Oxford Biomedical Research Centre Enabling translational research through partnership









Proof-of-Concept Phase-2a Clinical Trial of ANB020 (Anti-IL-33 Antibody) in the Treatment of Moderate-to-Severe Adult Atopic Dermatitis

Professor Graham Ogg University of Oxford United Kingdom

American Academy of Dermatology Annual Meeting

February 17th 2018

Conflicts of interest

Advisory boards, consultancies, research grants or equity with: AnaptysBio, Celgene, Eli Lilly, Novartis, Janssen, Orbit Discovery, UCB Pharma

Clinical study sponsored by AnaptysBio

Travel/registration costs for AAD: AnaptysBio

IL-33: Central Mediator of Type 2 Diseases

Key Role in Pathogenesis of Atopic Dermatitis

- IL-33 is a key cytokine in type 2 inflammatory responses to allergen
 - Responsible for activation of Th2 and ILC2
 - Functions upstream of IL-4, IL-5 and IL-13
 - Modulates mast cell degranulation
- IL-33 is rapidly released by epithelium upon allergen exposure
- Genetic association of IL-33 pathway mutations with type 2 diseases¹
- IL-33 is highly expressed in skin of atopic dermatitis patients with active disease²



ANB020: Anti-Human IL-33 Antibody

- ANB020 is humanized anti-human IL-33 monoclonal antibody
 - High affinity binding to human IL-33 with K_d of approximately 1 pM
 - Potent neutralizing activity with an IC₅₀ of approximately 1.5 nM
- Healthy volunteer Phase 1 trial (n=96) reported safety, pharmacokinetics and pharmacodynamics
 - Subjects dosed with 10mg to 750mg of ANB020 in single dose cohorts (n=48), 40mg to 300mg of ANB020 weekly for 4 weeks in multiple dose cohorts (n=24) and placebo (n=24)
 - *In vivo* half-life of approximately 16 days for both intravenous and subcutaneous administration
 - Pharmacodynamic effect persisted for 85 days at certain single dose levels of ANB020
 - ANB020 was generally well tolerated and no dose-limiting toxicities were observed



Single dose ANB020 healthy volunteer Phase 1 pharmacodynamic *ex vivo* assay measuring inhibition of IL-33 induced Interferon-gamma (IFN-g) relative to pre-dose levels

ANBO20 Phase 2a Atopic Dermatitis Proof-of-Concept Trial



- Study design:
 - Enrolled 12 moderate-to-severe adult atopic dermatitis patients inadequately controlled with topical corticosteroids
 - Single intravenous dose of placebo (Day -7) followed by a single 300 mg intravenous dose of ANB020 (Day 1)
 - EASI, 5-D pruritus, SCORAD, DLQI and IGA clinical scores determined at specific time points
- Study objective:
 - Demonstrate EASI-50 response in at least 50% of patients at Day 29 (primary endpoint)

Baseline Characteristics

Characteristic	Average (n=12)	
Age (years)	40.4 ± 13.5	
Male, number (%)	11 (91.7%)	
Caucasian race, number (%)	12 (100%)	
Body-Mass Index	26.14 ± 4.145	
EASI, score	32.25 ± 10.89	
IGA, 0-5 scale	4 ± 0.74	
SCORAD, score	64.79 ± 12.02	
Pruritus, 5-D score	19.1 ± 4.85	
DLQI, score	12.92 ± 6.54	

All 12 patients were inadequately controlled on corticosteroids pre-study

7 of 12 enrolled patients were treated with systemic immuno-modulators pre-study and presented with a baseline EASI score of 36 5 of 12 patients were not treated with systemic immuno-modulators pre-study and presented with a baseline EASI score of 27

EASI Scores Following Single ANB020 Dose Rapid response and all patients achieved EASI-50 on or before Day 57



Timepoint	Average % EASI Score Reduction*	% Patients Achieving EASI-50*	% Patients Achieving EASI-75*
Day -21 (Baseline)	0%	0	0
Day 1 (ANB020 Dosing)	4%	0	0
Day 15	58%	9 of 12 (75%)	3 of 12 (25%)
Day 29	61%	10 of 12 (83%)	4 of 12 (33%)
Day 57	62%	9 of 12 (75%)	5 of 12 (42%)
Day 78	62%	9 of 12 (75%)	2 of 12 (17%)
Day 113	55%	8 of 12 (67%)	2 of 12 (17%)
Day 140	45%	5 of 12 (42%)	3 of 12 (25%)

* Relative to baseline upon enrollment at Day -21

Time

Additional Efficacy Data 5-D Pruritus, SCORAD, DLQI and IGA Scores



IGA scores of zero or 1 (clear/almost clear skin) observed in 25% (3/12) of patients

Average % DLQI

Reduction*

0%

21%

43%

45%

48%

55%

35%

43%

Key Conclusions & Next Steps

- Rapid and persistent efficacy following single dose of ANB020
 - Rapid efficacy observed as early as Day 15
 - Efficacy was maximized between Day 29 and Day 57
 - All patients achieved at least EASI-50 response on or before Day 57
 - EASI responses consistent with 5-D pruritus, SCORAD, IGA and DLQI scores
- Disease severity does not limit ANB020 efficacy
 - ANB020 was similarly efficacious in patients with higher baseline EASI scores (treated with systemic immuno-modulators prestudy) versus lower baseline EASI score patients that did not require systemic therapy pre-study

• ANB020 was well-tolerated and no drug-related safety signals observed

- Most frequent adverse event was dizziness in 17% of patients post-placebo versus headache in 25% of patients post-ANB020
- A single serious adverse event of depression reported on Day 140 post-ANB020, which was consistent with the patient's pretrial history of depression, and was deemed not drug-related
- Next step: advance ANB020 into placebo-controlled, double-blind, randomized 200-300 adult moderate-to-severe atopic dermatitis Phase 2b trial
 - Assess different dose levels and dosing frequencies of subcutaneously-administered ANB020

Oxford Biomedical Research Centre Enabling translational research through partnership





NHS National Institute for Health Research



Acknowledgements

Oxford

Yi-Ling Chen Danuta Gutowska-Owsiak Melanie Westmoreland Teena MacKenzie Liliana Cifuentes Antonia Lloyd-Lavery

AnaptysBio

Allison Marquette Brian Kenney Marco Londei