Onco3R Therapeutics reports first pre-clinical data from its best-in-class precision oncology portfolio at the 2025 AACR-NCI-EORTC symposium

- *Three posters to be presented featuring pre-clinical data of potential best-in-class FGFR3 selective inhibitor, SMARCA2 selective inhibitor, and P53 Y220C reactivator*
- *Candidates for FGFR3 and SMARCA2 programs identified: IND enabling studies anticipated in mid-2026*

Leuven, Belgium, October 22, 2025. Onco3R Therapeutics, a clinical-stage immunology and oncology biotech company dedicated to transforming patients' lives with best-in-class medicines, today announced that it will present preclinical data from its FGFR3, SMARCA2 and P53 Y220C small molecules programs in 3 posters at the EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics, taking place October 22-26, 2025, in Boston.

"First generation precision medicines are often suboptimal in the clinic due to low target coverage, off-target toxicity and emergence of resistance. At Onco3R, our vision is to design best-in-class medicines to address the unmet needs left by first generation drugs and unlock the full potential of therapeutic targets" said François Gonzalvez, PhD, CSO and co-Founder of Onco3R Therapeutics.

"We are thrilled to present the first preclinical data from our lead oncology programs FGFR3, SMARCA2 and P53 Y220C. Each program has identified best-in-class molecules which offer the potential to deliver transformational efficacy and improved tolerability for patients. Our FGFR3 and SMARCA2 candidates, G-012 and G-141 respectively, have reached the optimum potency and selectivity profile to mitigate dose-limiting toxicities while maintaining maximum target coverage. This has translated into robust anti-tumor activity *in vivo*. The poster presentations will highlight data supporting the advancement of these two candidates towards the clinic, as well as the discovery of unique small molecule P53 reactivators."

"These compelling preclinical results further validate our patient-centric drug discovery approach, which integrates deep translational science with rational, structure-based and AI-augmented drug design", Pierre Raboisson, PhD, CEO and co-Founder of Onco3R Therapeutics said. "We look forward to advancing these two candidates and remain on track to initiate IND-enabling studies in mid-2026. The identification of these candidates, alongside the continued clinical progress of our SIK3 inhibitor O3R-5671 in autoimmune indications, reinforces Onco3R's strong strategic position. With a robust pipeline and clear execution momentum, we are confidently advancing toward our next value-driving milestones."

Presentation details

Title: Discovery of Best-in-Class FGFR3 small molecule inhibitors with high isoform selectivity and activity against gatekeeper mutations
Session:
Session: Poster Session C
Session Date and Time: Saturday, October 25, 12:30-4pm
Presenting author: Sandrine Vendeville, PhD

Key findings from preclinical studies include:

- G-012 demonstrated best-in-class potency and selectivity with favorable drug-like properties.

- Based on translational modelling, the compound reached the optimal selectivity against other FGFR isoforms to mitigate off-target toxicity and maintain maximal target coverage.
- G-012 showed robust anti-proliferative activity in FGFR3-driven cancer cells and induced significant tumor regression *in vivo*.
- G-012 is currently advancing in 14 days toxicology studies.
- IND-enabling studies are anticipated in mid-2026.

Title: Discovery of novel SMARCA2 small molecule inhibitors with best-in-class potency and selectivity for the treatment of SMARCA4-mutant cancers
Session: Poster Session C
Session Date and Time: Saturday, October 25, 12:30-4pm
Presenting author: Lijs Beke, PhD

Key findings from preclinical studies include:

- G-141 combined best-in-class cellular potency and selectivity to allow optimal target coverage and unlock the full therapeutic potential of SMARCA2 inhibition.
- The compound showed synthetic lethality in SMARCA4-deficient cells and induced robust anti-tumor activity *in vivo* without signs of SMARCA4-related toxicity.
- G-141 showed favorable drug-like properties and is currently advancing in 14 days toxicology studies.
- IND-enabling studies are anticipated in mid-2026.

Title: Discovery of a Best-in-Class small molecule p53 Y220C reactivator: Breaking through the potency ceiling
Session: Poster Session C
Session Date and Time: Saturday, October 25, 12:30-4pm
Presenting author: François Gonzalvez, PhD

Key findings from preclinical studies include:

- Onco3R patient-centric drug discovery approach identified unique small molecule P53 reactivators with best-in-class cellular potency.
- Onco3R leads exhibit the optimal potency and residence time to induce deep and sustain target engagement and fully unlock the tumor suppressive function of P53 in cells.
- This translated into robust anti-proliferative activity in P53 Y220C mutant cancer cell lines (single digit nanomolar IC50s) and tumor regression in a Y220C P53 mutant xenograft model.
- Further characterization of the lead candidates is ongoing.

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.

About O3R-5671

O3R-5671 has been developed 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, 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 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. O3R-5671 is currently being investigated in a first-in-human study in healthy volunteers with a SAD-MAD design.