

# **Analyst & Investor Presentation**

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# **Introduction and Agenda**

# **Dr. David Horn Solomon**

**Chief Executive Officer** 

# Agenda

#### **Introduction and Overview of Akari Therapeutics**

Dr. David Horn Solomon, Chief Executive Officer

#### Phase II Clinical Study of Coversin<sup>™</sup> in Patients with PNH

Anita Hill, M.D., PhD, MRCP, FRCPath, Consultant Haematologist for Leeds Teaching Hospitals NHS Trust, U.K., and Lead Clinician for the National PNH Service in England

#### **Duel C5 and Leukotriene B4 Programs**

Dr. Wynne Weston-Davies, Medical Director

#### **Coversin™ Long-Acting Data and Plan**

Dr. David Horn Solomon, Chief Executive Officer

#### **Closing Remarks and Q&A**

Dr. David Horn Solomon, Chief Executive Officer

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# Akari Overview

- Creating drugs for acute and chronic orphan inflammatory diseases by modulating the C5 and LTB4 pathways
- Lead drug candidate Coversin<sup>™</sup> successfully met primary endpoint in the Phase II clinical trial for paroxysmal nocturnal hemoglobinuria (PNH)
  - C5 inhibition is a well validated method of treatment in rare life-threatening diseases
  - Potential for differentiated product profile to address unmet needs in PNH
  - Following recent FDA Type B end of Phase II meeting, expect to initiate Phase III Q1 2018
- Coversin has potential in a wide range of diseases with unmet need
  - Dual complement & leukotriene inhibition
- Experienced management team
- Headquartered in New York and listed on NASDAQ (AKTX)
  - Clinical development operations in London, England

# Two separate development programs, each focused on distinct inflammatory pathways

#### Complement program

- Sub Q delivery differentiated against current IV standard of care
- PNH<sup>1</sup> Phase III planned Q1 2018
- aHUS<sup>2</sup> Phase II planned Q4 2017
- Once-weekly dosing molecule, Coversin LA™, in development –
   Phase I planned Q4 2018

#### Dual C5 & leukotriene B4 program

- Differentiated mechanism of action
- BP<sup>3</sup> & AKC<sup>4</sup> : projected Phase II starts planned H1 2018

<sup>1.</sup> PNH: Paroxysmal nocturnal hemoglobinuria

<sup>2.</sup> aHUS: Atypical hemolytic-uremic syndrome

<sup>3.</sup> BP: Bullous Pemphigoid

<sup>4.</sup> AKC: Atopic keratoconjunctivitis

## Akari Portfolio Builds on Complement Experience



#### Anticipated Near-Term Milestones

- PNH: Initiate first Phase III (anticipated Q1 2018)
- aHUS: Initiate Phase II (anticipated Q4 2017)
- AKC: Initiate Phase II (anticipated H1 2018)
- BP: Initiate Phase II (anticipated H1 2018)
- Coversin LA: Initiate once-weekly Phase I (anticipated Q4 2018)

# **COMPLEMENT PROGRAM**

### **Coversin – Differentiated Complement Inhibitor**

	Coversin™	Soliris <sup>®</sup> (Alexion Pharmaceuticals, Inc.)
Chemistry	Recombinant small protein	Antibody
Mechanism of action*	Blocks C5 & LBT4	Blocks C5
Administration	Subcutaneous	Infusion
Advantages	<ul> <li>Self-administration</li> <li>Potential reduction of transfusions</li> </ul>	<ul><li>Marketed product</li><li>Proven efficacy</li></ul>

\*Coversin and Soliris bind C5 at different binding sites. Roversi, P. et al., 2013. Jore, M. et al., Structural basis for therapeutic inhibition of complement C5, 2016.

## Phase III Program for PNH – First Trial Planned Q1 2018

- Two PNH Phase III clinical trials
  - Naïve patients (CAPSTONE)
  - Switch (ASSET)
- CAPSTONE: Naïve patients randomized to Coversin plus standard of care vs. standard of care
- ASSET: Eculizumab-treated patients randomized to remain on eculizumab or switch to Coversin
- FDA indicated safety and efficacy data for the proposed number of unique PNH patients on Coversin for over one year seems reasonable, subject to review of the actual data upon submission
- In ongoing discussion with regulators
- CAPSTONE currently planned to commence Q1 2018

## **Coversin Targeting Atypical Hemolytic Uremic Syndrome (aHUS)**

- Chronic and life-threatening genetic disease characterized by microangio-pathic hemolytic anemia, thrombocytopenia, and kidney injury
- Efficacy of C5 inhibition in aHUS demonstrated by the approval of eculizumab for this indication
- aHUS physicians have expressed support for once-daily Coversin
  - More therapeutic flexibility for episodic patients
  - Patient convenience
- Phase II trial up to 10 naïve patients at seven sites across Europe, projected to begin in Q4 2017

# **Dr. Wynne Weston-Davies**

**Medical Director** 

# DUAL C5 AND LEUKOTRIENE B4 (LTB4) PROGRAMS

#### Dual Leukotriene & Complement Inhibition by Coversin Has Potential in Wide Range of Diseases with Unmet Need



### Dual Action Coversin More Effective Than C5 or LTB4 Only

Dual action (Coversin) more effective than C5-only (saturated Coversin) or Zileuton (LTB4) alone in mouse model<sup>1</sup>



# Atopic Keratoconjunctivitis (AKC)



- Severe eye surface inflammation causing infiltration of immune cells such as neutrophils and T cells
- A cause of blindness worldwide
- Topical drugs, such as steroids or cyclosporin, often not effective or cannot be given chronically
- Both complement and LTB4 known to be involved
- Progresses to affect the cornea and may lead to loss of vision
- Phase I/II randomized, double masked, placebo-controlled trial at Moorfields Eye Hospital and Royal Liverpool Hospital planned to start H1 2018

## **Bullous Pemphigoid (BP) - Significant Unmet Need**



- Immune complex deposition initiates complement cascade and inflammatory process
- LTB4 recruits neutrophils to dermis-epidermis junction and amplifies inflammation
- Phase II open label trial planned to start in H1 2018 in three centers in Europe

# **Dr. David Horn Solomon**

**Chief Executive Officer** 

## **Coversin LA: Once Weekly Formulation**

Human PK simulation of free C5 following single dose injection potential for weekly dosing

# Inhibition of complement alternative pathway rabbit red blood cell lysis



- Terminal half life in humans estimated at four days based on pharmacokinetic (PK) data in mice and rats
- Clean initial toxicology profile comparable to unmodified Coversin
- Phase I clinical study planned for Q4 2018

Sources: Rupert Austin, Scaling PAS-Coversin PK from mouse and rat to man, BAST Inc. Limited, UCL Laboratories, December 2016

# Phase II Clinical Study of Coversin in Patients with PNH

# Anita Hill, M.D., PhD, MRCP, FRCPath

Consultant Haematologist for Leeds Teaching Hospitals NHS Trust, U.K., and Lead Clinician for the National PNH Service in England

## PNH is a Progressive Disease of Unregulated Complement Activity





#### Survival of Patients; Eculizumab Vs. Matched Normal Population



<sup>†</sup>Indications for transplantation were recurrent hemolytic crisis, aplastic anaemia and thromboembolism Hill A. ASH 2012; Peffault de Latour R. et al., Haematologica 2012;97:1666-1673

## Eculizumab Dosing of UK Patients September 2016

	Number of Patients			
Eculizumab dose	Leeds	King's	Total	% of Patients
Standard Dose				
900 mg	158	88	246	80.7%
Higher Dose				
1,200 mg	29	17	46	15.1%
1,500 mg	4	8	12	3.9%
1,800 mg	1	0	1	0.3%
Total	192	113	305	100.0%

305 total number of patients treated since approval of eculizumab; 276 patients currently being treated Data from the National PNH Service, UK

# Eculizumab Phase III – LDH Reduction to 1.5-1.8X ULN\* in Treated Patients



\* X ULN calculations derived by Akari from Hillman et al., 2006; NEJM 355(12):1237

## **COBALT Case Study**

- Patient: Female, aged 66
- History of severe aplastic anaemia for many years treated with immunosuppression, 1-2 units of PRBC monthly and frequent platelet transfusions
- Multiple complications including iron overload
- PNH diagnosed April 2016
- Not eligible for eculizumab or alternative investigational C5 inhibitor



- Started Coversin 4 months ago
- Has received 2 units of PRBC since starting Coversin
- Feels better, able to take walks and other physical activities that were not previously possible
- Self-injecting 45 mg once daily
- Now enrolled in CONSERVE

#### **Treatment Duration, Safety, and Tolerability of Patients Treated with Coversin**

**Eculizumab-resistant PNH patient (CONSENT)** 

22 Months

**Continuing Phase 2 PNH patients\*** 



- Drug well tolerated by patients
- No SAEs related to Coversin

Patient who did not complete Phase 2 study (COBALT)



#### Positive Response For 22 Months\* In Eculizumab-Resistant PNH Patient Treated With Coversin



No hemolytic episodes; no dose changes; symptom free; twice daily self injection

Patient treated pursuant to an approved clinical protocol in the Netherlands Saskia Langemeijer et al., 12 weeks safety and efficacy results of the novel C5 inhibitor Coversin in PNH with resistance to eculizumab due to complement C5 polymorphism, University of Radboud, Nijmegen, 2016

#### **COBALT Phase II PNH Trial Design**



#### **Selection Criteria**

- Male or female, >18 years
- 50 100 kg
- PNH confirmed by flow cytometry
- Complement inhibitor naïve

#### **Principal Outcome Measures**

- Safety
- Reduction in serum LDH: ≤1.8 x ULN by Day 28
- Quality of life
- Hemoglobin stabilization and transfusion reduction

#### **Demographics**

- 8 patients entered: 4 male, 4 female
- Age range at entry: 22 69 years
- 6 patients previously transfusion dependent

# **COBALT Phase II Clinical Trial Results**

- 8 patients entered trial and included in intention to treat (ITT) analysis
  - 5 patients have completed trial and entered long-term CONSERVE trial
  - 2 patients will complete by year-end 2017, and opted to join CONSERVE
  - 1 patient withdrawn at Day 43 due to suspected co-morbidity unrelated to Coversin treatment
- Trial met its primary efficacy endpoint (median LDH ≤1.8 x ULN by Day 28)
- All patients self-injected
  - 6 injecting once-daily, 1 injecting 12-hourly
  - Good compliance
- Coversin well tolerated with good safety profile
  - No treatment related serious adverse events (SAE)
  - 7 injection site reactions (ISRs) rated clinically significant (grade 2 or above) out of approx. 900 injections

#### **COBALT Overall Intention-To-Treat Result**



## **COBALT LDH x Upper Limit of Normal**



# **COBALT and CONSERVE Transfusion Results**

Patient	Transfusion Dependent?	Current Trial Status	Transfusion (Yes / No)
1	No	CONSERVE	No
2	Yes	CONSERVE	No
3	No	Withdrawn	No
4	Yes	CONSERVE	No
5	Yes	CONSERVE	No
6	Yes	CONSERVE	Yes; Reduced requirement
7	Yes	COBALT	Yes; Reduced requirement
8	Yes	COBALT	Yes; Reduced requirement

## Long-term CONSERVE Safety and Efficacy Study

- CONSERVE intended for all patients completing PNH and aHUS trials who opt to continue Coversin therapy
- In event of inadequate control (e.g., frank hemolysis, rising LDH, increasing symptoms) clinician has the option to divide the daily dose into 2 12-hourly doses, either temporarily or long-term, as an alternative to increasing dose
- Currently 5 patients in CONSERVE; 2 more patients will join this month
  - 1 to 9 months duration
  - 4 patients injecting once daily; 1 patient injecting 12-hourly
  - 4 patients on 45 mg; 1 patient on 30 mg
- CONSERVE database will contribute to the approval package after completion of Phase 3 program
- One patient with a rising LDH level was, as an alternative to higher dosing, moved to 12 hourly with a subsequent fall in LDH
- Median LDH of the other three patients at day 180 was 1.77x ULN

# **Closing Remarks and Q&A**

# **Dr. David Horn Solomon**

**Chief Executive Officer** 



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