FoRx Therapeutics Initiates First-in-Human Trial with Novel Anti-Cancer Drug FORX-428 Targeting DNA Damage Response

- Novel PARG inhibitor FORX-428 has shown best-in-class characteristics in preclinical studies
- Trial initially taking place in the U.S., following IND clearance
- Initial data expected in mid-2026 from open-label Phase 1 study in advanced solid tumors
- Milestone in drive to redefine cancer treatment with precision oncology therapy

Basel, Switzerland – August 11, 2025 – FoRx Therapeutics, a clinical-stage biotechnology company developing precision anti-cancer therapeutics, today announced the dosing of the first patient in a first-in-human clinical study of FORX-428, a novel PARG inhibitor designed to target and disrupt the DNA Damage Response (DDR) in advanced solid tumors.

The discovery that distinct genetic subsets of cancer are exceptionally vulnerable to drugs that interfere with the DDR led to the approval of PARP inhibitors more than 10 years ago, transforming cancer treatment. By pursuing a next-generation DDR target, called PARG, FoRx is seeking to further advance this strategy. PARG inhibition holds tremendous promise as a treatment option for patients whose cancers do not or no longer respond to PARP inhibitors.

Tarig Bashir, CEO of FoRx Therapeutics, said: "FoRx is built on the disruptive potential of PARG inhibition as a therapeutic strategy. FORX-428 has demonstrated exquisite anti-tumor efficacy in multiple preclinical *in vivo* tumor models, suggesting best-in-class potential. The entry of FORX-428 into clinical development is a major milestone in our mission to redefine cancer therapy by offering better treatment options for patients."

An initial data readout from the trial is expected by mid-2026. The open-label study, initially taking place in the United States, is evaluating safety, tolerability, pharmacokinetics, and preliminary efficacy in patients with advanced solid tumors who have exhausted standard-of-care options.

Manish R. Sharma, MD, Co-Director of Clinical Research at START Midwest and Principal Investigator on the trial said: "We are excited to have dosed the first patient with cancer in collaboration with FoRx Therapeutics. There is an unmet need to develop new therapies for advanced cancer patients with distinct DNA damage repair deficiencies or high replication stress. The PARG inhibitor, FORX-428, has a novel mechanism of action, and preclinical studies have shown it had impressive activity in cancers resistant to chemotherapy and PARP inhibitors."

FORX-428 received Investigational New Drug (IND) clearance from the U.S. Food and Drug Administration (FDA) on June 13, the first patient first visit (FPFV) was on July 22 and the first patient was dosed on August 6.

Jens Wuerthner, MD, PhD, Chief Medical Officer of FoRx Therapeutics, said: "The efficient pace from IND clearance to dosing the first patient is a testament to the dedication and coordination of our clinical, regulatory, operational, and research teams, including the team at START Midwest. We are thrilled to have begun investigating FORX-428 in patients with advanced cancer and believe this compound could be a significant advancement in solid tumor therapy."

FORX-428 is a proprietary, orally available small molecule drug designed to inhibit poly (ADP-ribose) glycohydrolase (PARG) to cause tumor cell death. PARG is a key DNA repair enzyme necessary for the survival of certain genetically defined cancers, harboring specific DDR deficiencies or high replication

stress. Preclinical studies demonstrated FORX-428 had robust anti-tumor activity across multiple solid tumor types underscoring the novel compound's outstanding potential in both monotherapy and combination settings. Importantly, FORX-428 was well tolerated, demonstrating drug-like pharmacology and a favorable safety profile.

FoRx Therapeutics (Basel, Switzerland) is a privately held clinical-stage biotechnology company pioneering precision therapeutics targeting the DNA Damage Response in treatment-resistant cancers. Its pipeline includes several small molecule programs addressing distinct DNA repair mechanisms, with the lead product candidate FORX-428, an oral small molecule PARG inhibitor, in Phase 1 testing to treat advanced solid tumors.

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