Ra Pharma

# Initial Data: RA101495 Phase 2 Program in Paroxysmal Nocturnal Hemoglobinuria (PNH)

27th June, 2017

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# RA101495: PNH
## Introduction

- 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)

# RA101495: PNH
# Phase 2 Program

- **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

# RA101495: PNH
## Phase 2 Initial Data: Executive Summary

- 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

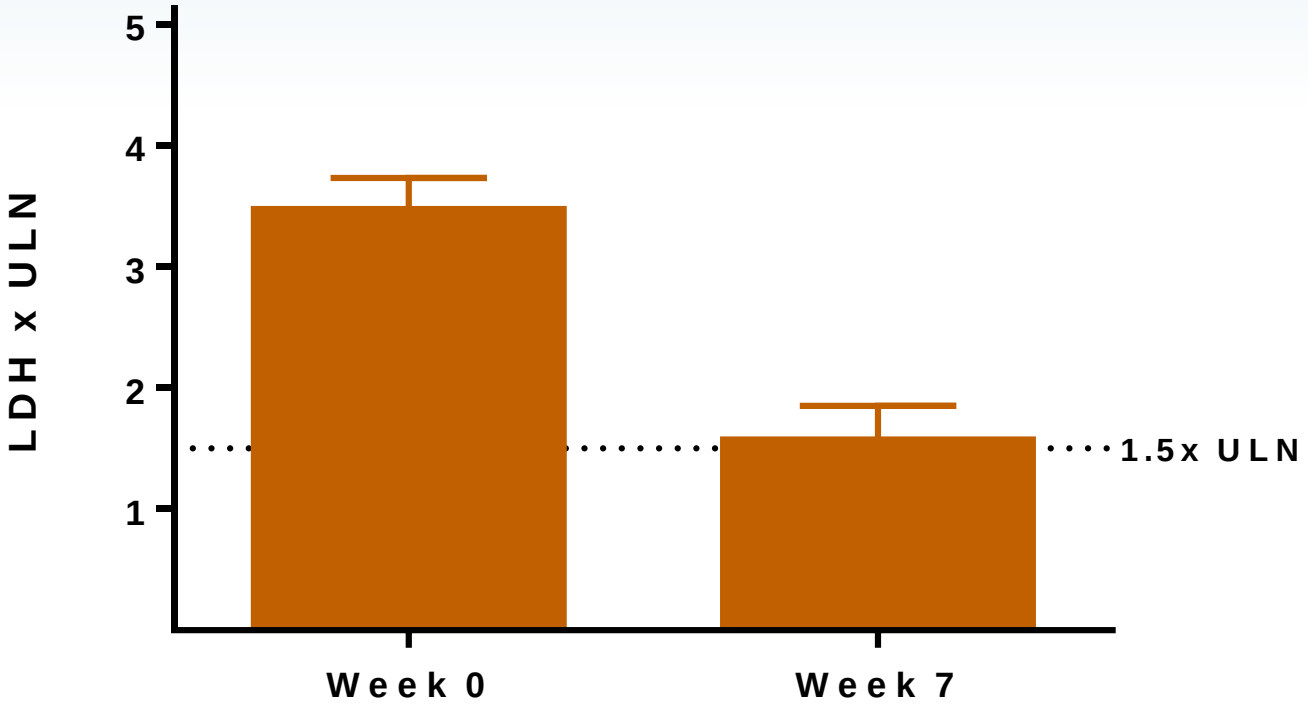
# RA101495: PNH
## Treatment-Naïve Patients (Cohort A): Demographics

- **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)

# RA101495: PNH
## Safety & Tolerability

- ✓ 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

# RA101495: PNH
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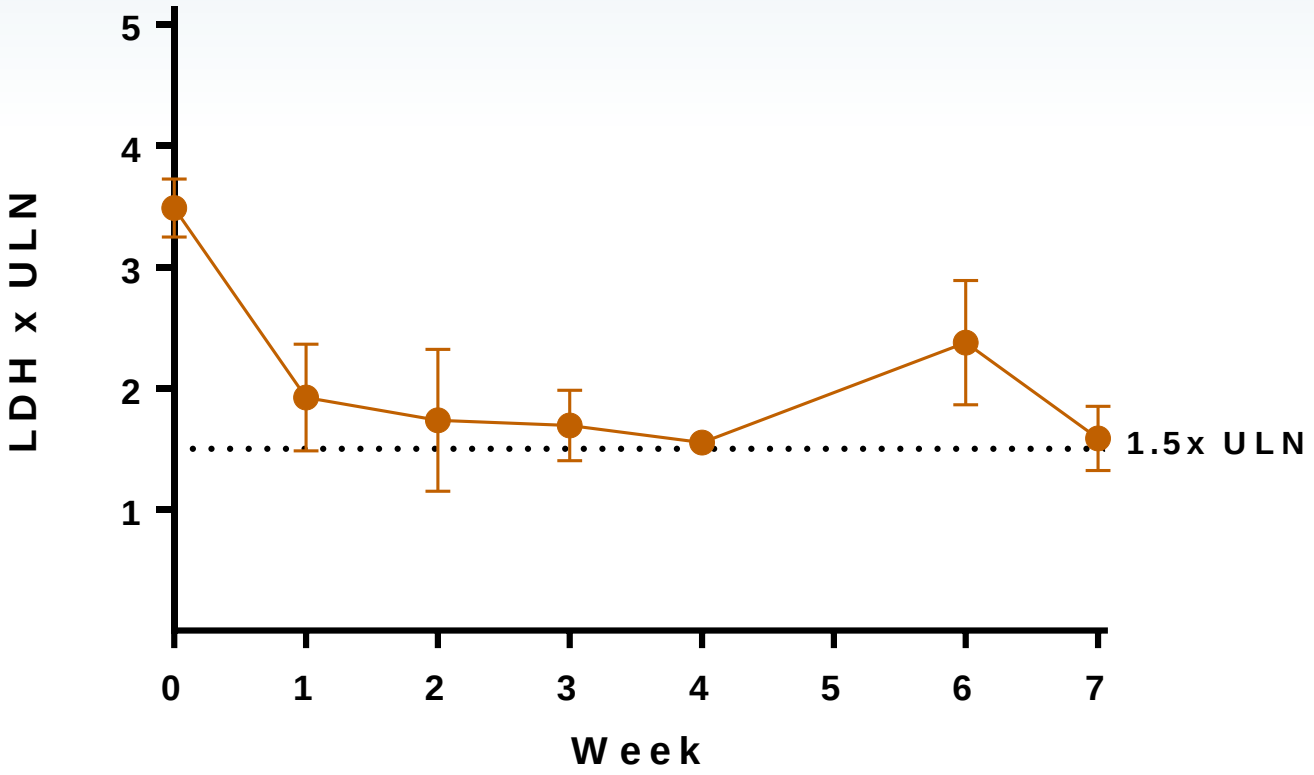
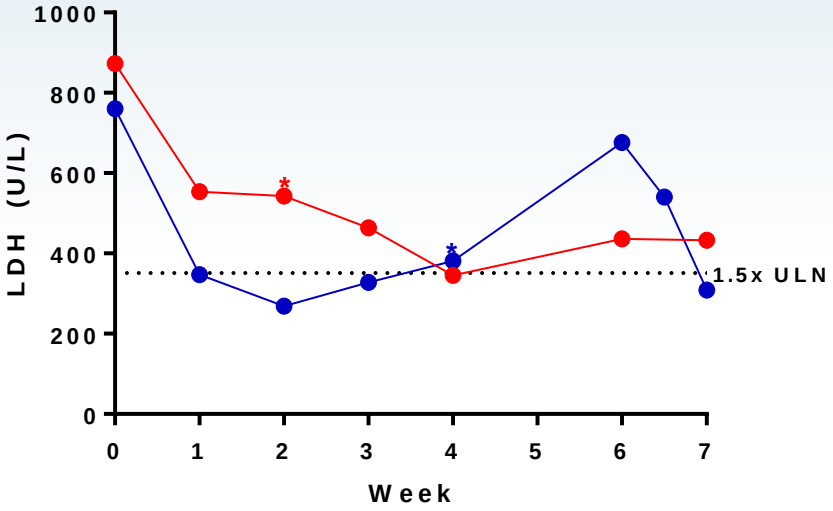
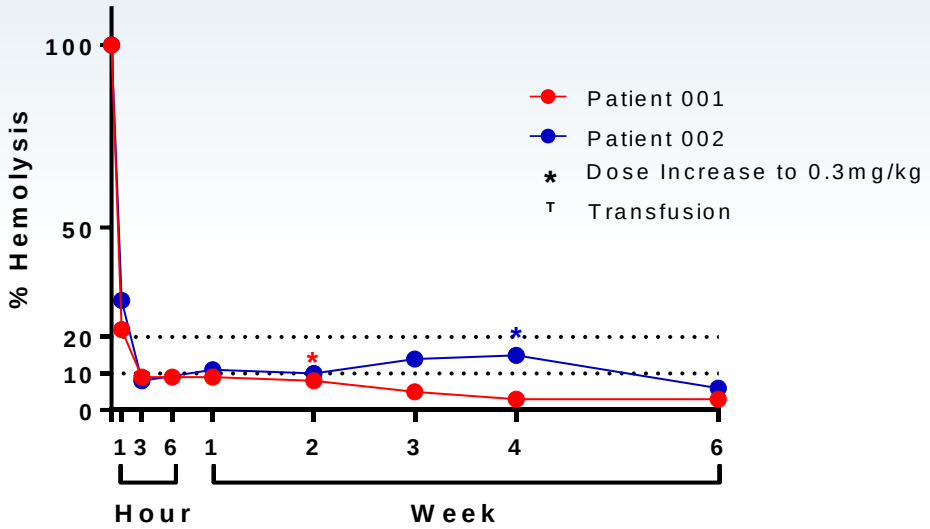


# RA101495: PNH
# Individual Data: Patients 001 and 002

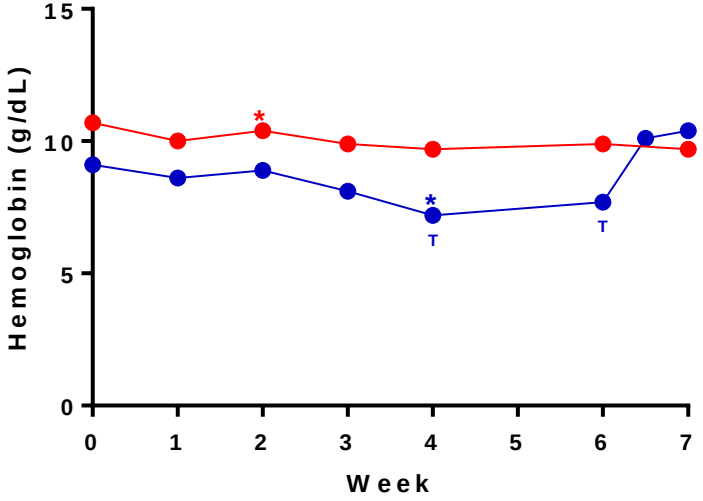
## LDH



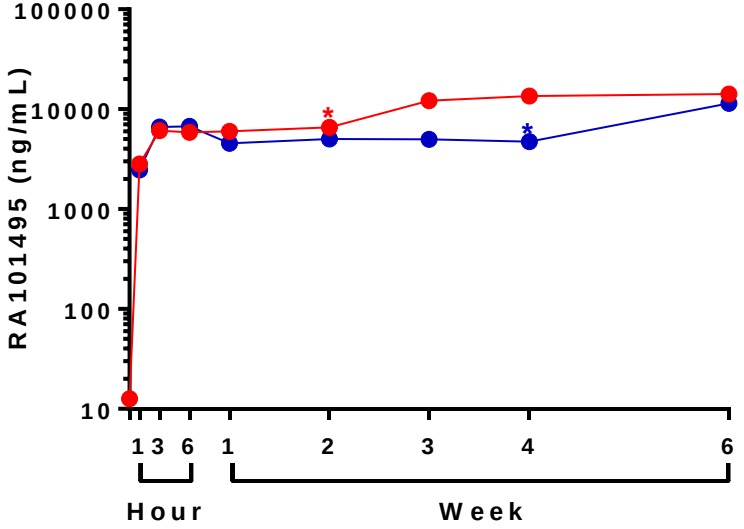

## Direct Hemolysis Assay (sheep RBC)




## Hemoglobin



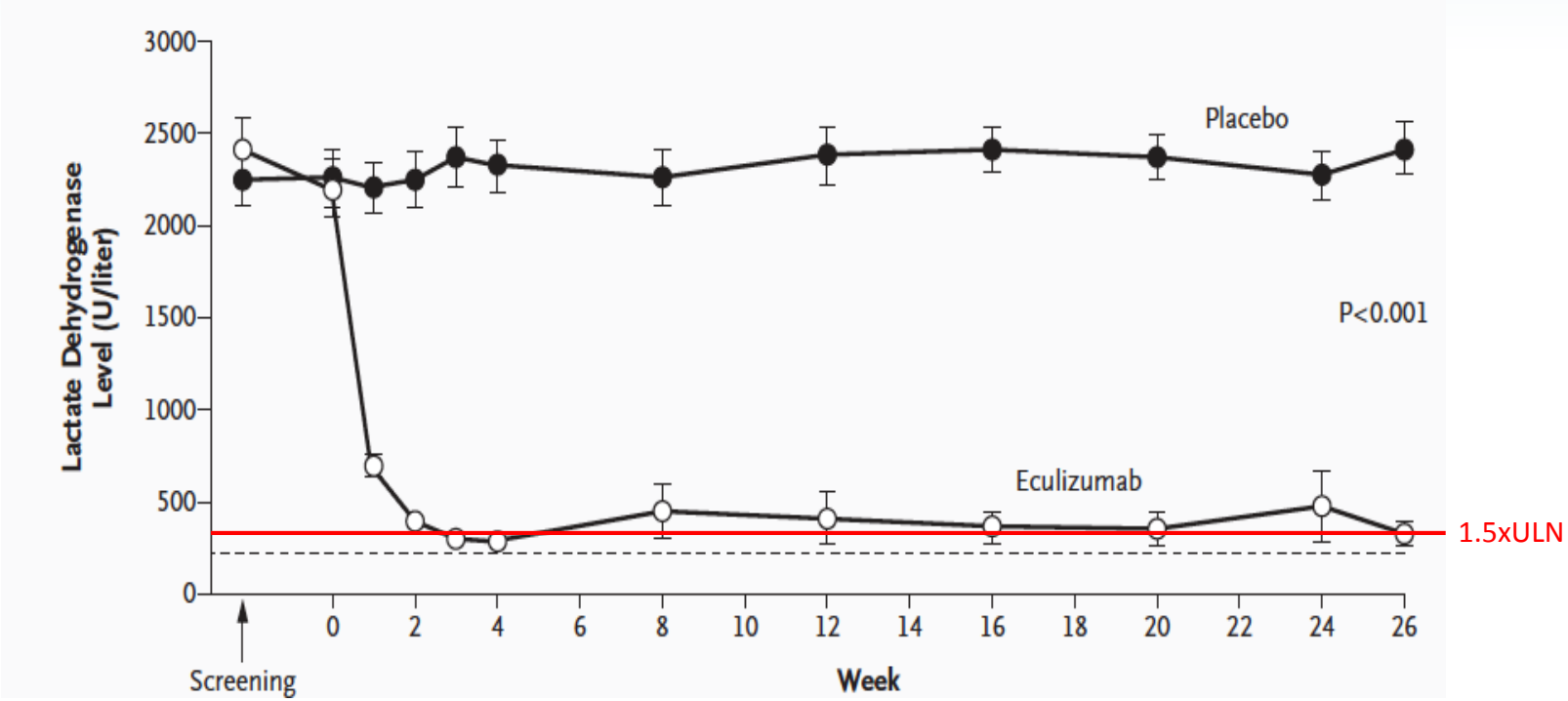

## Log Drug Levels




Scheduled visits W0,1,2,3,4,6. Other visits unscheduled

# TRIUMPH Trial:
# LDH Trajectory on Eculizumab

*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)*




Adapted from: Hillmen et al. *N Engl J Med*, 2006, 355;12

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# Q&A

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