UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Form 6-K

Report of Foreign Private Issuer
Pursuant to Rule 13a-16 or 15d-16
under the Securities Exchange Act of 1934

December 2021

Commission file number: 001-36288

Akari Therapeutics, Plc

(Translation of registrant's name into English)

75/76 Wimpole Street
London W1G 9RT
United Kingdom
(Address of principal executive offices)

Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F.

Form 20-F ☒ Form 40-F ☐

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulations S-T Rule 101(b)(1):_____

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulations S-T Rule 101(b)(7):_____

CONTENTS

On December 21, 2021, Akari Therapeutics, Plc updated its corporate presentation that it intends to use in conferences and meetings with investors. A copy of the presentation is attached hereto as Exhibit 99.1 and is incorporated herein by reference.

Exhibit No.

99.1 Corporate presentation dated December 2021.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Akari Therapeutics, Plc
(Registrant)

By: /s/ Clive Richardson
Name: Clive Richardson
Chief Executive Officer and
Chief Operating Officer

Date: December 21, 2021

Exhibit 99.1


AKARI
THERAPEUTICS
Combined Inhibition Of
Complement & Leukotriene Pathways
To Treat Inflammatory Diseases
December 2021

Forward-Looking Statements

Certain statements in this presentation constitute contains "forward-looking" statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. These forward-looking statements reflect our current views about our plans, intentions, expectations, strategies and prospects, which are based on the information currently available to us and on assumptions we have made. Although we believe that our plans, intentions, expectations, strategies and prospects as reflected in or suggested by those forward-looking statements are reasonable, we can give no assurance that the plans, intentions, expectations or strategies will be attained or achieved. Furthermore, actual results may differ materially from those described in the forward-looking statements and will be affected by a variety of risks and factors that are beyond our control. Such risks and uncertainties for our company include, but are not limited to: needs for additional capital to fund our operations, our ability to continue as a going concern; uncertainties of cash flows and inability to meet working capital needs; an inability or delay in obtaining required regulatory approvals for nomacopan (Coversin) and any other product candidates, which may result in unexpected cost expenditures; our ability to successfully develop nomacopan as a treatment for COVID-19-related pneumonia and to successfully commercialize any product in that indication; our ability to obtain orphan drug designation in additional indications; risks inherent in drug development in general, and risks specific to the development of potential treatments for COVID-19-related illnesses; uncertainties in obtaining successful clinical results for nomacopan and any other product candidates and unexpected costs that may result therefrom; difficulties enrolling patients in our clinical trials; failure to realize any value of nomacopan and any other product candidates developed and being developed in light of inherent risks and difficulties involved in successfully bringing product candidates to market; inability to develop new product candidates and support existing product candidates; the approval by the FDA and EMA and any other similar foreign regulatory authorities of other competing or superior products brought to market; risks resulting from unforeseen side effects; risk that the market for nomacopan may not be as large as expected; risks associated with the impact of the outbreak of COVID-19; risks associated with the SEC investigation; inability to obtain, maintain and enforce patents and other intellectual property rights or the unexpected costs associated with such enforcement or litigation; inability to obtain and maintain commercial manufacturing arrangements with third party manufacturers or establish commercial scale manufacturing capabilities; the inability to timely source adequate supply of our active pharmaceutical ingredients from third party manufacturers on whom the company depends; unexpected cost increases and pricing pressures and risks and other risk factors detailed in our public filings with the U.S. Securities and Exchange Commission, including our most recently filed Annual Report on Form 20-F filed with the SEC on March 31, 2020.

The statements made in this presentation speak only as of the date stated herein, and subsequent events and developments may cause our expectations and beliefs to change. Unless otherwise required by applicable securities laws, we do not intend, nor do we undertake any obligation, to update or revise any forward-looking statements contained in this presentation to reflect subsequent information, events, results or circumstances or otherwise. While we may elect to update these forward-looking statements publicly at some point in the future, we specifically disclaim any obligation to do so, whether as a result of new information, future events or otherwise, except as required by law.

The trademarks included herein are the property of the owners thereof and are used for reference purposes only. Such use should not be construed as an endorsement of such products.

This presentation shall not constitute an offer to sell or the solicitation of an offer to buy, nor shall there be any sale of these securities in any state or other jurisdiction.

Akari Overview
Targeting Inflammatory Diseases With Unmet Need

- **Lead drug, first in class, differentiated bifunctional mechanism of action**
  - Nomacopan directly inhibits complement C5 **and** leukotriene B4 (LTB4)
  - Targeting inflammatory indications where blocking both proinflammatory mediators may be more effective than inhibiting either pathway alone

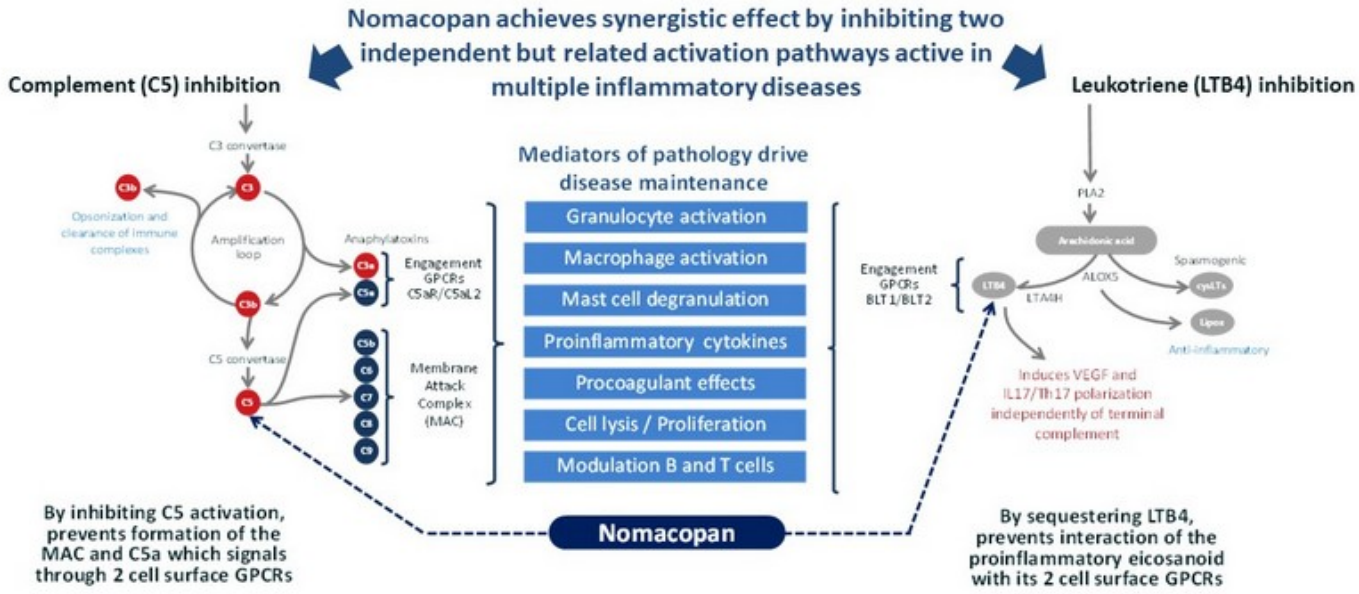
Only dual inhibitor of C5 & LTB4 in complement treatment space

- **Positive clinical and safety data – with two open Phase 3 clinical studies:**
  - **Bullous Pemphigoid** – severe dermatological orphan condition
  - **Pediatric HSCT-TMA** – ultra orphan indication and gateway into broader TMA space

- **Development pipeline - large markets with partnering upside:**
  - **Back of eye (long-acting PAS-nomacopan)** – Geographic Atrophy (dry AMD) large market, no treatments
  - **Surface of eye (topical)** – dry eye remains poorly treated for severe patients
  - **Pulmonary (inhaled)** – focus on treating exacerbations across multiple severe respiratory diseases

HSCT-TMA: Hematopoietic Stem Cell Transplant-Related Thrombotic Microangiopathy

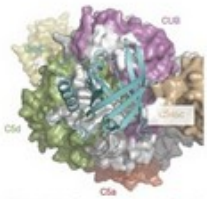
Nomacopan's Competitive Advantage: Synergistic Inhibition of Two Key Effectors Driving Autoinflammation



Nomacopan's Mechanism of Action is Highly specific, Well Understood and Supported by Clinical Efficacy Data

Effective Complement Inhibition

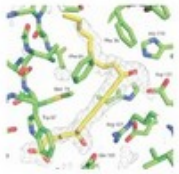
- **Tight binding** – nomacopan inhibits activation of complement C5 in a similar way to eculizumab **(K_D 0.1-1nM)**
- **Terminal complement fully inhibited** during long-term self-administration of nomacopan by paroxysmal nocturnal hemoglobinuria (PNH) patients
- **Nomacopan reduced transfusion dependence by 79%** in transfusion dependent PNH patients (vs. 50-60% with eculizumab*)



Top view of nomacopan (Cyan) bound to C5 Jore et al. 2016

Effective Leukotriene Inhibition

- **Unique mode of action :** by tightly sequestering LTB4 within body of protein 'ligand capture' (**K_D 0.1nM**), prevents LTB4 receptor mediated cell activation
- **Drug effect:** Nomacopan 3X more effective in *ex vivo* neutrophil chemotaxis model than U75302, an LTB4 receptor inhibitor



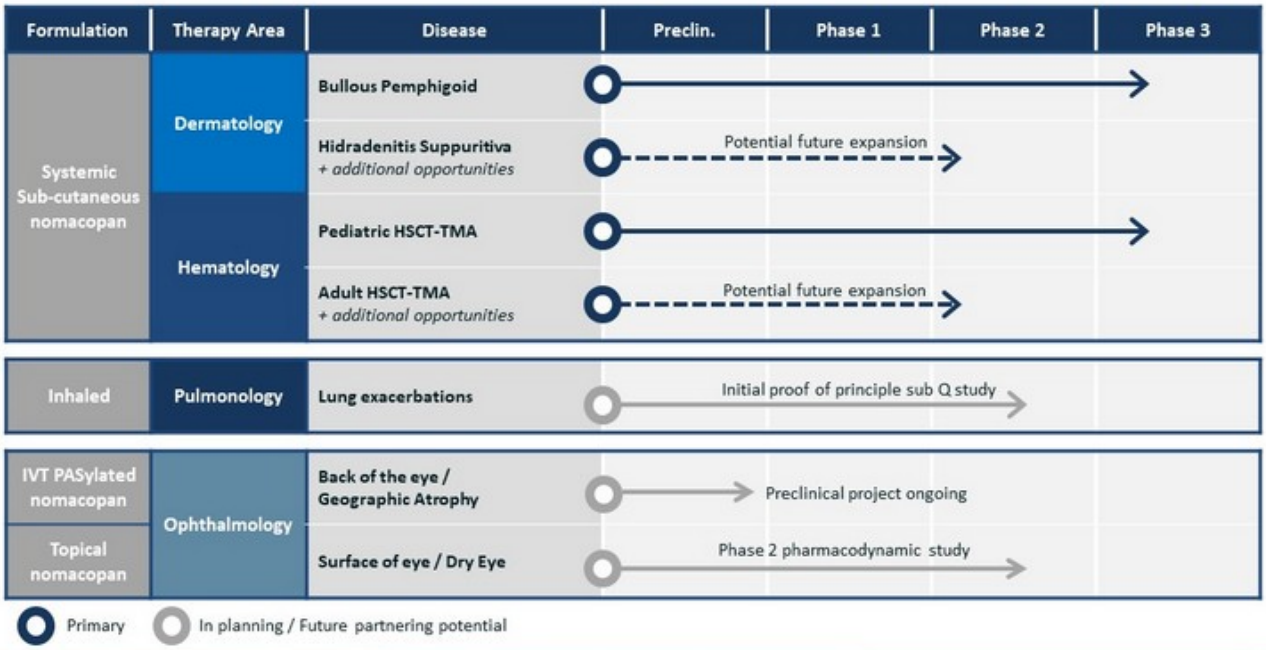
Nomacopan binding to LTB4 Roversi et al. 2013

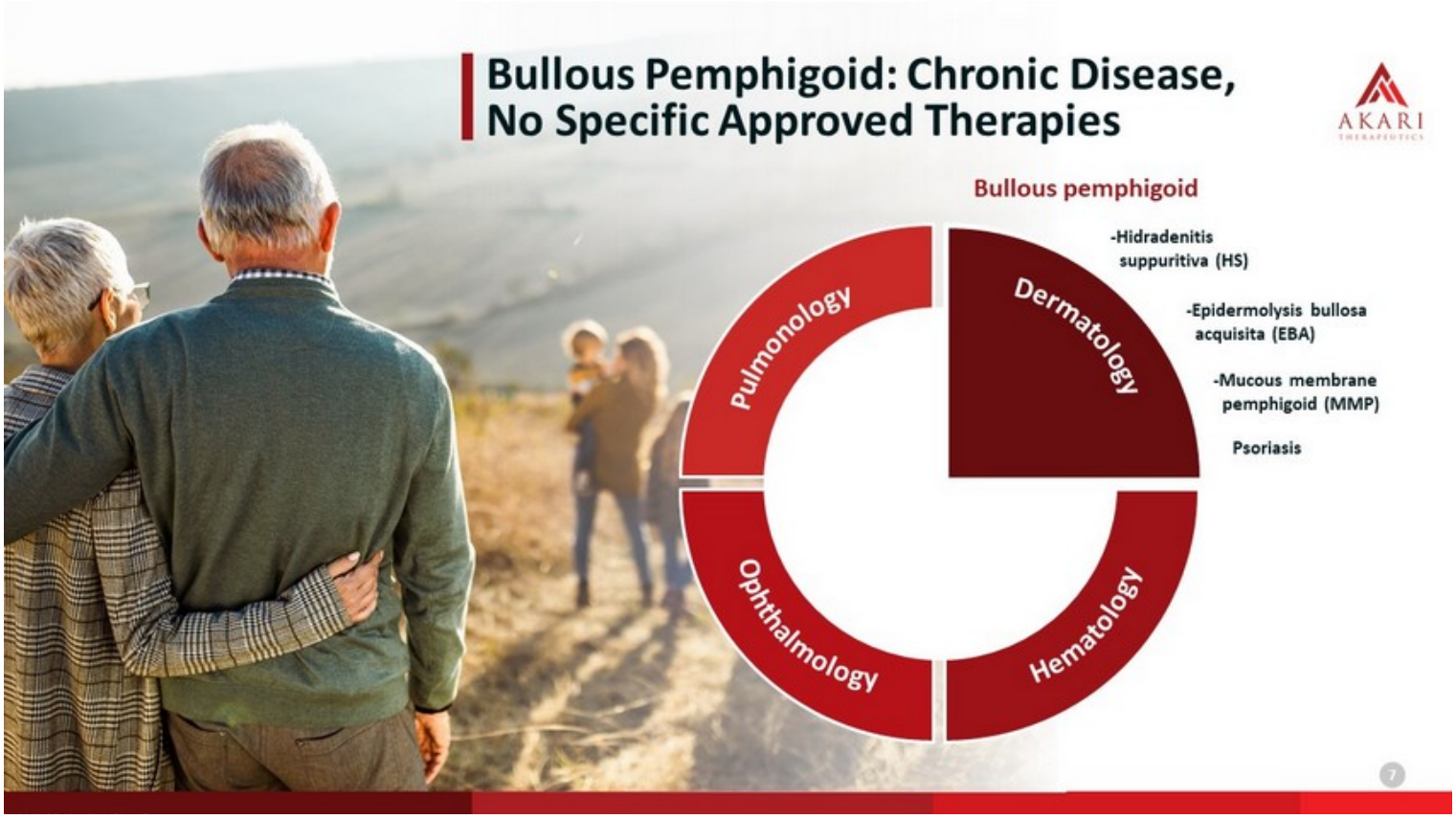
Positive Safety Profile

- Total of >35 cumulative patient years nomacopan exposure with only one reported possibly drug-related SAE (a urinary tract infection)

* Brodsky et al., 2008, SHEPHERD study, Hillmen et al 2013 - Phase III study of eculizumab and ravulizumab (Wook Lee et al., 2019) transfusion independence respectively increased from 21% to 66% of and 23% to 74% of patients over first 6 months of treatment

Clinical Pipeline Progressing Into Phase 3 Studies




Bullous Pemphigoid: Chronic Disease, No Specific Approved Therapies
AKARI THERAPEUTICS
Bullous pemphigoid
Pulmonology
Dermatology
Ophthalmology
Hematology
-Hidradenitis suppuritiva (HS)
-Epidermolysis bullosa acquisita (EBA)
-Mucous membrane pemphigoid (MMP)
Psoriasis
7

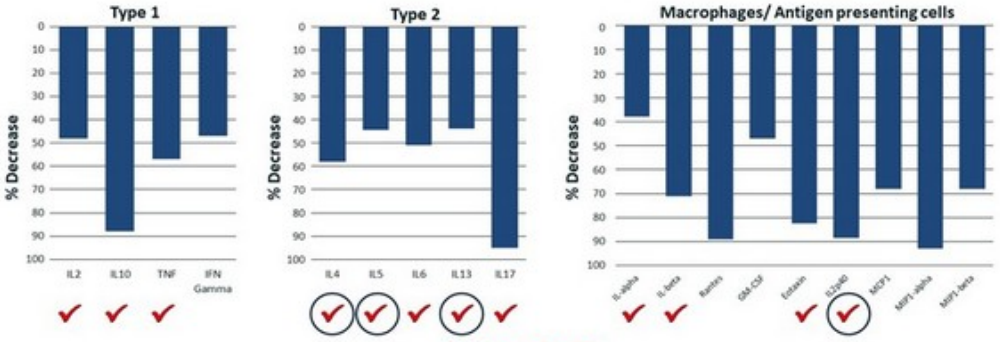
Bullous Pemphigoid is an Auto-Immune Blistering Skin Disease with Few Treatment Options and no Biological Therapies

Unmet Need	**High dose oral corticosteroid (OCS) use associated with approximately 3-fold increase in mortality** • Need for rapidly efficacious steroid-sparing therapy
Prevalence	**Most common auto-immune blistering skin disease** • 120K patients in US+EU; 75% are moderate/ severe • Majority of cases in elderly
Cause	**Auto-antibodies to epidermal basement membrane proteins leads to separation of dermis/epidermis** • In animal models C5 & LTB4 initiate and maintain inflammatory drive in BP with cell recruitment leading to blisters
Treatment	**No specific approved therapies** • SOC for moderate/severe patients is high dose OCS / superpotent topical steroids
Status	**Phase 3 initiated** • Nomacopan has designated Orphan and Fast Track status for BP

Nomacopan's Dual C5 & LTB4 MOA Together Act Upstream Of Most Competitors in Development in Bullous Pemphigoid

In animal models Nomacopan inhibits multiple cytokines implicated in BP, as well as the direct effector mechanisms mediated by C5 and LTB4

Inflammatory markers inhibited by nomacopan in polymicrobial sepsis mouse model



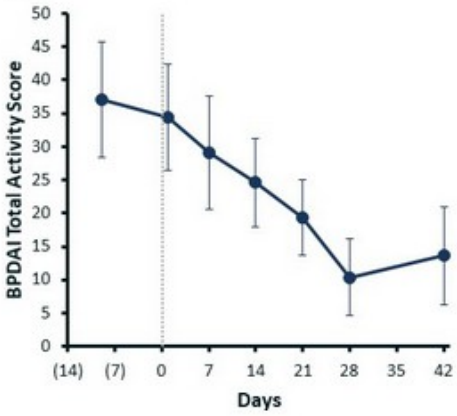
- Nomacopan's upstream mode of action differentiated in BP
- Other drugs in development for BP primarily operate downstream of nomacopan, inhibiting specific cytokines/chemokines or immunoglobulins
- Dupilumab (Dupixent) inhibits IL-4 & IL-13 and benralizumab (Fasenra) inhibits IL-5, and ustekinumab (Stelara) inhibits IL12 and IL23 (via IL12p40). See left

Nomacopan (coversin) data adapted from Figs. 1, 2 & 3 of *Huber-Lang et al. J Immunol 2014; 192:5324–5331;*
BP activity taken from *Le Jan et al 2019*: IL17, IL22, IL6 and IL23 raised in blister fluid; TGFbeta raised in serum; *Solz et al 2017*: IL31 elevated in serum and blister fluid

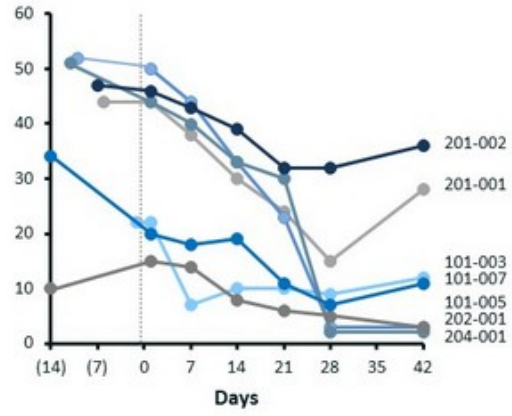
Phase 2: Rapid Reduction in BPDAI Activity Scores On Nomacopan

Single arm (n = 9); 42 days treatment; mild - moderate active BP; endpoints safety (primary) and BPDAI/QoL at Day 42

Mean BPDAI Activity + 90% CI



Individual Patients BPDAI Activity

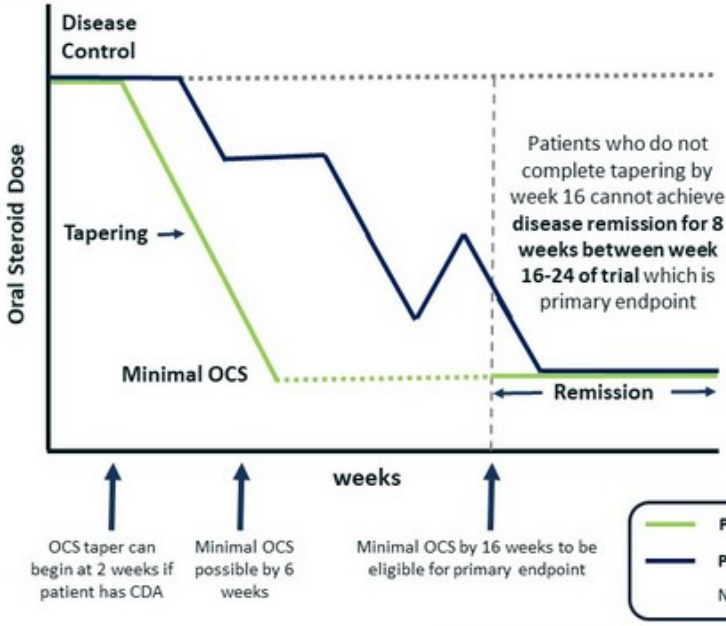


Phase 2 Observations

- **Rapid clinical response**
- **7 of 9 patients were responders**
- Clinical response similar to potent oral steroids
- 3 patients exhibited essentially complete remission within 6 weeks of treatment
- No reported grade 3, 4 or 5 treatment-related Adverse Events
- Results underpin ongoing Phase 3 trial with rapid steroid tapering

- All prior treatment, including steroids, withdrawn circa one week prior to initiation of treatment with nomacopan
- Addition of <30g/week low dose 0.1% lesional mometasone, a moderate topical steroid, was permitted from study initiation through Day 21. Mometasone may stabilize mild BP - but is not sufficiently potent to control moderate or severe BP

BP Phase 3 Trial Design Summary – and example response of two putative patients in the trial



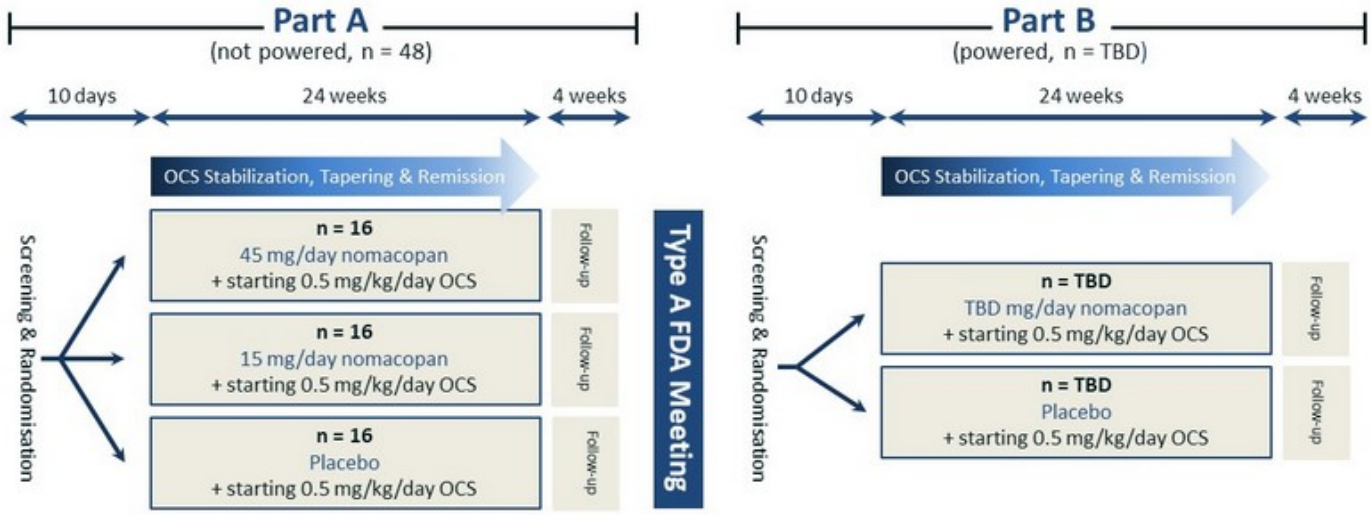
- Recruiting moderate and severe patients with oral corticosteroids (OCS) as current standard of care
- Systemic oral steroid - starting 0.5mg/kg/day
- Steroid tapering and disease remission phases
- Home monitoring to decrease patient burden
- Nomacopan likely to be additive to OCS, as each therapy impacts different immune pathways
- Testing 45mg (fully inhibiting C5 & LTB4) and 15mg (partially inhibiting C5 & fully inhibiting LTB4) vs single 30mg dose used in Phase 2

Patient 1: tapers to minimal OCS by 8 weeks and remains in disease remission

Patient 2: does not taper to minimal OCS by 16 weeks and fails primary endpoint

Note : if achieve wk16 remission but not maintained to week 24 also fail primary end point

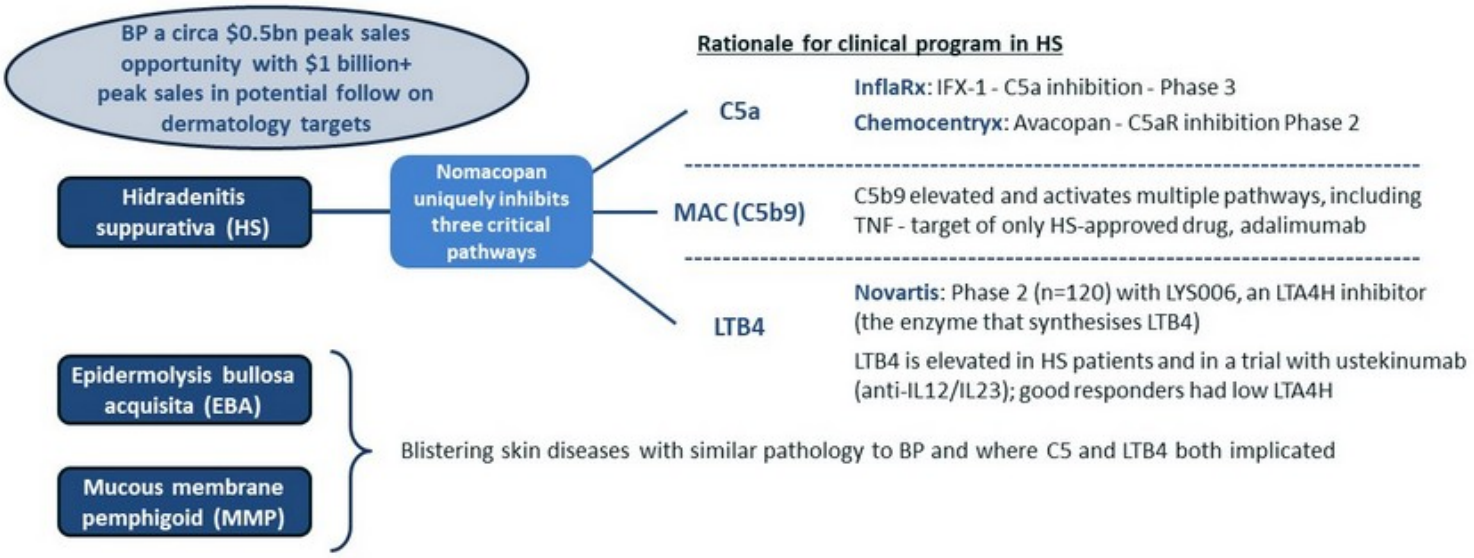
BP Phase 3 Design Provides Interim Readout After Part A



Primary endpoint: Achievement of Complete Disease Remission (Cr_{on}) on minimal OCS therapy (0.1mg/kg/day) for 8 weeks or more by Week 24

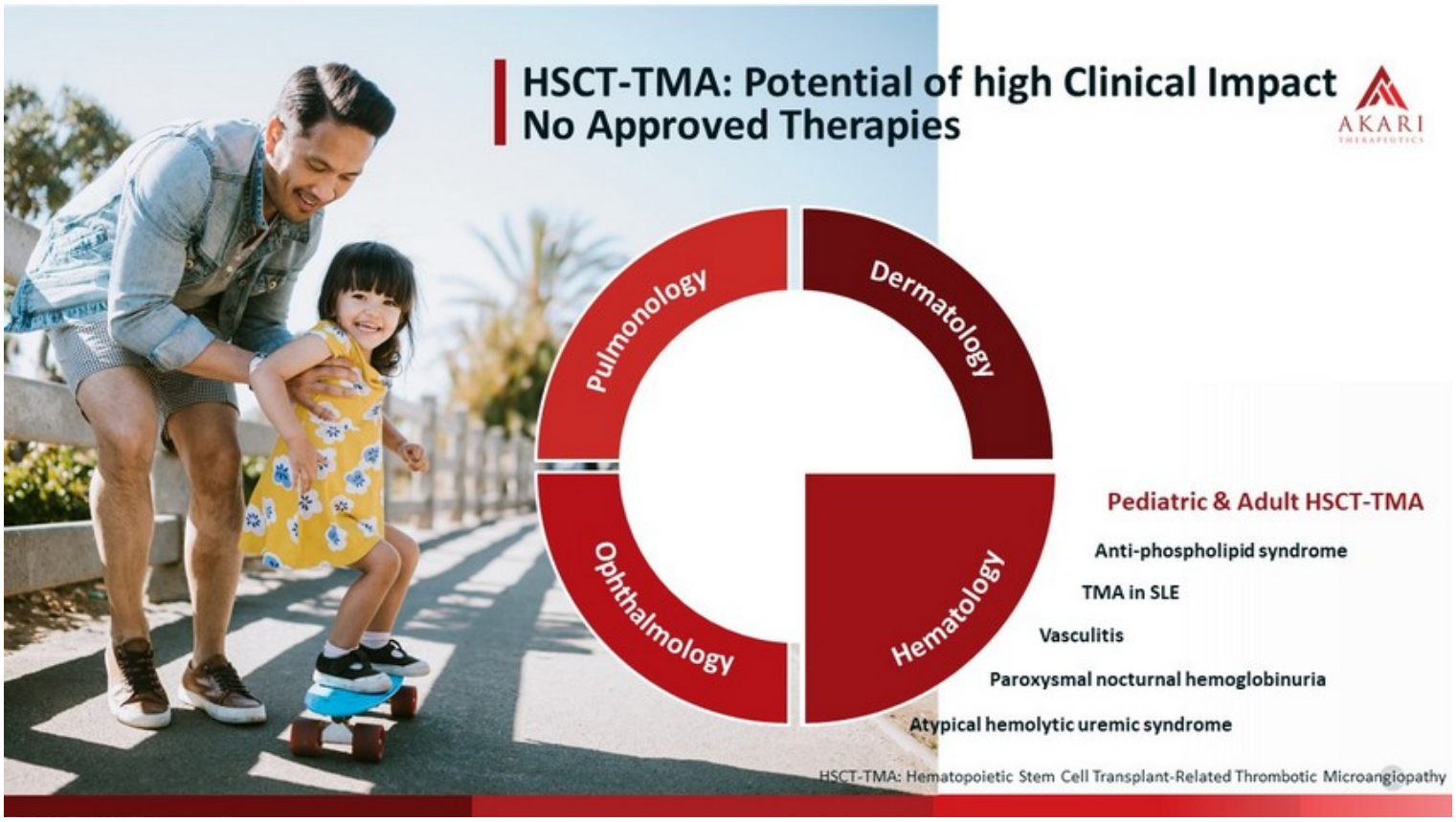
[CRon = Absence of new or established lesions and absence of pruritic symptoms while patient is receiving minimal therapy (≤ 0.1 mg/kg/day OCS) for at least 8 weeks]

Additional Dermatology Indications for Nomacopan



HS : Other mediators being directly targeted include IL17, IL23, IL1alpha and CXCR1/2 which are downstream to and likely to be inhibited by nomacopan (in addition to its direct effect on C5 and LTB4

REFERENCES: *Kanni et al., 2018*: Complement activation in hidradenitis suppurativa; *Frew et al., 2019*: Topical, systemic and biologic therapies in hidradenitis suppurativa; *Penno et al., 2020*: Lipidomics profiling of hidradenitis suppurativa skin lesions reveals lipoxygenase pathway dysregulation and accumulation of proinflammatory leukotriene B4; *Blok et al., 2016:* Ustekinumab in hidradenitis suppurativa


HSCT-TMA: Potential of high Clinical Impact
No Approved Therapies
AKARI
THERAPEUTICS
Pulmonology
Dermatology
Ophthalmology
Hematology
Pediatric & Adult HSCT-TMA
Anti-phospholipid syndrome
TMA in SLE
Vasculitis
Paroxysmal nocturnal hemoglobinuria
Atypical hemolytic uremic syndrome
HSCT-TMA: Hematopoietic Stem Cell Transplant-Related Thrombotic Microangiopathy

HSCT-TMA (Pediatric & Adult): Potential To Reduce Mortality In Aggressive Disease

Unmet Need

High mortality rate of up to 80% associated with severe pediatric HSCT-TMA

- Need for rapid, complete & sustained C5 & potentially LTB4 inhibition

Prevalence

~10K pediatric HSCT and ~60K adult HSCT performed in US + EU annually

- TMA diagnosed in up to 30% of HSCT
- 50% of the HSCT-TMA cases are severe

Cause

Vicious cycle of inflammation leads to progressive organ damage and death

- Complement activation leads to endothelial tissue injury, a prothrombotic state
- LTB4 shown to impact GVHD progression and activate endothelial surfaces and neutrophil extracellular traps (NETs) exacerbating prothrombotic state and elevating inflammation

Treatment

No approved therapies (SOC transfusions and immunosuppressants)

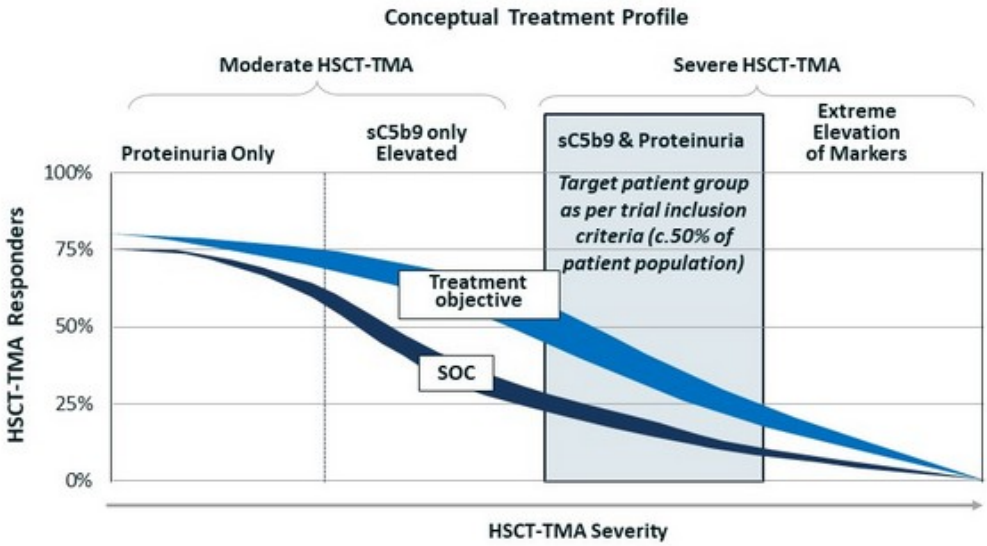
- Off-label use of eculizumab especially in US – used at higher dosing level than in PNH

Status

Phase 3 study ongoing in pediatric population

- Nomacopan has designated Orphan and Fast Track status for HSCT-TMA

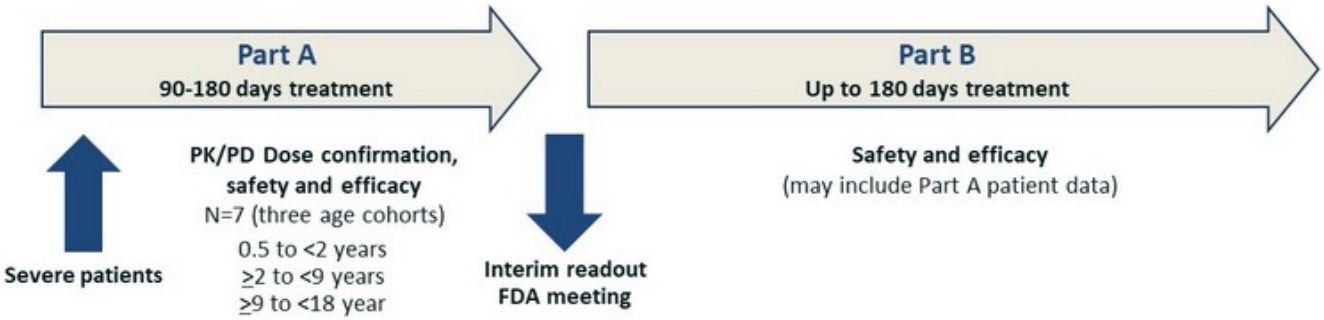
Pediatric HSCT-TMA Phase 3 Program Goals: Transfusions, Renal Function, Survival



- Targeting severe HSCT-TMA with elevated sC5b9 and proteinuria
- Early diagnosis and intervention critical to optimize responder outcomes
- Target population *c.*50% of patients with HSCT-TMA
- Treatment goals
  - Decrease transfusions
  - Renal improvement
  - Increase survival

Source: Conceptual graphic based on review of treatment literature, including Jodele et al Blood 2014 and Jodele et al., *Transfus Apher Sci* 2016; 54: 181-190

Pediatric HSCT-TMA Open-Label Phase 3 Study:



Primary Endpoints

- Response-based end point
- Reduced transfusion dependence and renal improvement

Additional Hematology Indications for Nomacopan

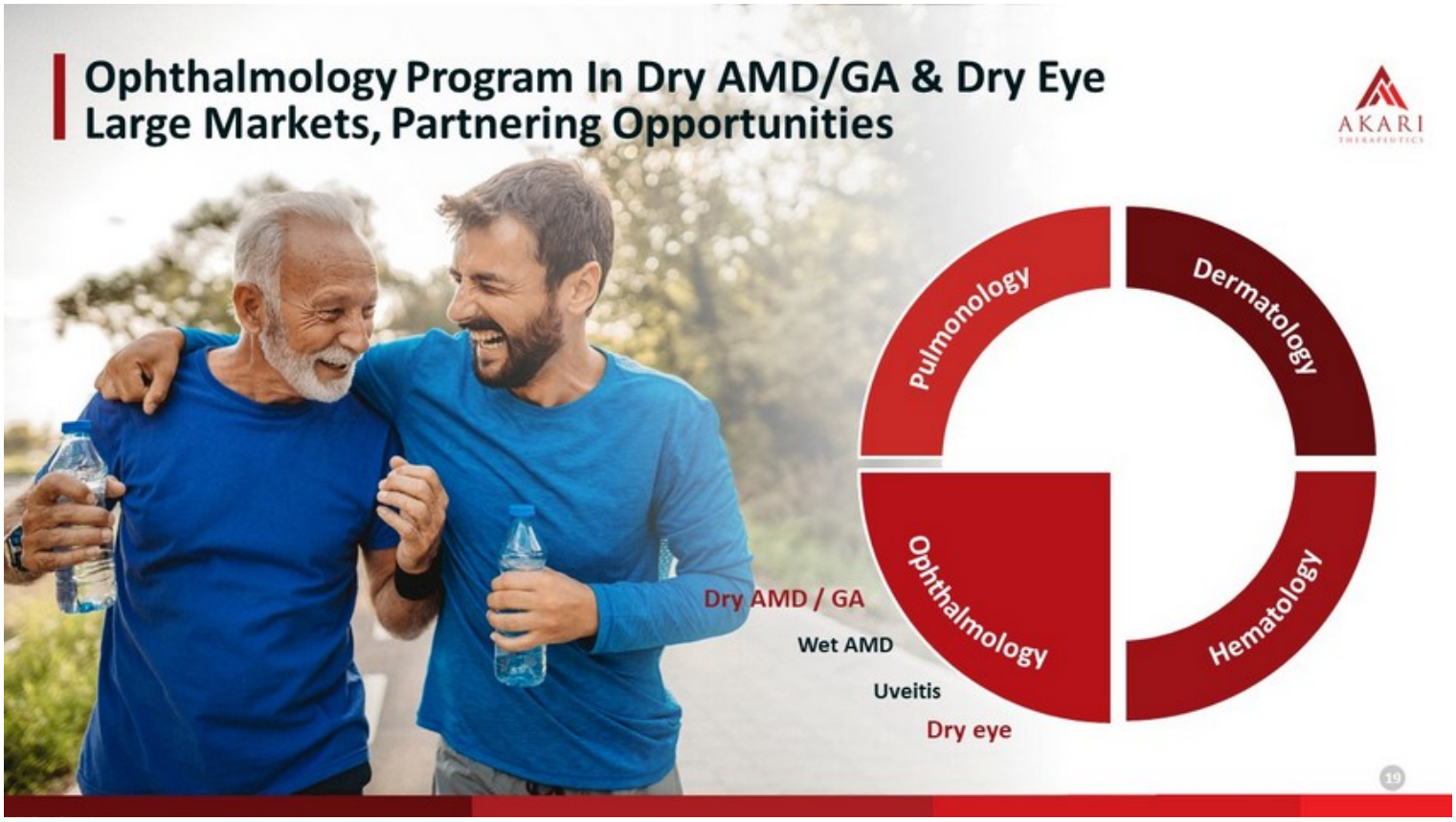
$1 billion peak sales in potential follow on hematology targets

$100M* market → **$500M* market** → **>$1bn total markets****

Pediatric HSCT-TMA → **Adult HSCT-TMA** →

- **Atypical Hemolytic Uremic Syndrome**
  - In aHUS *ex-vivo* model, C5b9 elevated on endothelial cells exposed to aHUS patient serum. LTB4 also increases C5b9 deposition. Nomacopan reduces C5b-9 deposition to normal levels
- **Anti-phospholipid syndrome**
  - In APS model nomacopcan reduces induced thrombi in mouse by 90% compared to normal human serum. Both C5 & LTB4 likely to play a role in disease[1]
- **TMA+SLE, Vasculitis, etc.**
  - C5 and LTB4 implicated in wide range of endothelial and kidney diseases. Ongoing *ex vivo* study at Ohio State University (OSU)

* US and EU5 markets only
** Initial and follow-on indications; company sources
Note : market size projection are company estimates based on existing treatments and prevalence
[1]Romay-Penabad et al., *Lupus* 2014; 23:1324-1326


Ophthalmology Program In Dry AMD/GA & Dry Eye
Large Markets, Partnering Opportunities
AKARI
THERAPEUTICS
Pulmonology
Dermatology
Ophthalmology
Hematology
Dry AMD / GA
Wet AMD
Uveitis
Dry eye
19

Topical Nomacopan: Surface of the Eye Inflammatory Diseases

- Nomacopan superior to dexamethasone and cyclosporin in experimental immune conjunctivitis; suppresses pro inflammatory Th2 and Th9 cells
- LTB4 significantly elevated in tear fluid of allergic conjunctivitis patients and C5 and LTB4 receptors detected in conjunctiva
  - Supports potential treatment role for nomacopan
- Phase 1/2 study in AKC*, a severe form of conjunctivitis, showed :
  - Nomacopan administered as eye drops twice daily for 56 days was comfortable and well tolerated
  - No drug related SAEs

In many of the surface of the eye inflammatory conditions, totaling up to $3bn, patients with more severe disease lack effective treatment options

- **Open IND** : Exploring optimal target disease for topical nomacopan, with options including Mucous Membrane Pemphigoid (autoimmune pathology related to BP) and severe forms of Dry eye


Orphanet Journal of Rare Diseases

LETTER TO THE EDITOR — Open Access

Dual inhibition of complement component 5 and leukotriene B4 by topical rVA576 in atopic keratoconjunctivis: TRACKER phase 1 clinical trial results

Allergy — EUROPEAN JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY

LETTER | Open Access

Allergic eye disease: Blocking LTB4/C5 in vivo suppressed disease and Th2 & Th9 cells

Malihe Eskandarpour, Xiaozhe Zhang, Alessandra Micera, Sarah Zaher, Frank D. P. Larkin, Miles Nunn, Stefano Bonini, Wynne Weston-Davies, Virginia L. Calder

First published: 06 October 2021 | https://doi.org/10.1111/all.15128

* Atopic Keratoconjunctivitis

Note : market size projections are company estimates based on existing treatments and prevalence

Potential for Long-Acting PASylated-Nomacopan in Back of the Eye Diseases, Including Geographic Atrophy/Dry AMD (GA)

- C5 & LTB4 receptors both identified in retina and a target for treatment across multiple back of the eye diseases including GA, uveitis and DME
- In experimental autoimmune uveitis, a back of the eye inflammatory disease, long-acting PAS nomacopan significantly reduced inflammation
- Inhibition of LTB4 significantly also reduces VEGF-A production, which can cause damaging choroidal neovascularization
- Long-acting PAS-nomacopan has potential to extend dosing interval

No approved treatment for GA: potential ~$10bn+ market

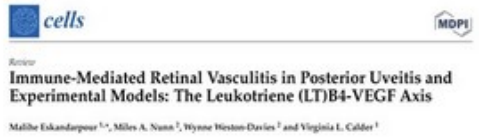
Pre-clinical program being extended for long-acting engineered PAS-nomacopan, with anticipated H1 2022 data, to enable:

- Optimal dosing and new PAS constructs to further extend hydrodynamic radius, half life and hence residency time - a key patient issue
- CMC optimization for back of the eye PAS formulation; objectives include further enhancing product quality, removing histopathology inconsistency and progressing to GMP manufacturing


Am J Pathol. 2021 Feb;191(2):320-334. doi: 10.1016/j.ajpath.2020.10.010. Epub 2020 Nov 4.

Leukotriene B 4 and Its Receptor in Experimental Autoimmune Uveitis and in Human Retinal Tissues: Clinical Severity and LTB 4 Dependence of Retinal Th17 Cells

Malihe Eskandarpour [1], Yi-Hsing Chen [2], Miles A Nunn [3], Sarah E Coupland [4], Wynne Weston-Davies [3], Virginia L Calder [3]


cells

MDPI

Review

Immune-Mediated Retinal Vasculitis in Posterior Uveitis and Experimental Models: The Leukotriene (LT)B4-VEGF Axis

Malihe Eskandarpour [1,*], Miles A. Nunn [2], Wynne Weston-Davies [2] and Virginia L. Calder [1]

Potential Advantages of Treating Geographic Atrophy (GA) with Long-Acting PASylated-nomacopan

Current Situation

- Complement C5 and C3 inhibition for treatment of GA looks promising
- APL-2 (anti-C3) from Apellis in submission to FDA, and Zimura (anti-C5) from Iveric in pivotal Phase 3

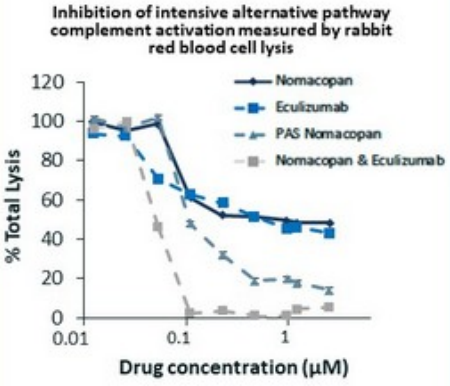
  However, both drugs:
  - Have mixed clinical response in reduction in lesion growth
  - Cause higher incidence of new cases of choroidal neovascularization (CNV) than sham, requiring additional intravitreal injection rescue treatment (VEGF inhibitors)
  - Standard treatment requires an injection every month into the eye, which is challenging for patients

Potential Improvement

- PASylated-nomacopan therapy has potential for:
  - Improved efficacy due to complement inhibition and additional anti-inflammatory activity by inhibiting elevated LTB4 in eye
  - Fewer new cases of neo vascularization – reducing need for anti-VEGF treatments
  - Decreased injection frequency from current once monthly therapies

PAS-nomacopan: highly effective C5 inhibitor

- Nomacopan C5 binding is very tight (K_D 0.1-1 nM)[1,2]
- PAS-nomacopan inhibits C5 more effectively than nomacopan in lysis model

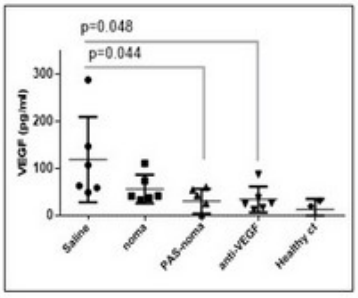


[1]Roversi et al., *J Biol Chem*. 2013;288:18789–18802;
[2]Macpherson et al., *J Biol Chem*. 2018; 293:14112-14121;

PASylated-nomacopan: Potentially Improved Clinical Response and Safety by Reducing CNV Risk in GA Patients

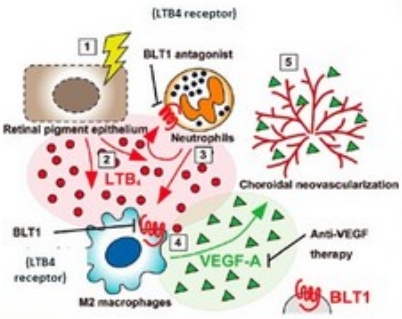
- PAS-nomacopan inhibits C5 **and** LTB4, which has additional potent anti-inflammatory benefits in animal models
  - In experimental uveitis, PAS-nomacopan reduced retinal inflammation by 58% compared to saline and 42% compared to anti-VEGF[1]
- **By reducing VEGF, PAS-nomacopan may reduce risk of CNV conversion in GA patients and associated rescue therapy**
- Higher incidence of damaging CNV(neovascularisation) in GA patients across APL-2 (Apellis) and Zimura (Iveric) clinical studies. This may then require treatment with additional rescue injections of VEGF inhibitors
- PAS-nomacopan in mouse model of severe uveitis:
  - Inhibited VEGF[1] (top panel) by preventing cell activation of M2 macrophages by LTB4 released by damaged retinal pigment epithelium (RPE)[2] (lower panel)
- In laser-induced neovascularisation mouse model, single PAS-nomacopan dose saw significant CNV reduction (p=0.02), in line with Eylea (anti-VEGF)[3]

REFERENCES: [1]Eskandarpour et al. *Cells* 2021; 10:e396; [2]Sasaki et al. *Int Immunol.* 2019;37:607-615; [3]Model performed by IRIS Pharma



Nomacopan and PAS-nomacopan reduce VEGF levels in mouse model of severe uveitis:

PAS-nomacopan has comparable effect to anti-VEGF antibody



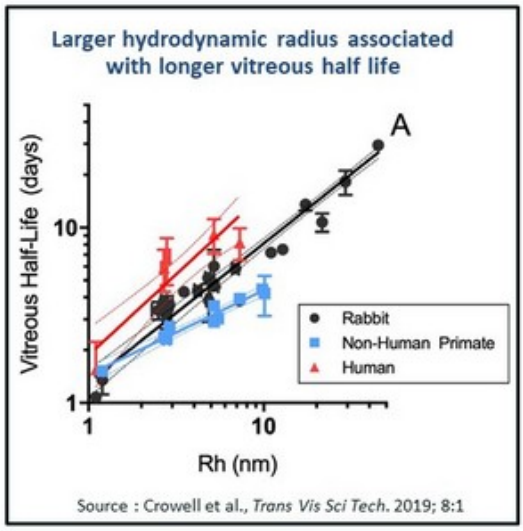
Mechanism VEGF inhibition by PAS-nomacopan:

1 & 2) RPE damage by lipid oxidation products causes synthesis LTB4, which recruits neutrophils and monocytes to retina
3 & 4) Paracrine/autocrine loop through BLT1 also recruits M2 macrophages which secrete VEGF-A
5) Acceleration of CNV due to elevated VEGF-A

Source : Sasaki et al

Potential for PAS-nomacopan to Extend Dosing Interval for Intravitreal Eye Injections, Increasing Safety & Convenience

- PASylation of nomacopan provides major half-life extension with same potent binding to C5 and LTB4 as compared to parent drug nomacopan
- Addition of PAS (a proline, alanine, serine repeat) greatly increases nomacopan's hydrodynamic radius (Rh) and molecular weight (MW); increasing half-life, leading to potential reduced injection frequency
- PAS600-nomacopan MW is 68kDa; but apparent MW by size exclusion chromatography is c.580kDa with a hydrodynamic radius of 9.3nm[1]
  - Competitive vitreal and retinal rabbit half life of 5-6 days* based on standard rabbit PK eye model
  - PAS-nomacopan relatively soluble and can be injected with a standard 30-gauge needle at concentrations > 60mg/ml (e.g. 6 mg for a 0.1ml injection)
  - Potential for 3 monthly injections using PAS-600 nomacopan
- Additional pre-clinical programs including tox and studies with PAS-nomacopan constructs with a larger hydrodynamic radius to further reduce injection frequency
- APL-2 (C3 inhibition) and Zimura (C5 inhibition) both have dosing constraints : C3 is at 30x level of C5 in the eye[2] and Zimura due to its viscosity requires 2 injections of 0.1ml for 4mg dosing[3]

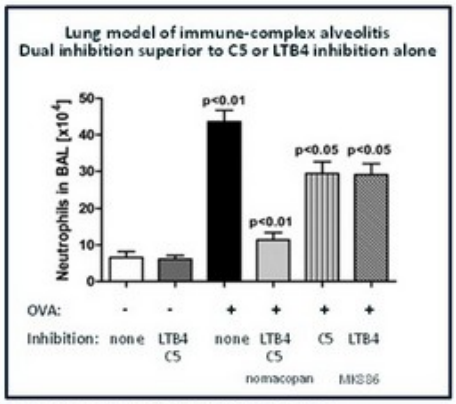


(1) Kuhn et al., *Bioconjugate Chem.* 2016; 27:2359-2371
(2) Mandava et al., *Retina* 2020;61: e39
(3) Jaffe et al, Ophthalmology 2020

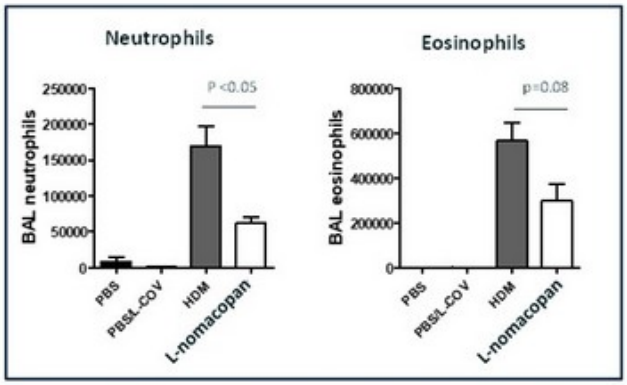
*Est rabbit vitreal half life of 2.5-2.9 days for Lucentis and 3.9 to 4.6 for Eylea : Garcia-Quintanilla et al 2019 and Park et al, IOVS 2016


Potential Across Multiple Pulmonary Indications
Large Markets, Partnering Opportunities
AKARI
THERAPEUTICS
Severe asthma
COVID-19
COPD
PAH
Pulmonology
Dermatology
Ophthalmology
Hematology
25

Inhibition of C5 & LTB4 by Nomacopan Established Across Multiple Pulmonary Indications in Preclinical Models



Source : Roversi et al (2013) JBC 288: 18789 - 18802



Source: Akari preclinical study with Imperial College, London- House Dust Mite challenge in Mice

- Leukotriene pathway validated in the lung. Zileuton® (general leukotriene inhibitor) approved in **severe asthma**
- Preclinical lung models show additive effects of C5 and LTB4 inhibition by nomacopan
- LTB4 inhibition by L-nomacopan reduced neutrophil & eosinophil recruitment to bronchoalveolar
- Nebulized nomacopan provides median particle size <5µM for deep lung delivery

Targeting Improved Treatment of Severe Lung Exacerbations

Inadequate current treatment options

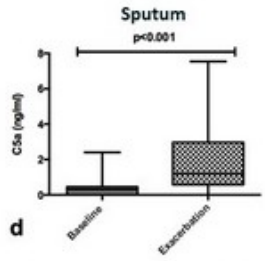
- High prevalence of respiratory inflammatory disease
  - 2nd most common global cause of death
  - **Carries high personal & health care costs**
- Exacerbations drive clinical visits and hospital admissions, particularly in winter

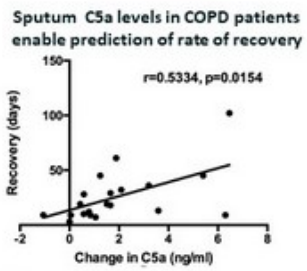
Patients live in fear :

- Need for a treatment specific for hyperinflammatory response
- Ability for patients to administer a simple inhaled therapy to **preempt full scale exacerbations**
- **Improved patient control** when standard therapy fails

Complement (C5) and Leukotriene (LTB_4) strongly implicated in **driving hyperinflammatory response**

24 COPD patients at baseline and on exacerbation





COVID pneumonia observational study

- Plasma levels of C5a, C5b9 and LTB4 elevated
- Levels of C5a (p = 0.001) and C5b9 (p = 0.019), significantly higher in patients that worsened from moderate to severe
- Potential biomarkers for disease progression

Note : Westwood J-P et al. *ERJ Open Res.* 2016; 2:00027-2016

Akari Summary

Platform Molecule

- Dysregulation of complement and leukotriene pathways implicated across a wide range of poorly treated inflammatory diseases
- Multiple formulations (Sub-Q, topical, inhaled, long-acting PAS-nomacopan) provides risk diversification and flexibility in terms of partnering / collaborations

Validated Therapeutic Approach

- Recent $1 billion+ acquisitions* focused on complement-mediated diseases

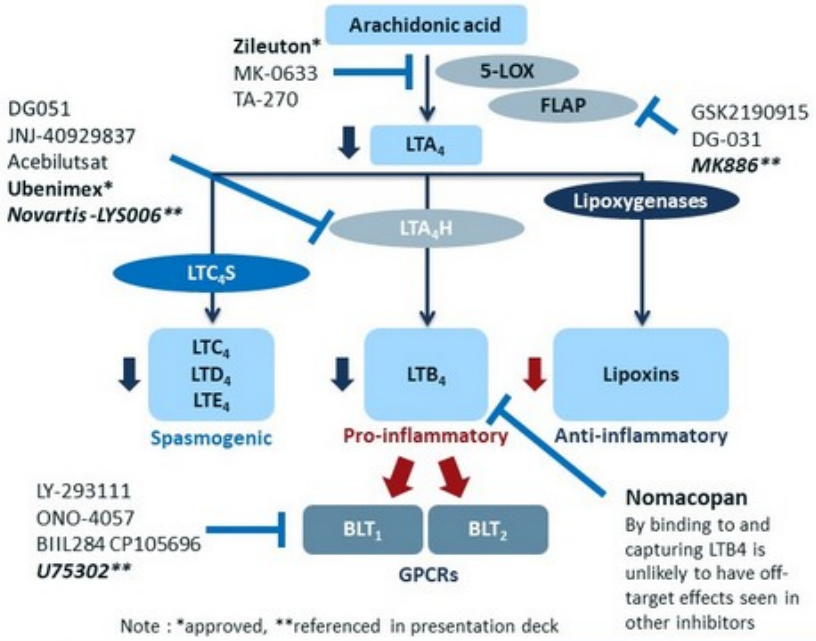
Late stage

- Late-stage orphan programs in pivotal studies
- Lead indications are gateways to high potential follow-on indications
  - Earlier-stage programs in blockbuster indications

* Acquisitions of RA Pharma by UCB, Achillion by Alexion and Alexion by AstraZeneca


Appendix

LTB4 Ligand Capture: Nomacopan's Advantageous & Unique Mode of Action (MOA)



Note : *approved, **referenced in presentation deck

Off-Target Effects of Other Inhibitors

5-LOX / FLAP inhibitors

- Reduces anti-inflammatory lipoxins

BLT1/BLT2 antagonists

- Realization that anti-inflammatory mediators also signal through BLT1/BLT2

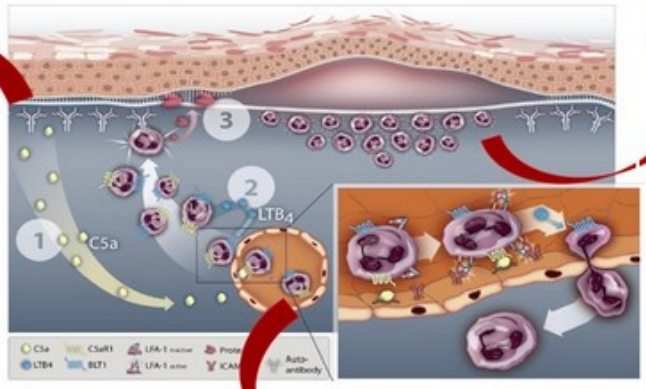
LTA_4H inhibitors

- Secondary anti-inflammatory role for LTA_4H in degrading pro-inflammatory/ remodelling mediator PGP

Note: LTB4 capture by nomacopan is external to cell so will not interfere with recently described anti-inflammatory effects of LTB4 within cells

Interaction Of C5 & LTB4 in Bullous Pemphigoid Pathology

1. Autoantibodies directed against dystonin (BP230) and type XVII collagen (BP 180) are deposited at the dermal-epidermal junction (DEJ); this leads to the formation of C5a



3. Activation of neutrophils at the DEJ by the deposited autoantibodies induces the release of proteases which degrade proteins of the DEJ and compromise dermal-epidermal adhesion.

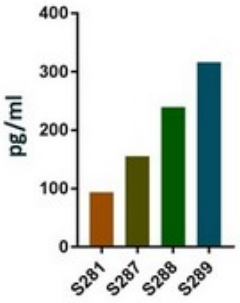
2. C5a binds with C5aR1 on neutrophils in dermal blood vessels and induces the release of LTB4. LTB4 further amplifies the recruitment of neutrophils and directs their migration to the DEJ.

Sadik et al., Semin Immunol 37:21-29 (2018)

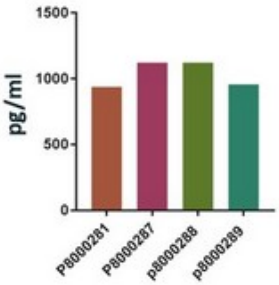
Rational for Nomacopan in Bullous Pemphigoid Preclinical Efficacy & Elevated C5a/LTB4 (In BP Patients)

Elevated levels of LTB4 and C5a indicate activation of complement and synthesis of LTB4 in blisters

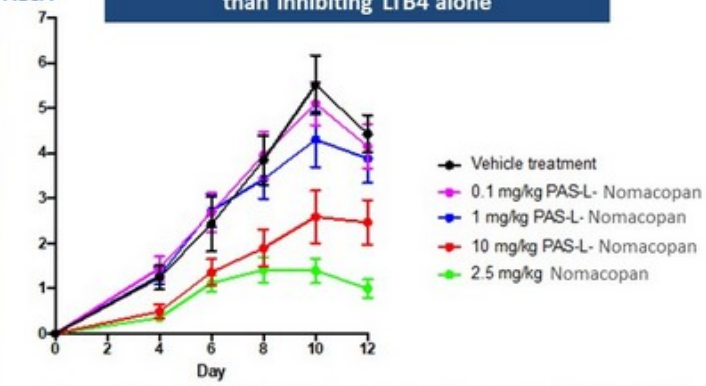
LTB4 levels
Human blister fluid



C5a levels in
blister fluid diluted 1:25



Nomacopan inhibiting C5+LTB4 more effective than inhibiting LTB4 alone

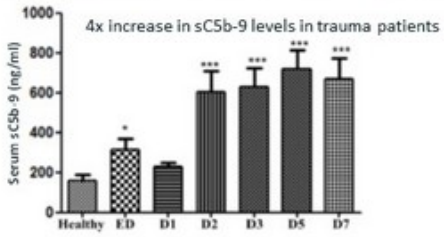


- Mouse model of BP-like epidermolysis bullosa acquisita (EBA)
- ~80% reduction in absolute body surface area affected by blisters (ABSA) on Nomacopan (SQ) compared to vehicle
- Long acting LTB4-only Nomacopan (10 mg/kg) ameliorates blister formation, but less effective than molar equivalent dose of Nomacopan (2.5 mg/kg) inhibiting C5 + LTB4

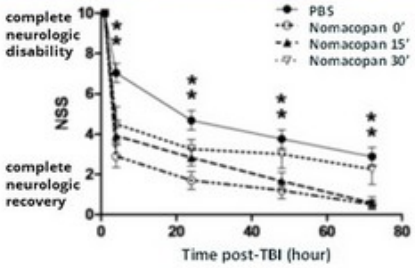
Preclinical passive mouse model of epidermolysis bullosa acquisita (EBA)

Cooperative Research & Development Agreement (CRADA) With US Army In Trauma

USAISR study of complement level in trauma patients



Nomacopan (OmCI) reduces neural damage in mouse trauma model



- Ongoing collaboration with U.S. Army Institute of Surgical Research (USAISR) to evaluate nomacopan activity in pig model of blast injury and haemorrhagic shock
- Nomacopan reduced secondary neuroaxonal loss and promoted neurologic recovery after traumatic brain injury (in mice)
- Nomacopan does not require special handling and can be carried at ambient temperature; may facilitate use in prehospital settings
- C5 and LTB4 inhibition by nomacopan for treatment of trauma is supported by a large body of literature reflecting the harmful role for both these inflammatory mediators in early pathophysiology of trauma & haemorrhagic shock

Early complementopathy predicts the outcomes of patients with trauma; Li Y, et al. Trauma Surg Acute Care Open 2019;4:e000217
Inhibition of the Membrane Attack Complex of the Complement System Reduces Secondary Neuroaxonal Loss and Promotes Neurologic Recovery after Traumatic Brain Injury in Mice; J Immunol 2014; 192:2339-2348

Active Pipeline Program Expansion

Engineered Nomacopan

- New chemical entity with extended patent protection
- Long-acting PASylated nomacopan with potential for weekly Sub-Q and in frequent IVT dosing
- Tissue targeted : nomacopan linked to peptides which bind to specific disease related tissue such as neuromuscular junction
- Ligand specific: C5 or LTB4 inhibition only for diseases that do not require inhibition of both mediators

Other lipocalin molecules

- Votucalis captures histamine uniquely preventing activation of all four histamine receptors which can induce diverse pathophysiological processes, including chronic pain, itch and inflammation. Potential for topical delivery.


AKARI
THERAPEUTICS
Combined Inhibition Of
Complement & Leukotriene Pathways
To Treat Inflammatory Diseases
December 2021