Rani Therapeutics Announces Positive Topline Results from Phase 1 Study of RT-102 in Osteoporosis

August 10, 2022

- RT-102 was generally well-tolerated, with no RaniPill™-related adverse events -

- Bioavailability of PTH delivered via the RaniPill was found to be 300-400% greater than PTH delivered via subcutaneous injection -

- Improved RaniPill design enabled 95% drug delivery success rate -

SAN JOSE, Calif., Aug. 10, 2022 (GLOBE NEWSWIRE) -- Rani Therapeutics Holdings, Inc. (“Rani Therapeutics” or “Rani”) (Nasdaq: RANI), a clinical-stage biotherapeutics company focused on the oral delivery of biologics and drugs, today announced positive topline results from the single-ascending dose portion of its Phase 1 clinical study of RT-102, a RaniPill capsule containing a proprietary formulation of human parathyroid hormone (PTH) analog PTH (1-34) for the potential treatment of osteoporosis (“Study Part 1”). Study Part 1 achieved all of its endpoints, with RT-102 being generally well-tolerated and demonstrating high oral bioavailability of Rani’s PTH analog.

“I am delighted to share the results of Part 1 of our Phase 1 study of RT-102, which demonstrated not only that RT-102 was generally well-tolerated, but also that the bioavailability of PTH delivered using the RaniPill was greater than the bioavailability of PTH delivered subcutaneously in this study – specifically RT-102 delivered PTH with between 300-400% greater bioavailability than subcutaneous Forteo® (teriparatide) in the study. Based on these results, we believe RT-102 has the potential to be an effective oral treatment option for patients with osteoporosis comparable to the current injectable standard of care,” said Talat Imran, Chief Executive Officer of Rani. “Importantly, this marks the first results of our second Phase 1 clinical trial, following on the positive results we previously announced for RT-101, the RaniPill capsule containing octreotide. Our RaniPill platform has now been tested in more than 80 healthy volunteers, and the incremental enhancements we have made to the RaniPill design have further increased drug delivery success rate. We plan on sharing these results with the U.S. Food and Drug Administration and, subject to a successful IND filing, initiating a Phase 2 trial for RT-102 in the U.S. in 3Q 2023.”

The single-center, open label, Study Part 1 of RT-102 was conducted in Australia. The study evaluated the safety, tolerability, and pharmacokinetics (PK) of RT-102 in healthy adult female volunteers. Of the 39 Of the 39 participants, 15 were administered RT-102 containing a single 20µg dose of PTH and 14 were administered RT-102 containing a single 80µg dose of PTH, while a control group of 10 participants received a single 20µg subcutaneous injection (SC) of Forteo (teriparatide), a commercial formulation of PTH for SC administration. The endpoints of the study were safety and tolerability, and measurements of serum concentrations of RT-102 in healthy adult female volunteers.

Phase 1 Topline Results

Safety Data

- RT-102 was generally well-tolerated, with no RaniPill-related adverse events (AEs) observed in study participants:
  - 0% (0/15) of participants dosed with RT-102 20µg experienced drug-related AEs.
  - 14% (2/14) of participants dosed with of RT-102 80µg experienced drug-related AEs.
  - 50% (5/10) of participants dosed with 20µg of Forteo SC experienced drug-related AEs.
  - There were no serious adverse events (SAEs) noted during Study Part 1.

Per protocol, in instances where the RaniPill capsule did not exit the stomach within 7 hours, participants were excluded from the study. Based on the exclusion criteria, three participants were excluded from Study Part 1, one of whom experienced bloating, and one additional subject was excluded due to vomiting the capsule intact. In all instances, the capsule remnants passed from all participants who ingested the RaniPill capsule.

Across our two clinical studies of the RaniPill platform (Phase 1 clinical study of RT-101, a RaniPill capsule containing octreotide, and Study Part 1 of RT-102), 81 subjects received the RaniPill capsule and no RaniPill-related AEs were observed in participants in the studies.

Pharmacokinetics

- Oral RT-102 (20µg and 80µg) delivered PTH with 300%-400% greater bioavailability than PTH delivered by Forteo SC (20µg).
- RT-102 20µg delivered PTH with lower, more sustained peak serum levels and higher area under the curve (AUC) than Forteo SC 20µg.

	Forteo SC 20µg	**RT-102 20µg**	**RT-102 80µg**
Cmax (pg/mL)	128 ± 20	98 ± 10	971 ± 223
Tmax (hr)	0.217	1.13	0.994
AUC (h*pg/mL)	126 ± 64	342 ± 36	2600 ± 649
Relative BA (5)	N/A	~300%	~400%

- Although the Study Part 1 did not include a head-to-head comparison with abaloparatide (Tymlos®), RT-102 80µg

demonstrated a PK profile similar to abaloparatide at 80µg as reported in the package insert for Tymlos. Specifically:

- abaloparatide at 80µg has a Cmax of 812 ± 118, while RT-102 80µg had a Cmax of 971 ± 223.
- abaloparatide at 80µg has an AUC of 1622 ± 641, while RT-102 80µg had an AUC of 2600 ± 649.

Device Performance

- Two versions of the RaniPill were used during Study Part 1: Version C, which was used in Rani's Phase 1 study of octreotide (which also utilized a Version A and Version B); and Version D, the latest iteration of the RaniPill.
- New RaniPill Version D demonstrated a higher drug delivery success rate than Version C:
  - 95% (20/21) of participants received successful drug delivery when ingesting RaniPill Version D.
  - 75% (6/8) of participants received successful drug delivery when ingesting RaniPill Version C.

The device performance analysis does not include participants excluded from the study per protocol, as drug delivery was not measured in such participants.

Rodent Study

In addition to Study Part 1 of RT-102, we also conducted a 6-week pharmacodynamic (PD) study of the RT-102 drug substance (DS) PTH (1-34) to evaluate the effect of daily RT-102 DS intraperitoneal (IP) injections on bone mineral density (BMD) in a rodent model of osteoporosis. The study compared two control groups of rodents undergoing sham surgery (N=10) and ovariectomy (OVX) (N=10) receiving no drug, to three OVX groups each dosed with 5 mcg/kg per day of either RT-102 DS (N=10), teriparatide (N=10), or abaloparatide (N=10).

The study found that, following six weeks of treatment:

- RT-102 DS increased BMD in a rat model of osteoporosis.
- RT-102 DS delivered via the RaniPill IP route of administration was biologically active comparable to SC injected PTH analogs.

Rani Therapeutics

Rani Therapeutics is a clinical stage biotherapeutics company focused on advancing technologies to enable the development of orally administered biologics. Rani has developed the RaniPill™ capsules, which are a novel, proprietary and patented platform technology, intended to replace subcutaneous injection or intravenous infusion of biologics and drugs with oral dosing. Rani has successfully conducted several preclinical and clinical studies to evaluate safety, tolerability and bioavailability using RaniPill capsules. For more information, visit ranitherapeutics.com.

Forward-Looking Statements

This presentation and the accompanying oral statements contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 as contained in Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act. Forward-looking statements are based on information available at the time those statements are made or on management's good faith beliefs and assumptions as of that time with respect to future events, and are subject to risks and uncertainties that could cause actual performance or results to differ materially from those expressed in, or suggested by, the forward-looking statements. In light of these risks and uncertainties, the forward-looking events and circumstances discussed in this presentation and the accompanying oral statements may not occur and actual results could differ materially from those anticipated or implied in the forward-looking statements. These risks and uncertainties include Rani Therapeutics Holdings, Inc.'s ("Rani," "we," "us," or "our") future financial performance, including our expectations regarding our revenues, cost of revenues, operating expenses, and our ability to achieve and maintain future profitability, those risks inherent in the preclinical and clinical development process and the regulatory approval process, the risks and uncertainties in commercialization and gaining market acceptance, our ability to complete development of the RaniPill® HC or any redesign and conduct additional preclinical and clinical studies of the RaniPill HC or any future design of the RaniPill to accommodate higher target payloads, the risks associated with protecting and defending our patents or other proprietary rights, the risk that our proprietary rights may be insufficient to protect our product candidates, the risk that we will be unable to obtain necessary capital when needed on acceptable terms or at all, our ability to enter into strategic partnerships and to achieve the potential benefits of such partnerships, competition from other products or procedures, our reliance on third-parties to conduct our clinical and non-clinical trials, our reliance on single-source third-party suppliers to manufacture clinical, non-clinical and any future commercial supplies of our product candidates, our ability to continue to scale and optimize our manufacturing processes by expanding our use of automation, our expectations regarding the period during which we qualify as an emerging growth company under the JOBS Act, the extent and duration of the COVID-19 pandemic and the conflict between Ukraine and Russia, our expectations regarding customer demand for our product candidates, increased regulatory requirements and other factors that are set forth in our filings with the Securities and Exchange Commission ("SEC"), including under the caption "Risk Factors" in our Quarterly Report on Form 10-Q for the quarter ended March 31, 2022, which was filed with the SEC on May 11, 2022, and our other public filings made with the SEC and available at www.sec.gov.

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