable.

Based upon the strong data from the TV03 study, TopiVert is preparing to progress the oral TOP1288 formulation into a proof of concept study in UC.

Ajay Duggal, TopiVert's Chief Medical Officer, commented: "We are delighted with the clinical progress made with our TOP1630 and TOP1288 NSKI programmes in ophthalmology and IBD respectively. Our recently reported strong proof of concept data for TOP1630 in dry eye syndrome validates our NSKI technology in the treatment of inflammatory disease. For our IBD program, using an innovative trial design, we have successfully demonstrated that drug can be delivered into the colon tissue at pharmacologically relevant concentrations. This is an exciting time for TopiVert as we look forward to progressing the clinical development of both our lead programmes in areas of high unmet medical need."

Professor Simon Travis, (Professor of Clinical Gastroenterology, University of Oxford), commented: "These results put TopiVert in a unique position in the development of oral topical anti-inflammatories for treatment of IBD. The colon biomarker and PK data generated with the oral formulation of TOP1288, together with the fact that there was minimal systemic absorption, demonstrate effects through truly local action. This phenomenon has not been demonstrated before. Although efficacy still needs to be established, the results obtained strongly support progression to the next stages of development"

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About TopiVert

TopiVert is a clinical-stage biotechnology company developing narrow spectrum kinase inhibitors as novel, locally-acting medicines for the treatment of chronic inflammatory gastrointestinal (GI) and ocular diseases. The Company's lead GI programme, TOP1288 for the treatment of ulcerative colitis, has recently demonstrated strong safety, PK and PD data in a Phase 1 study with an oral formulation. The Company's lead ophthalmology programme, TOP1630 for dry eye syndrome (DES), has also reported compelling results in a Phase 1/2a proof of concept study in the US. Current therapies for these debilitating inflammatory diseases provide inadequate long-term control in a high proportion of patients and considerable unmet medical need remains. The Company commenced operations in early 2012 and its investors include SV Health Investors, Touchstone Innovations, NeoMed and Johnson & Johnson Innovation – JJDC, Inc.

About Narrow Spectrum Kinase Inhibitors (NSKIs)

NSKIs are novel small molecules characterised by broad, potent anti-inflammatory activity and minimal systemic exposure. Specifically, NSKIs are potent inhibitors of a select range of pivotal kinases involved in inflammatory cascades of both innate and adaptive immunities. Simultaneous targeting of multiple inflammatory components leads to a synergistic activity profile with broad anti-inflammatory

effects. NSKIs are designed to have low systemic bioavailability so that their exposure to the body's healthy tissues is reduced, thereby providing enhanced safety and tolerability. Together, these attributes make NSKIs ideal treatment candidates for chronic inflammatory diseases where long term therapy demands a sustained effect accompanied by excellent safety and tolerability.

About IBD and ulcerative colitis

Inflammatory bowel disease (IBD) is a term used to describe several diseases that involve inflammation of the gastrointestinal tract. The two most common forms of IBD, Crohn's disease and ulcerative colitis, together affect over 4 million people worldwide. They are both chronic relapsing conditions that cause bloody diarrhoea, abdominal pain and significant reductions in a patient's quality of life. While their causes are not fully understood, these diseases are characterised by an abnormal inflammatory reaction that leads to damage of the intestinal wall.

Current treatments for ulcerative colitis involve administration of oral, rectal or intravenous/subcutaneous anti-inflammatory and immunomodulatory therapies, including biologics. Despite these products being effective in treating active disease in some patients, their long-term use is often hampered by safety and tolerability issues. Furthermore, at least 40% of patients have poorly controlled disease and around 15% may require surgery to manage the disease.

About Dry Eye Syndrome

Dry eye syndrome (DES), also known as dry eye disease, keratoconjunctivitis sicca (KCS) or keratitis sicca, is an inflammatory eye disease characterised by dryness on the surface of the eye. It is usually a chronic problem and it can be debilitating in severe cases. It is also one of the most common eye diseases, with almost 19 million sufferers in the US alone and over 300 million worldwide¹. DES becomes more common with age, with a third of elderly people suffering from this ailment.

¹ Market Scope®, 2013 Report on the Global Market for Dry Eye Products