Initial Data: RA101495 Phase 2 Program in Paroxysmal Nocturnal Hemoglobinuria (PNH)
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RA101495 is a peptide inhibitor of complement C5

More convenient and flexible treatment regimen as compared to IV infusion

- Subcutaneous product for once-daily self-administration
- Provided in a single-use self-injector containing a pre-filled syringe (29G needle)
- Stable at room temperature for up to 30 days in-home use

High level of investigator support

Phase 2 trial designed to study safety and efficacy, and to establish a dosing regimen for Phase 3

- Initial data in eculizumab-naïve patients supports opening a cohort comprised of patients currently treated with eculizumab (“switch” cohort)
Goal: Dose-finding study to evaluate the safety, tolerability, preliminary efficacy, pharmacokinetics, and pharmacodynamics of RA101495 in patients with PNH

Design: Open-label (12 weeks) with long-term extension

Global Program addressing 3 PNH populations
- Eculizumab Naïve (Cohort A); n=8-12
- Eculizumab Switch (Cohort B); n=6-8
- Eculizumab Inadequate Responders; n=6-8

Dose-Finding Regimen
- Loading dose: 0.3mg/kg s.c. on Day 1
- Starting dose: 0.1mg/kg s.c. once daily for the first 2 weeks
- Up-titration: from the week 2 visit onwards, if LDH is ≥ 1.5xULN, the dose is increased to 0.3mg/kg s.c. once daily

Primary Efficacy Endpoint: Change in lactate dehydrogenase (LDH) from baseline to the mean level from Week 6 to Week 12
• Three eculizumab-naïve patients enrolled in cohort A, of which two have completed 7 weeks of follow-up
• No safety or tolerability concerns identified
• Near-complete inhibition of hemolytic activity achieved
• Rapid declines in LDH observed; mean LDH at Week 7 = 1.6 x ULN
• One transient episode of breakthrough hemolysis associated with inter-current illness
• 100% compliance with once-daily s.c. self-administration
• Enrollment of additional cohort A patients continues
• Based on these initial data, cohort B (eculizumab switch) is now open to enrollment
Patient 001 (56-year old female)
- PNH diagnosed April 2017
- No transfusions prior to enrollment
- Granulocyte clone size = 80%
- RBC clone size = 25%
- Baseline LDH = 873 U/L (3.7 x ULN)

Patient 002 (65-year old female)
- PNH diagnosed April 2017
- Transfusion-dependent prior to enrollment
- Granulocyte clone size = 99%
- RBC clone size = 47%
- Baseline LDH = 760 U/L (3.2 x ULN)
100% compliance with once daily subcutaneous self-administration at home (monitored remotely by smartphone)

- No serious adverse events
- No related adverse events
- No injection site reactions
- No dosing interruptions
- No drug discontinuations
RA101495: PNH
Mean Lactate Dehydrogenase (LDH)

LDH Central Lab ULN = 234 U/L

Week 0

1.5x ULN

Week 7

LDH Central Lab ULN = 234 U/L
RA101495: PNH
Mean Lactate Dehydrogenase (LDH)
RA101495: PNH
Individual Data: Patients 001 and 002

LDH

Hemoglobin

Direct Hemolysis Assay (sheep RBC)

Log Drug Levels

Scheduled visits W0,1,2,3,4,6. Other visits unscheduled.
After completion of the weekly loading regimen (W0 - W4), mean LDH levels on eculizumab exceed 1.5 x ULN at every time point except the final visit (W26).
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