Onco3R Therapeutics Announces Completion of First Multiple Ascending Dose Cohort in Phase 1 Trial of Novel SIK3 inhibitor O3R-5671

Dosing of first MAD cohort in Phase 1 trial of O3R-5671 complete with no drug related adverse events

Pharmacokinetic profile demonstrates long half-life and low intersubject variability

Pharmacodynamic data from single ascending dose cohorts indicative of profound and sustained TNFα inhibition at low doses

Leuven, Belgium. December 3, 2025. Onco3R Therapeutics, a clinical-stage immunology and oncology biotech company dedicated to transforming patients' lives with best-in-class medicines, today announced the successful completion of the first multiple ascending dose (MAD) cohort of subjects in the Phase 1 trial of its novel SIK3 inhibitor O3R-5671. Four single ascending dose (SAD) cohorts have also been completed.

In each of the SAD cohorts, six subjects received a single oral dose of O3R-5671 between 5mg - 35mg. In the first MAD cohort, six subjects received 5mg O3R-5671 once a day for 14 days. Pharmacokinetic and safety data support investigating a higher dose in the second MAD cohort of the study, which is planned to initiate in early December.

Pharmacokinetic data generated to date demonstrate that O3R-5671 has a flat PK profile, a highly attractive attribute of this drug candidate, with a long half-life. Drug exposure in the SAD cohorts is dose proportional with low variability between subjects. A food effect cohort demonstrated that O3R-5671's PK profile is consistent with or without food indicating that there will be no food restrictions in future patient clinical studies. Data from the first MAD cohort demonstrate that O3R-5671's attractive PK profile is maintained at day 14 with drug exposure approximately two times higher than the same single 5mg dose.

The safety profile of O3R-5671 is highly encouraging with a low rate of drug related adverse events reported to date. Importantly, no drug related adverse events have been reported in the 25 and 35mg SAD cohorts or in the 5mg MAD cohort and there have been no clinically significant abnormalities on ECG, vital signs or physical examination.

Pharmacodynamic data from the SAD cohorts demonstrate that O3R-5671 potently inhibits TNFα in a dose dependent manner and that maximal inhibition (approximately 90%) is achieved between 25mg and 35mg, the highest dose that has been examined to date. Furthermore, drug levels 24 hours after dosing at 25 and 35mg doses maintained inhibition of TNFα by more than 75%.

"We are very encouraged by the PK, safety and PD data that have been generated to date in the first in human study of O3R-5671" said Pierre Raboisson, PhD, CEO and Founder of Onco3R Therapeutics. "These data exceed the expectations we had for O3R-5671 before we entered the clinic, and we are excited about the prospect of completing this important study and embarking on patient studies in 2026. In addition to potently inhibiting TNFα, our non-

clinical data also demonstrate that O3R-5671 potently inhibits IL-23 and IL-12 which, along with TNFα, are implicated in the pathogenesis of a variety of autoimmune diseases including ulcerative colitis, Crohn's disease and psoriasis."

He added, "We are highly motivated to discover and develop drugs that will make significant improvements to the lives of patients living with autoimmune diseases and cancer. Specifically for patients with autoimmune diseases, O3R-5671 has the potential to become a safe, effective and convenient therapeutic option and we are looking forward to its continued development."

About O3R-5671
O3R-5671 has been designed based on more than 12 years of preclinical and clinical data on SIK inhibitors for autoimmune diseases. O3R-5671 is a highly selective SIK3 inhibitor, which has been designed to avoid the toxicities associated with inhibiting SIK1 and SIK2. Furthermore, O3R-5671 does not inhibit other kinases and has demonstrated a highly attractive profile in an extensive safety panel. Preclinical data demonstrated that O3R-5671 inhibits the release of the pro-inflammatory cytokines TNFα and IL-23 and promotes the release of the immunomodulatory cytokine IL-10. These data, along with data from animal models of autoimmune diseases, indicate that O3R-5671 has the potential to treat a variety of autoimmune diseases including ulcerative colitis, Crohn's Disease, psoriasis, psoriatic arthritis and rheumatoid arthritis.

About the Phase 1 trial of O3R-5671
The first-in-human study is evaluating O3R-5671 in healthy volunteers using a single ascending dose (SAD) and multiple ascending dose (MAD) design. In addition to assessing safety and pharmacokinetics, the trial includes extensive biomarker tests that will provide insights into how O3R-5671 modulates immune responses. The results from the trial will inform the design of subsequent patient trials across a range of autoimmune diseases, which are planned to commence in 2026.

About Onco3R Therapeutics
At Onco3R Therapeutics, we are driven by our purpose to transform the lives of patients with autoimmune diseases and cancer through precision-designed, best-in-class therapies. With over 150 years of combined R&D experience, our team brings deep expertise in disease biology, drug discovery & development, and translational science. We focus on clinically validated targets and select the right therapeutic modality, small or large molecules, to address the underlying disease biology with best-in-class therapies. Our mission is to develop safer, more effective medicines in oncology and immunology that truly make a difference for patients. By integrating learnings from past clinical challenges and applying cutting-edge technologies, we aim to de-risk clinical development and accelerate the delivery of innovative treatments with real-world impact. The company is based in the biotech cluster in Leuven, Belgium. For more information, visit www.onco3r.com or follow us on LinkedIn.