TopiVert demonstrates proof of concept in Phase 1/2a study of TOP1630 in the treatment of dry eye syndrome

- ***TOP1630 improved multiple symptom and sign endpoints in both environmental and controlled challenge settings***
- ***TOP1630 demonstrated excellent safety and placebo-like tolerability and comfort profiles***

London, UK, 28 November 2017: 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 (GI) and ocular diseases, today announces successful results from its Phase 1/2a proof of concept study of TopiVert's TOP1630 ophthalmic solution for the treatment of dry eye syndrome (DES). TOP1630 improved multiple symptom and sign endpoints in both an environmental setting and in the Controlled Adverse Environment (CAE®; Ora, Inc.) challenge. Furthermore, TOP1630 demonstrated excellent safety and placebo-like tolerability and comfort profiles.

NSKIs target key kinases in the signalling cascade in inflammatory cells, leading to synergistic inhibition of pathways involved in innate and adaptive immunities. The Company's lead NSKI for ophthalmology, TOP1630, is retained in target inflammatory cells in the cornea and conjunctiva when administered as eye drops and has only minimal systemic exposure, making it an ideal topical eye therapy.

The Phase 1/2a proof of concept study was a randomised, double-masked, parallel-group trial of 0.1% TOP1630 or placebo topical ophthalmic solution TID (three times daily) conducted in 61 subjects with moderate to severe DES in the US who were randomised to 28 days treatment. Safety assessments included adverse event (AE) query, slit-lamp biomicroscopy and visual acuity. Efficacy assessments included environmental and CAE® change in DES symptoms and ocular surface staining.

In the study, TOP1630 delivered statistically significant results across multiple signs and symptoms endpoints in DES starting at day 15, the first study assessment point. All analyses reported are pre-specified, (i.e., no *post hoc* or subgroup analyses). Symptoms showing significant improvements for TOP1630 versus placebo included improvement in worst DES symptom (diary, $p=0.03$), ocular discomfort ($p=0.02$ CAE only), grittiness/foreign body sensation (on four independent assessment scales, each $p<0.05$) and ocular pain ($p=0.02$). Total ocular surface (all regions), corneal sum and conjunctival sum staining improved with TOP1630 compared to placebo (each $p<0.05$).

There were no safety findings, with TOP1630 shown to be safe and very well tolerated with a placebo-like profile. Importantly, this included no noticeable instillation site pain and discomfort.

Professor John Sheppard, Professor of Ophthalmology, Eastern Virginia Medical School said: *"The TOP1630 study generated frontline data showing consistent effects across both signs and symptoms,*

with placebo-like tolerability. I believe these characteristics define a very promising benefit–risk profile, and therefore highly likely to prove beneficial to patients and desirable for prescribing eye care providers."

DES is a common inflammatory disorder of the front of the eye associated with considerable morbidity. A major unmet medical need remains for a more effective and better tolerated therapy for this debilitating disorder which affects over 300 million worldwide[1]. TOP1630 has the potential to provide rapid symptomatic relief together with long term efficacy in the treatment of the signs and symptoms of DES.

Ajay Duggal, TopiVert's Chief Medical Officer, commented: *"TOP1630, our lead NSKI in ophthalmology, has delivered compelling data in a Phase 1/2a proof of concept study for the treatment of dry eye syndrome. We believe that the consistency of effect demonstrated across a range of sign and symptom endpoints, from multiple assessment scales and all from pre-specified analyses, coupled with the placebo-like tolerability profile sets a new benchmark for DES treatments. This exciting programme is now ready for late stage development in an area of high unmet medical need."*

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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 completed a Phase 2a proof of concept study with a rectal formulation and a Phase 1 study with an oral formulation. The Company's lead ophthalmology programme, TOP1630 for dry eye syndrome (DES), has recently 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 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 worldwide[1]. 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