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Rezolute Presents RZ358 Clinical Data-Validated Model of the Pharmacokinetics and Glycemic Response in Congenital Hyperinsulinism at Pediatric Endocrine Society 2020 Annual Meeting

REDWOOD CITY, Calif., June 01, 2020 (GLOBE NEWSWIRE) -- **Rezolute, Inc. ("Rezolute" or "the Company")** (OCTQB:RZLT) recently announced that it has validated pharmacokinetic (PK) and pharmacodynamic (PD) models of its lead clinical asset, RZ358. Phase 2a data in adult and pediatric patients with congenital hyperinsulinism (HI) were shown to be predicted by the constructed models, and demonstrated that RZ358 raises glucose into a normal target range in a disease- and exposure-dependent manner, consistent with its known allosteric mechanism of action. The data were accepted as an oral presentation at the Pediatric Endocrine Society (PES) 2020 Annual Meeting, held virtually.

A Population PK (PopPK) and subsequent empirical exposure-response (ER) model were constructed using pooled PK, PD, and continuous glucose monitoring (CGM) data from all clinical studies conducted with RZ358. Pediatric simulations were performed using allometrically scaled PK parameters derived from adult data. The clinical data were well-described by the model, which was in turn used to characterize results from two completed Phase 2a open-label studies (X358602 and X358605) in adult (n=10) and pediatric (≥ 12 years; n=4) patients with congenital HI. In these studies, serial measurements of RZ358 and extended CGM were collected before and after intravenous administration of single (1, 3, 6, 9 mg/kg) and dual (3+6 mg/kg) doses of RZ358, respectively. PK/PD modeling was performed to describe RZ358 levels and exposure-response relationships in the CHI population.

Patient data was consistent with PK/PD models. First, empirical glucose levels were well-described in the model as a function of RZ358 levels, which were in turn dose-proportional and well-described by the PK model. RZ358's approximately 15-day half-life demonstrates the potential for once- to twice-monthly dosing. Observed pediatric PK fell within the ~90% prediction interval of simulated data, indicating that drug levels in children can be extrapolated from adults. Second, RZ358's exposure-response profile was disease state-dependent: RZ358 resulted in a sustained ~50% increase in glucose into a target range of 70-180 mg/dL in patients with pronounced baseline hypoglycemia (median subset; n=7), whereas the subset of patients with relatively normal overall baseline blood glucose (median; n=7) remained within their starting normoglycemic range. Lastly, the model demonstrated an exposure-response relationship; importantly, target concentrations (EC_{50}) were well-characterized and are predicted to be achieved at clinically-relevant dose regimens that are being tested in an ongoing Phase 2b study (RZ358-606 RIZE study) in

pediatric and adult patients with congenital HI.

“RZ358 is particularly well-suited as a potential treatment for congenital HI in both adults and children, as supported by congruence between its mechanism of action and its predictable results in a heterogenous patient group. The magnitude and timing of hypoglycemia varies among patients with congenital HI, so a built-in buffer provided by the unique mechanism of action of RZ358 may offer a differentiated way to safely counteract insulin activity, hypoglycemia, and hypoketosis without causing hyperglycemia,” said Brian Roberts, M.D., head of clinical development at Rezolute. “Results also demonstrated that drug levels in children with congenital HI can be extrapolated from adult data, which we will take into consideration as we advance into late-stage clinical development in increasingly younger patients with congenital HI,” he concluded.

A copy of the presentation, titled “Single Dose Studies of RZ358 in Patients with Congenital Hyperinsulinism: Results of Population PK/PD Modeling and Simulation in Adult and Pediatric Patients” is available here.

Ann Arbor Pharmacometrics Group (A2PG) conducted the PK/PD modeling referenced above.

About Rezolute, Inc.
Rezolute is advancing targeted therapies for rare, metabolic, and life-threatening diseases. Its lead clinical asset, RZ358, is in Phase 2b development as a potential treatment for congenital hyperinsulinism, a rare pediatric endocrine disorder. Its pipeline also includes RZ402, an orally available plasma kallikrein inhibitor in late-stage preclinical development for the treatment of diabetic macular edema, which the Company intends to advance into clinical trials after the IND has been filed. For more information, visit www.rezolutebio.com or follow us on Twitter.

About Congenital Hyperinsulinism
Congenital hyperinsulinism is a rare, genetic, pediatric endocrine disorder that leads to the inappropriate secretion of the hormone insulin by the pancreas. High levels of insulin in the blood result in episodes of low blood sugar or hypoglycemia with associated suppression of ketone bodies, the only other potential source of fuel to the glucose-dependent brain. Repeat episodes and/or dangerously low blood sugars increase the risk of neurological and developmental complications, including persistent feeding problems, learning disabilities, recurrent seizures, and/or brain damage, or even death. Existing medical options were not developed for CHI and are often either ineffective since certain groups of patients do not respond to these therapies or are associated with substantial side effects that discourage compliance and lead to suboptimal treatment outcomes. Surgical removal of the pancreas is also an option, but this approach is invasive, may require repeat surgery, and ultimately leads to the development of lifelong insulin-dependent diabetes.

About RZ358
RZ358 is an intravenously administered human monoclonal antibody that binds with high potency and selectivity to an allosteric site on the insulin receptor. RZ358 counteracts the effects of elevated insulin at its target tissues by diminishing the binding and downstream signaling of insulin at its receptor. This unique mechanism of action gives properties of reversibility and graded activity, which are dependent on the extent of insulin elevation. Therefore, RZ358 is ideally suited as a potential therapy for hyperinsulinism, and it is being

developed to treat the hypoglycemia associated with diseases such as CHI.

RZ358 received Orphan Drug Designation in the United States and European Union. Rezolute is currently evaluating RZ358 in the RIZE trial, a Phase 2b clinical trial in patients with CHI.

Forward-Looking Statements
This release, like many written and oral communications presented by Rezolute, Inc. and our authorized officers, may contain certain forward-looking statements regarding our prospective performance and strategies within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. We intend such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995, and are including this statement for purposes of said safe harbor provisions. Forward-looking statements, which are based on certain assumptions and describe future plans, strategies, and expectations of the Company, are generally identified by use of words such as "anticipate," "believe," "estimate," "expect," "intend," "plan," "project," "seek," "strive," "try," or future or conditional verbs such as "could," "may," "should," "will," "would," or similar expressions. Our ability to predict results or the actual effects of our plans or strategies is inherently uncertain. Accordingly, actual results may differ materially from anticipated results. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this release. Except as required by applicable law or regulation, Rezolute undertakes no obligation to update these forward-looking statements to reflect events or circumstances that occur after the date on which such statements were made.

Media Contact
Amy Jobe, Ph.D.
LifeSci Communications
+1 315 879 8192
ajobe@lifescicomms.com

Investor Contact
Corey Davis, Ph.D.
LifeSci Advisors
+1 212 915 2577
cdavis@lifesciadvisors.com

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