Combined inhibition of complement and leukotriene pathways to treat inflammatory diseases

AKARI THERAPEUTICS

September 2020

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

- Focused on treating inflammatory diseases through inhibition of complement and leukotriene pathways
  – Lead molecule, nomacopan, inhibits both C5 (complement) and LTB4 (leukotriene)
- Two lead clinical programs in Phase 3 – targeting orphan diseases with no approved treatments:
  – **Bullous Pemphigoid**: severe dermatological condition of the elderly
  – **HSCT-TMA**: severe microangiopathy, targeting pediatric population
- **COVID–19 pneumonia**: planned integrated international clinical programs
- **Ophthalmology**: Phase 1/2a study in AKC; back of the eye indications in preclinical development
- Lead programs expected to have clear regulatory paths to pivotal studies, fast-to-market potential, and target peak sales of $500m+ including initial and follow-on indication potential
- Multiple upcoming clinical readouts expected in 2020 and 2021

AKC: Atopic Kerato-conjunctivitis; HSCT-TMA: Hematopoietic Stem Cell Transplant-Related Thrombotic Microangiopathy

Nomacopan: unique de-risked immunomodulator in Phase 3 development for orphan indications

Nomacopan Platform

- Unique mode of action by directly inhibiting C5 and LTB4 with additive proinflammatory effects
- Rapid clinical response demonstrated in multiple inflammatory disorders
- 35+ cumulative years patient safety data
- Clear path to potential BLA submissions, including three Orphan and two Fast-Track designations

Late Stage Target Indications

Pediatric HSCT-TMA
Phase 3
Potential fast path to approval

Bullous Pemphigoid
Phase 3
$300M + peak sales opportunity

COVID-19 pneumonia
+ chronic lung diseases
>$1 billion market opportunity*

* Initial and follow-on indications; company sources

Nomacopan competitive advantage: Synergistic C5 and LTB4 inhibition

INDEPENDENT ACTIVATION PATHWAYS SIGNAL CONTINUALLY IN DEVELOPING & ESTABLISHED DISEASE

C3 convertase

C3b

C3

Opsonisation

Amplification loop

C3b

C5 convertase

C5

Anaphylatoxins

C3a

C5a

Engagement GPCRs C5aR/C5aL2

C5b

C6

C7

C8

C9

Membrane Attack Complex

MEDIATORS OF PATHOLOGY DRIVE DISEASE MAINTENANCE

- Granulocyte activation
- Mast cell degranulation
- Proinflammatory cytokines
- Procoagulant effects
- Cell lysis / Proliferation
- Modulation B and T cells

Engagement GPCRs BLT1/BLT2

PLA2

Arachidonic acid

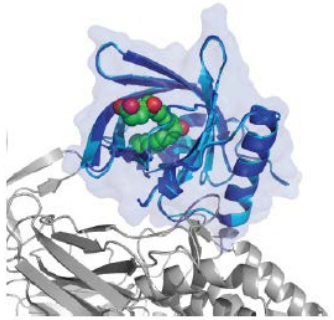
LTB4

LTA4H

ALOX5

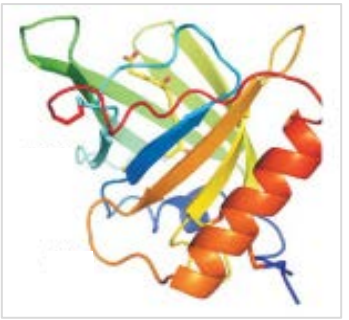
cysLTs

Lipox



Crystal structure of nomacopan simultaneously bound to C5 and LTB4

Nomacopan



Crystal structure of nomacopan bound to LTB4

Interruption of effector mechanisms expected to inhibit innate and acquired immune responses contributing to disease

Leukotriene (LTB4) and complement (C5) activation both implicated in Akari's target conditions

- Complement activation causes direct cell/tissue damage & activates leukocytes most potently neutrophils. C5 inhibition is an approved treatment for several diseases via Eculizumab
- LTB4 is a powerful neutrophil attractant, active at sites of inflammation. LTB4 inhibition is an approved treatment for inflammation in the lung via Zileuton

Category	Disease	Expected Effect By Inhibiting C5		Expected Effect By Capturing LTB4
		C5a GPCRs*	sC5b9	LTB4 GPCRs
Dermatology	**BP**	• Reduced recruitment of cells mediating epithelial inflammation	• Reduced deposition in epithelial basement membrane	• Reduced recruitment of cells that mediate epithelial inflammation
Hematology	**HSCT-TMA**	• Reduced inflammatory and prothrombotic state of endothelium	• Reduced deposition in kidney endothelium	• Associated with GVHD • LTB4 present at high concentrations in diseased kidney
Eye	**Surface / Back of Eye**	• Reduced inflammatory state conjunctival epithelium and cornea • Reduced retinal inflammatory cells	• Unknown	• Drives T cell differentiation to effector Th17. LTB4 present at high concentrations • Reduced release of VEGF
Lung	**COVID-19 pneumonia**	• Reduced inflammatory and prothrombotic state endothelium	• Reduced deposition in lung and vascular endothelium	• LTB4 at high concentrations in diseased lung. Molecule inhibiting LTB4 (Zileuton) approved in severe asthma

* G protein-coupled receptors

Clinical development strategy: Fast-to-market, targeting indications with unmet need

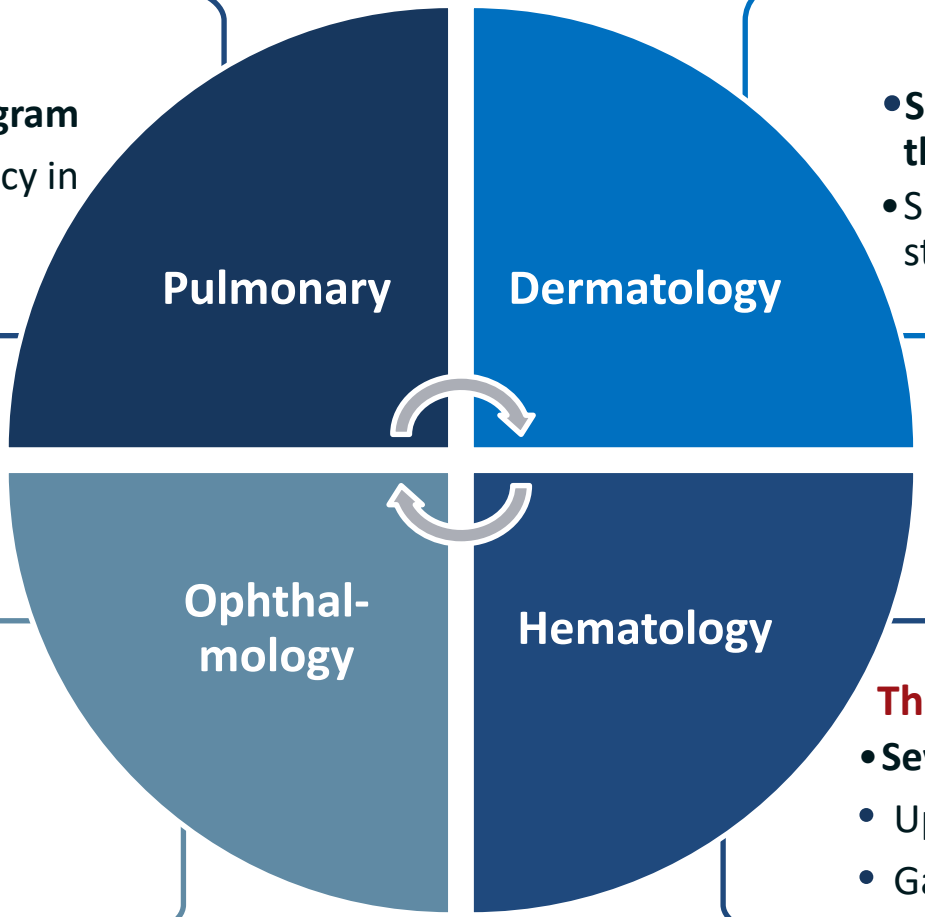
AKARI THERAPEUTICS

COVID-19 Pneumonia / Lung

- **International COVID-19 pneumonia program**
- Preclinical evidence of nomacopan efficacy in multiple lung conditions

Bullous Pemphigoid (BP)

- **Severe dermatological disease, primarily in the elderly**
- Side effect concerns with current SOC – steroids



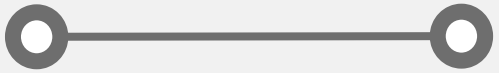
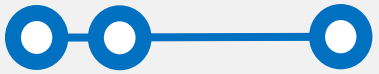
Atopic Kerato-conjunctivitis (AKC)

- **Debilitating surface of the eye disease**
- Preclinical other back of the eye indications - evidence of nomacopan efficacy in uveitis and

Thrombotic Microangiopathy (HSCT-TMA)

- **Severe disease – pediatric focus**
- Up to 80% mortality rate on current SOC
- Gateway into other TMAs

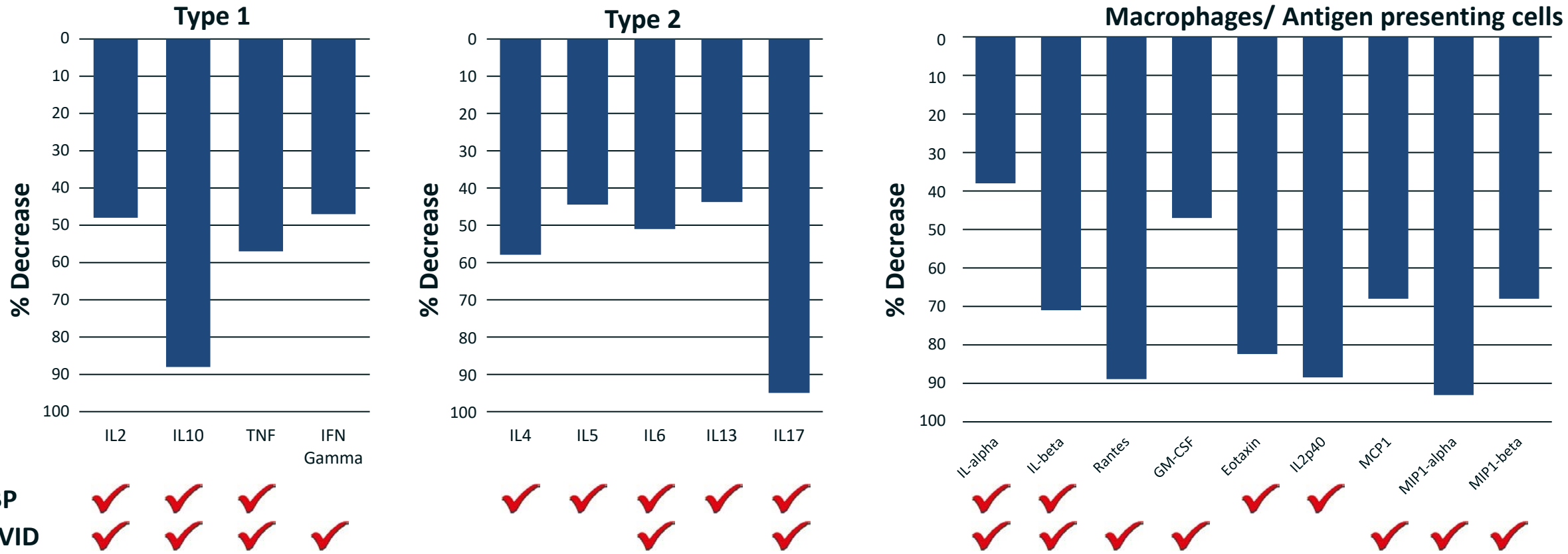
Nomacopan: Three active Phase 2/3 programs

Category	Disease	Preclinical / Phase 1 / Phase 2 / Phase 3	Results	Planned Upcoming Milestones
Dermatology	Bullous Pemphigoid		• Phase 2: 7/9 patients responded • ODD* (FDA)	• Phase 3 to initiate 1H/2021
Hematology	Thrombotic Microangiopathy		• Phase 3 IND Open • ODD and FTD* (FDA)	• Initiate recruitment Q4 2020. Deferred due to COVID-19
	Paroxysmal Nocturnal Hemoglobinuria		• 19 patients treated • High levels of transfusion independence	• Deprioritized • Additional data expected Q4 2020
Pulmonary	COVID-19 pneumonia		• Supportive preclinical data • Initial smaller safety studies	• Ongoing studies : H2 2020 readouts
Ophthalmology	AKC / Back of the Eye		• Topical nomacopan: good safety profile, well tolerated • Positive pre-clinical data	• Further recruitment COVID-19 dependent

* ODD: Orphan Drug Designation; FTD: Fast Track Designation

Nomacopan inhibits downstream cytokine & chemokine signaling cascades implicated in BP and COVID pathology

Inflammatory markers inhibited by nomacopan in polymicrobial sepsis mouse model



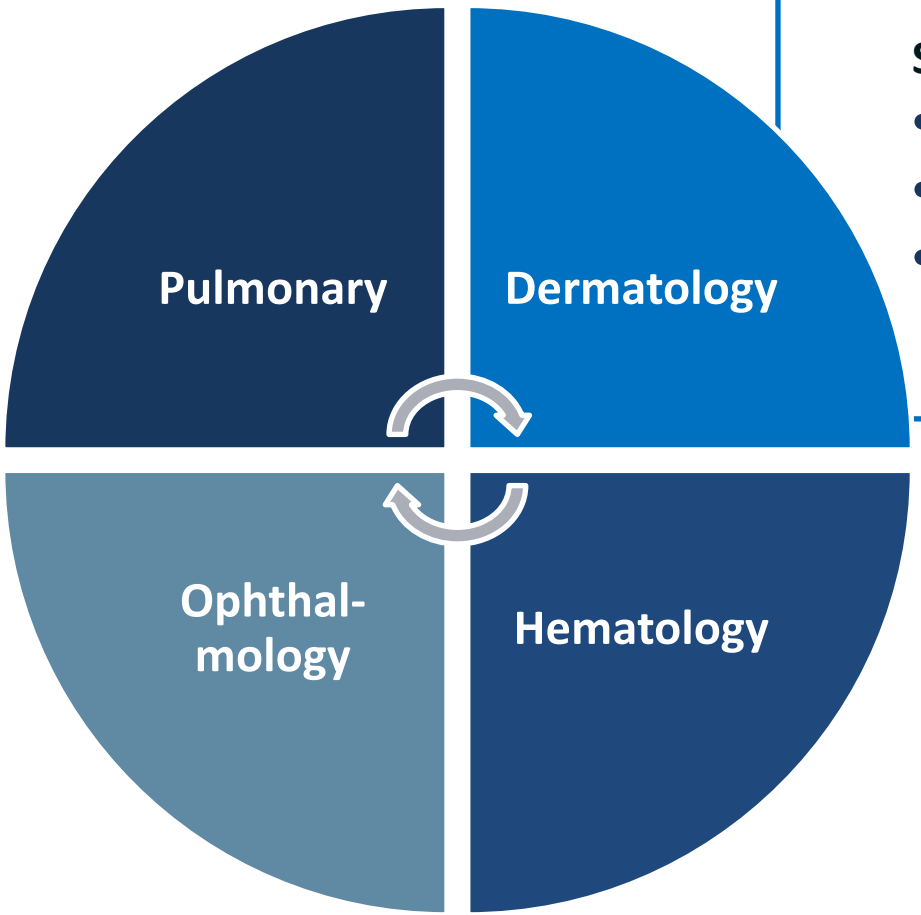
Source:

Nomacopan (coversin) data adapted from Figs. 1, 2 & 3 of Huber-Lang et al. J Immunol 2014; 192:5324 – 5331 ;

COVID activity taken from : Mehta P et al. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet, March 16 2020; 395(10229): 1033 – 1034;

BP activity taken from Le Jan et al 2019: IL17, IL22, IL6 and IL23 raised in blister fluid; TGFbeta raised in serum; Salz et al 2017: IL31 elevated in serum and blister fluid;

Bullous Pemphigoid:
Chronic disease with no approved therapies



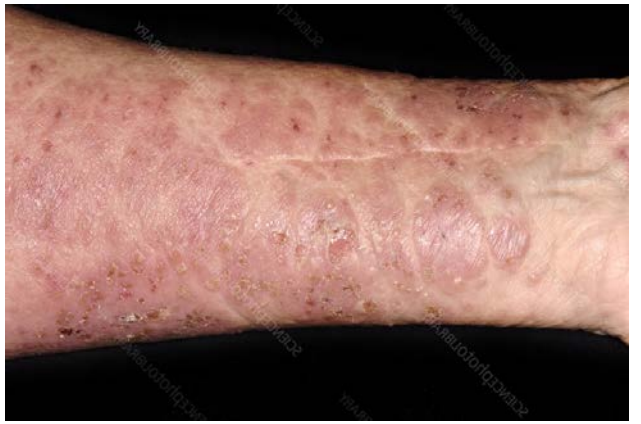
Bullous Pemphigoid (BP)

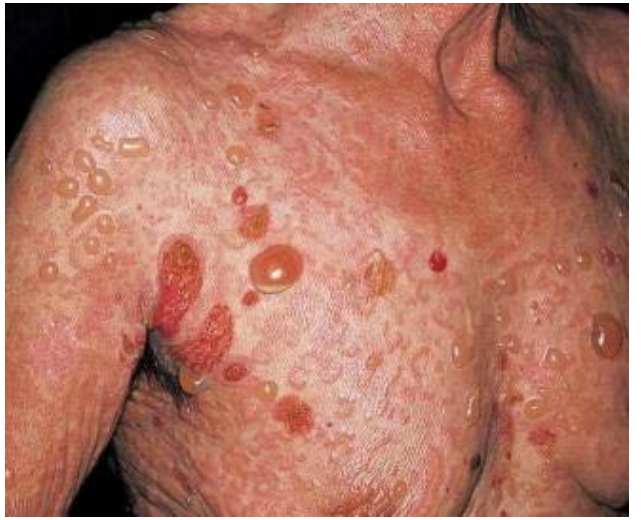
Severe dermatological disease of the elderly

- Side effect concerns with current SOC – steroids
- C5 and LTB4 elevated
- Phase 2 complete, supporting entry into Phase 3 expected to commence H1 2021

Bullous Pemphigoid: Auto-immune blistering disease with no approved therapy

Unmet Need	**High dose OCS* use associated with approximately three-fold increase in mortality in this patient group** • Need for efficacious therapy that has rapid onset of action and is steroid-sparing
Prevalence	**Most common auto-immune blistering skin disease** • ~18 in 100,000; 75% are moderate/ severe • Majority of cases in elderly aged 70+ years
Cause	**Auto-antibodies in the epidermal membrane zone leads to separation of dermis / epidermis** • Elevated C5 & LTB4 levels at site of blisters
Treatment	**No approved therapies** • Use of topical corticosteroids for mild cases • High dose OCS or superpotent topical steroids first line for moderate to severe patients





* OCS: Oral corticosteroids

Completed Bullous Pemphigoid Phase 2 study in mild-to-moderate disease

Study Design

- Single arm (n = 9); 42 days treatment
- Active BP; newly diagnosed or recurrent

Treatment

- Nomacopan SQ dosing
- **Day 1**: 60 mg and 30 mg 12 hours later
- **Days 2-42**: 30 mg once daily

Endpoints

- **Primary:** Safety
- **Secondary**: Efficacy evaluated by BPDAI
  BPDAI & QoL at day 42

Phase 2 Results

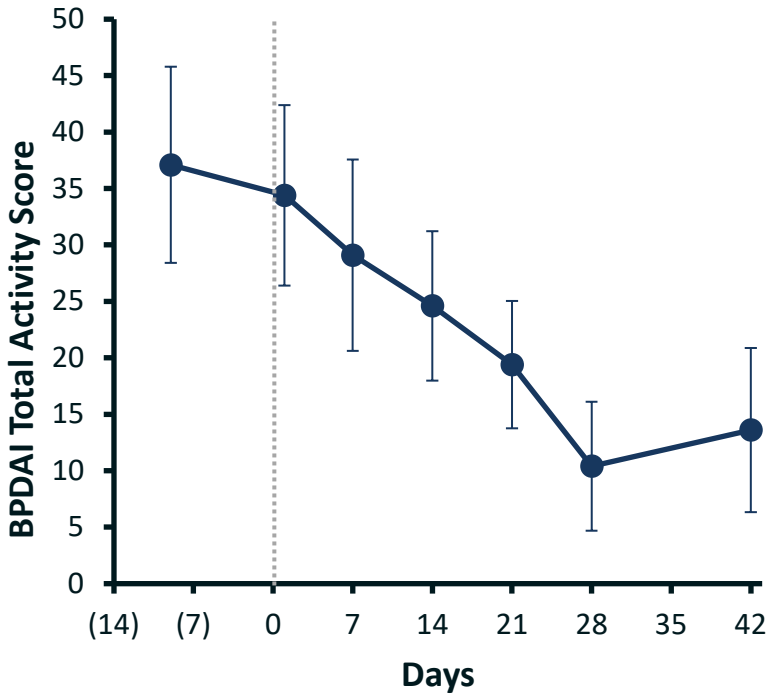
- 7 of 9 patients responded
  - 3 showing > 80% reduction in BPDAI activity
  - 3 showing ~ 40% reduction in BPDAI activity by Day 42
  - 2 of 9 patients were non-responders
- No reported grade 3, 4 or 5 treatment-related AEs

- Day 1 to 21: nomacopan (30 mg once daily) + lesional mometasone only
- Day 21 to 42: nomacopan only
- Any use of mometasone or any other steroid after Day 21 considered rescue therapy

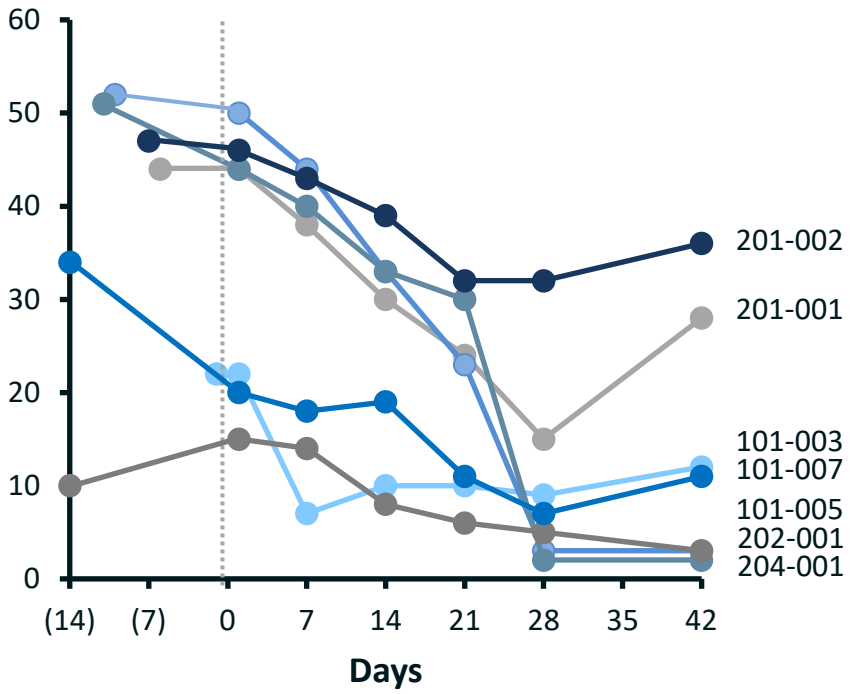
Phase 2 Responder BPDAI activity scores (n=7) and Phase 2 observations ahead of Phase 3 initiation

AKARI THERAPEUTICS

Mean BPDAI Activity + 90% CI



Individual Patients BPDAI Activity



Phase 2 Observations

- Rapid clinical response
- Quantum of response similar to potent oral steroids
- Indications that remission may be achievable with 6 weeks of treatment
- Good safety profile; well tolerated
- Supports Phase 3 design of rapid steroid tapering

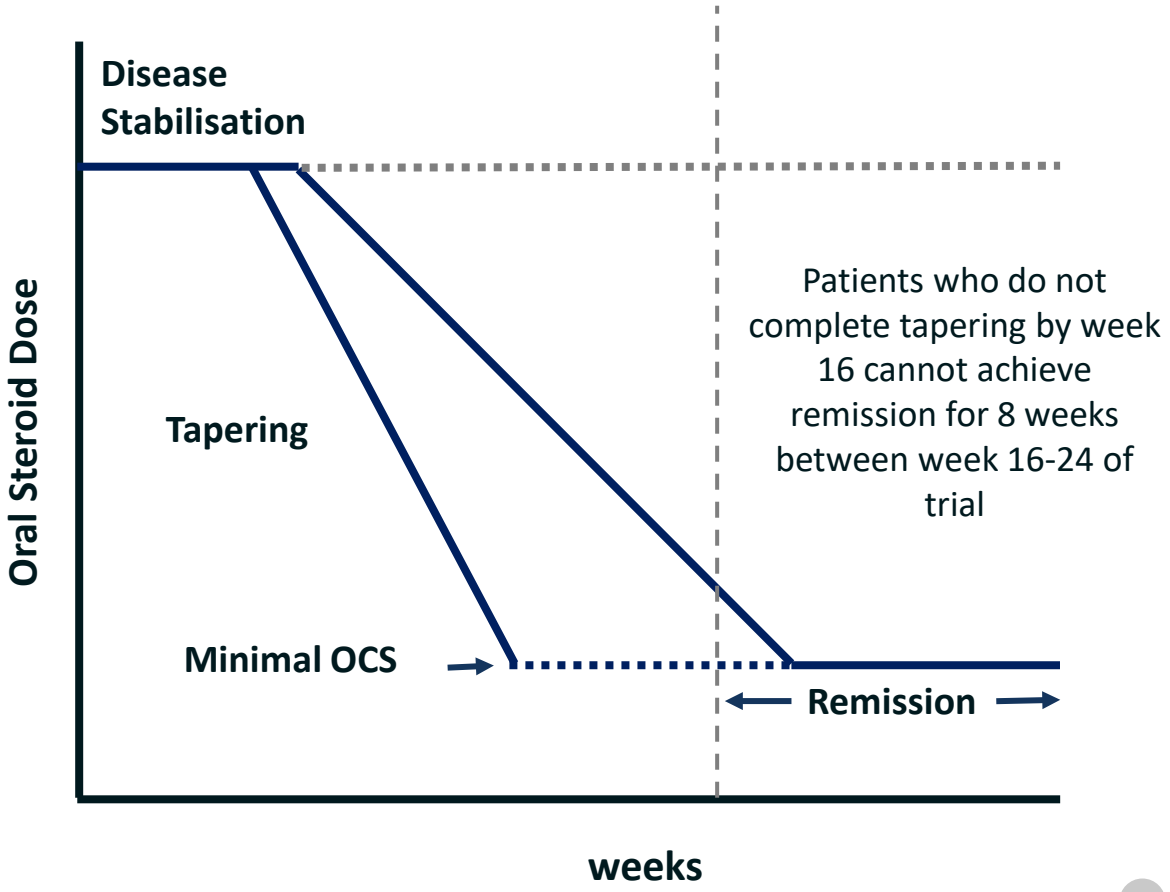
- Prior treatment withdrawn approximately one week prior to treatment with nomacopan
- Lesional mometasone permitted until Day 21. Mometasone is a moderate topical steroid that was given at a low dose which can help to stabilize mild BP but is not used to control moderate or severe BP

BP Phase 3 versus Phase 2 design

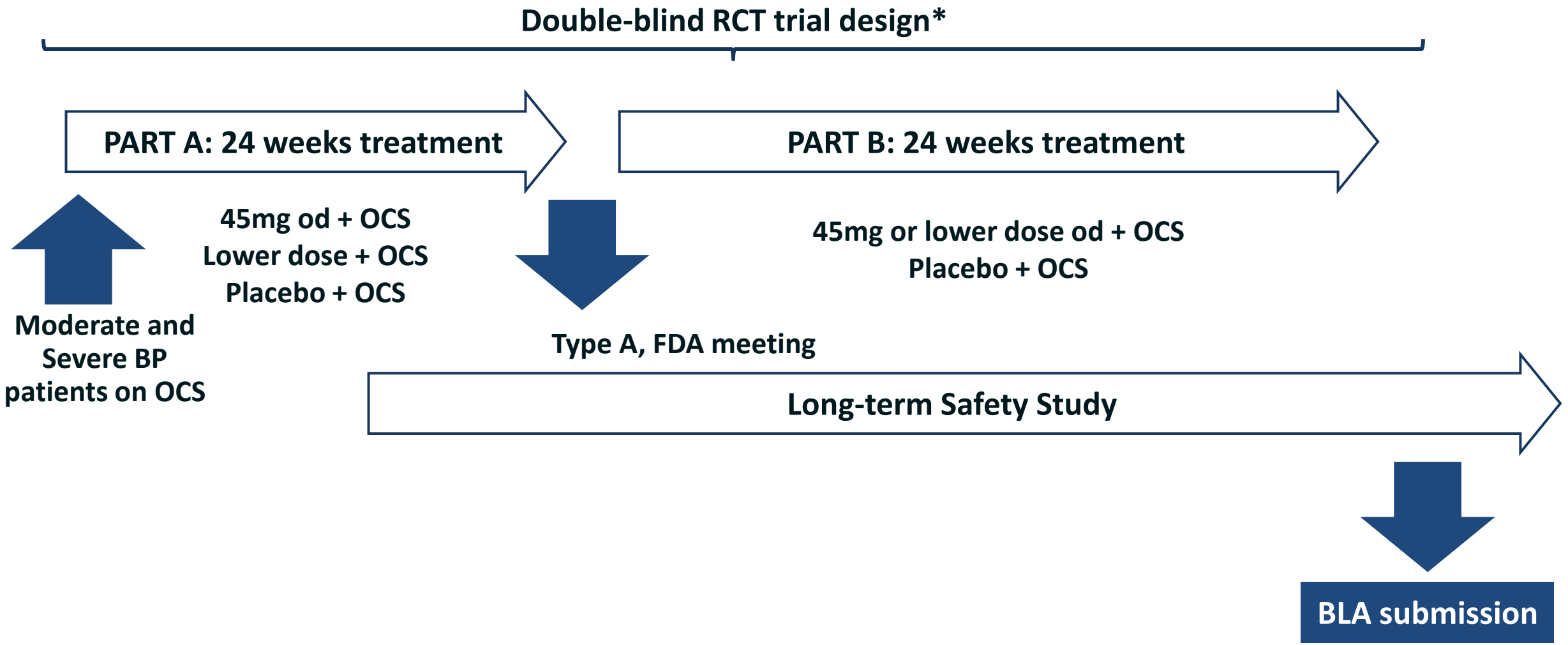
Phase 3 Vs Phase 2 Design

- Longer treatment period
- Steroid tapering and disease remission phases
- Higher dosing nomacopan
- Home monitoring to decrease patient burden
- Inclusion / exclusion criteria tailored to maximize patient recruitment while avoiding patients who may not reach end of trial

Phase 3 Design

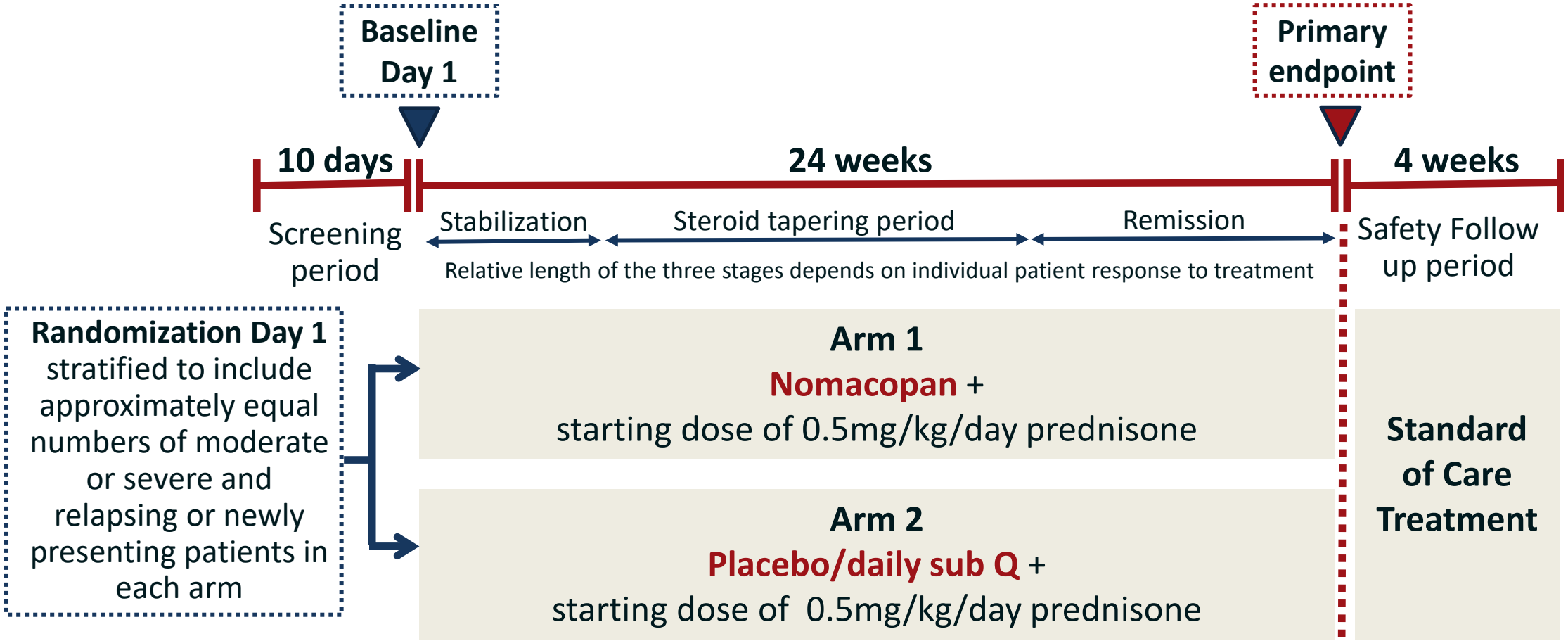


Proposed Phase 3 BP study design



* Patient inclusion, endpoints etc. is the same for Part A and Part B

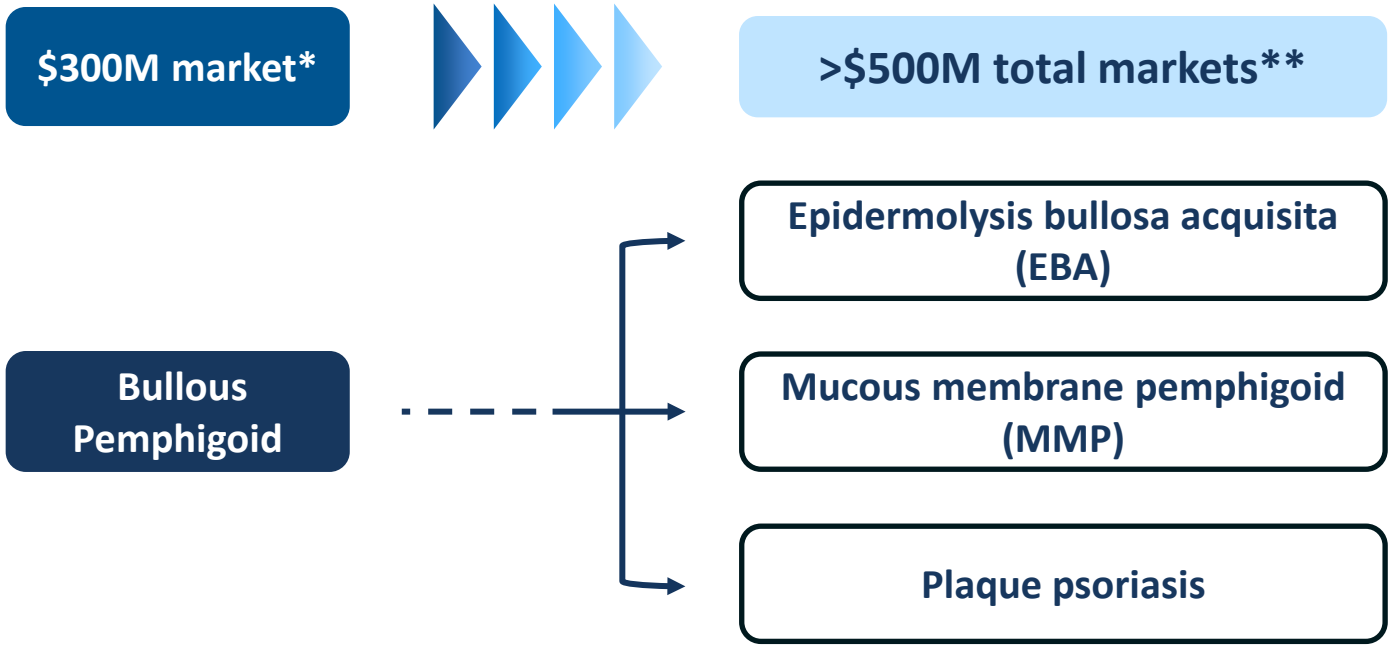
BP Phase 3 Part B design schematic



Primary endpoint: Complete remission while patient is receiving minimal therapy for at least 2 months. Minimal therapy is defined as less than or equal to 0.1mg/kg/day of prednisone

Bullous Pemphigoid: Gateway to other indications

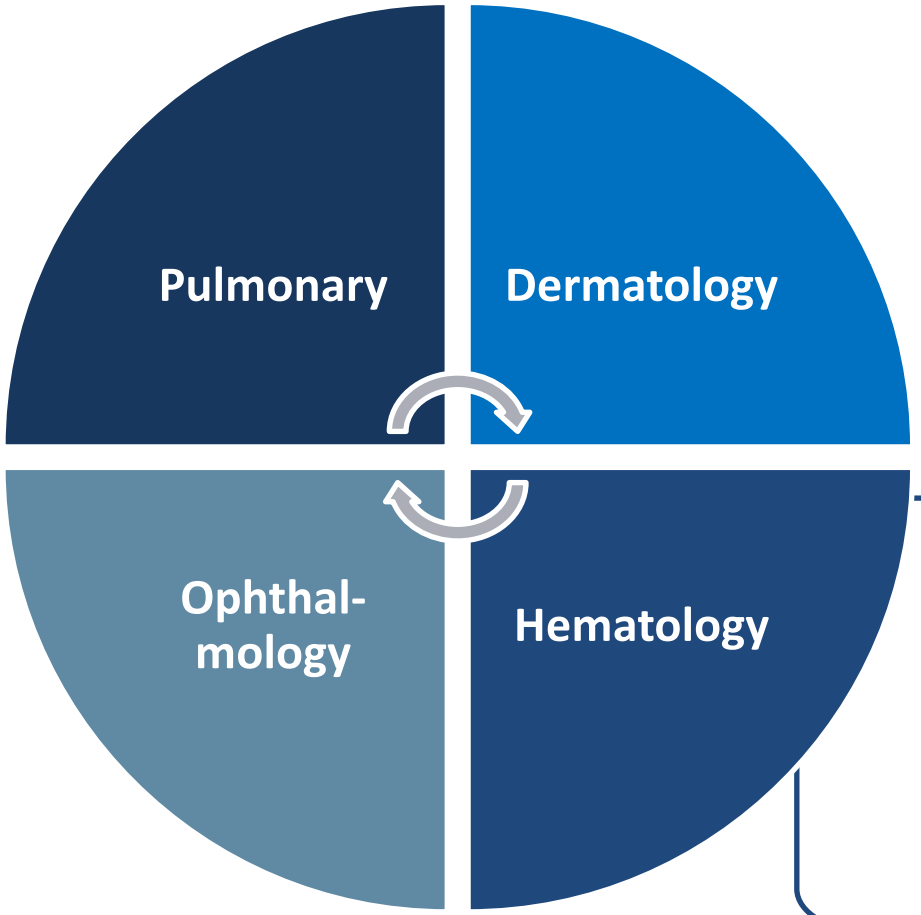
Success in BP may lead to multiple similar-sized follow-up market opportunities



- Competitors operate downstream of nomacopan, inhibiting specific cytokines, chemokines or immunoglobulins
- Other biologicals believed to have not subsequently progressed into further development: (ligelizumab - anti Ig E, mepolizumab - IL5 inhibition, Eotaxin-1 antibody, Anti-IL17a mAb)
- Dupilumab (IL-4 and IL-13 inhibitor) currently being explored in a Phase 2/3 BP study

* US and EU5 markets only
** Initial and follow-on indications; company sources

HSCT-TMA:
High clinical impact, no approved therapies



Thrombotic Microangiopathy (HSCT-TMA)

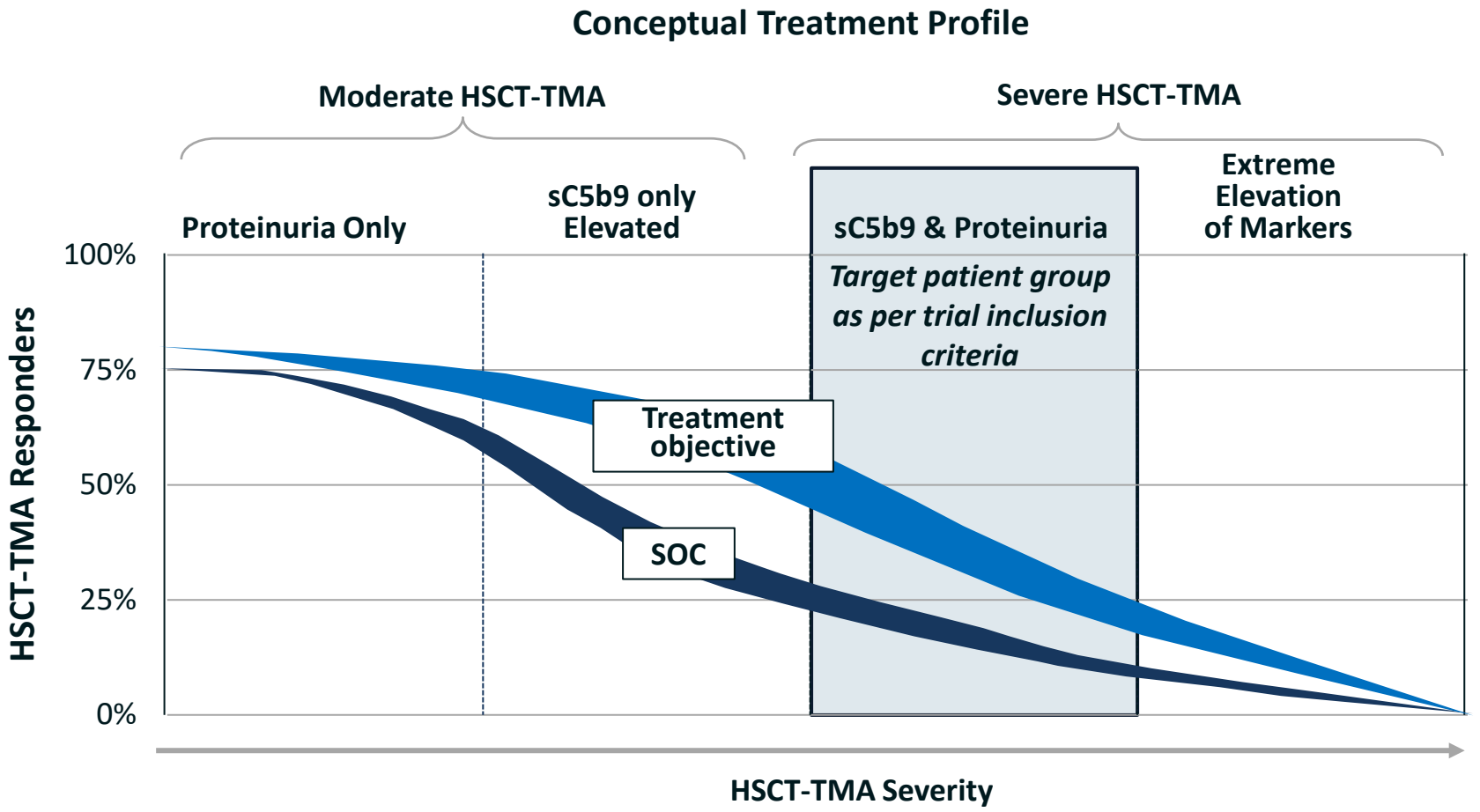
Severe disease – focused on pediatric population

- Up to 80% mortality rate on current SOC
- Phase 3 pivotal study initiated
- Gateway into a broad range of other TMAs

HSCT-TMA:
Potential for significant clinical impact

Unmet Need	**High mortality rate of up to 80% associated with severe 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 complement activation leads to endothelial tissue injury, a prothrombotic state and progressive organ damage and death** • LTB4 may activate endothelial surfaces and Neutrophil Extracellular Traps (NETs) exacerbating prothrombotic state and elevated inflammation • LTB4 may impact GVHD progression, which often co-exists with HSCT-TMA
Treatment	**No approved therapies** • Off-label use of eculizumab – especially in USA

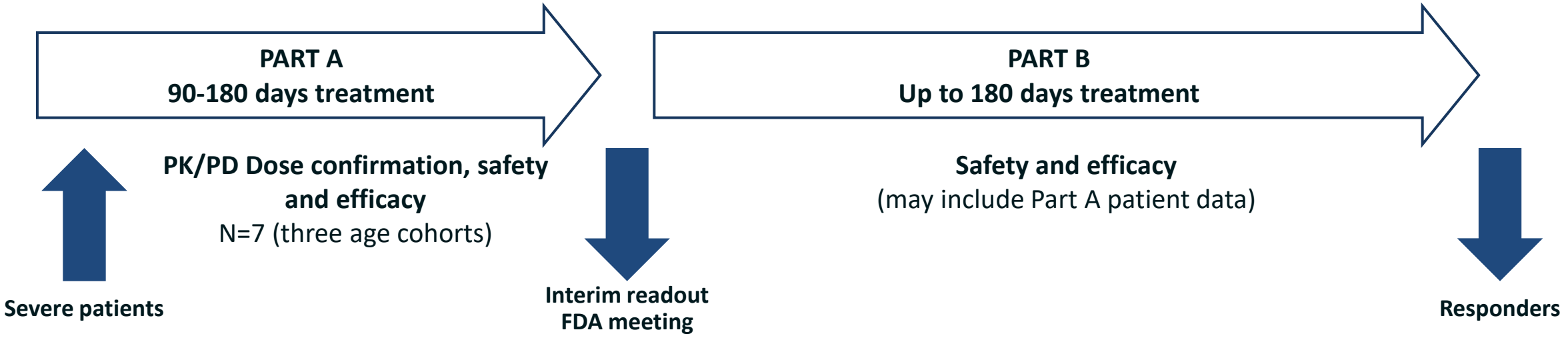
HSCT-TMA pivotal program
Targeting pediatric patients with severe disease



- Targeting severe HSCT-TMA with elevated sC5b9 and proteinuria
- HSCT-TMA patients with extreme elevation of markers unlikely to respond to therapy
- 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

Pediatric HSCT-TMA pivotal study design



Primary Endpoints

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

Regulatory

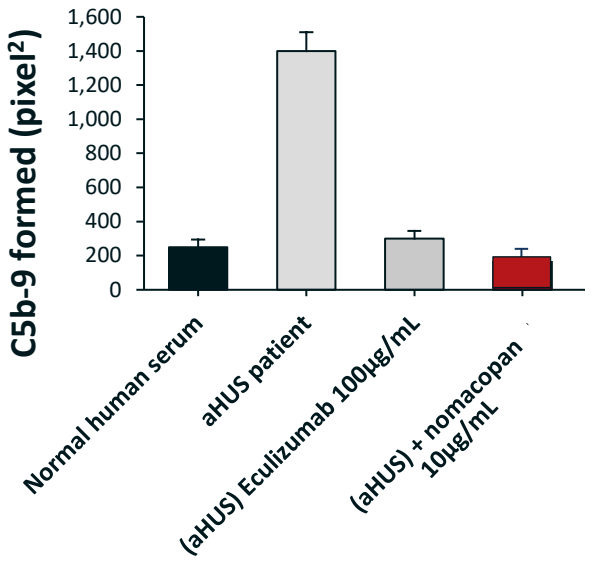
- Fast Track for paediatric HSCT-TMA (FDA)
- Orphan status (FDA) for adult and pediatric HSCT-TMA
- FDA Model Informed Drug Development (MIDD) program completed

Anticipated that initiation of recruitment delayed to end of 2020 due to COVID-19

Nomacopan potential across multiple TMAs

Nomacopan equipotent to Eculizumab in aHUS endothelial cell surface model

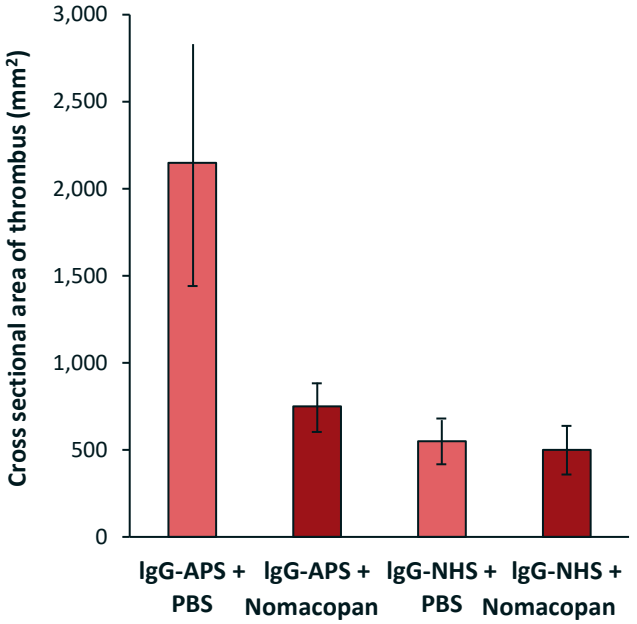
Effect of C5 inhibitors on aHUS serum-activated C5b-9 deposition on ADP-activated HMEC-1



- *Activation of endothelial cell surface by ADP*
- *Expose cells to normal serum or aHUS patient serum*

Significant response with nomacopan in antiphospholipid disease model

Nomacopan reduces area of thrombus



- *Mean cross-sectional area of induced thrombi in mice treatment groups at time of surgery*
- *APS: antiphospholipid syndrome; NHS: normal human serum; PBS: phosphate buffered saline*

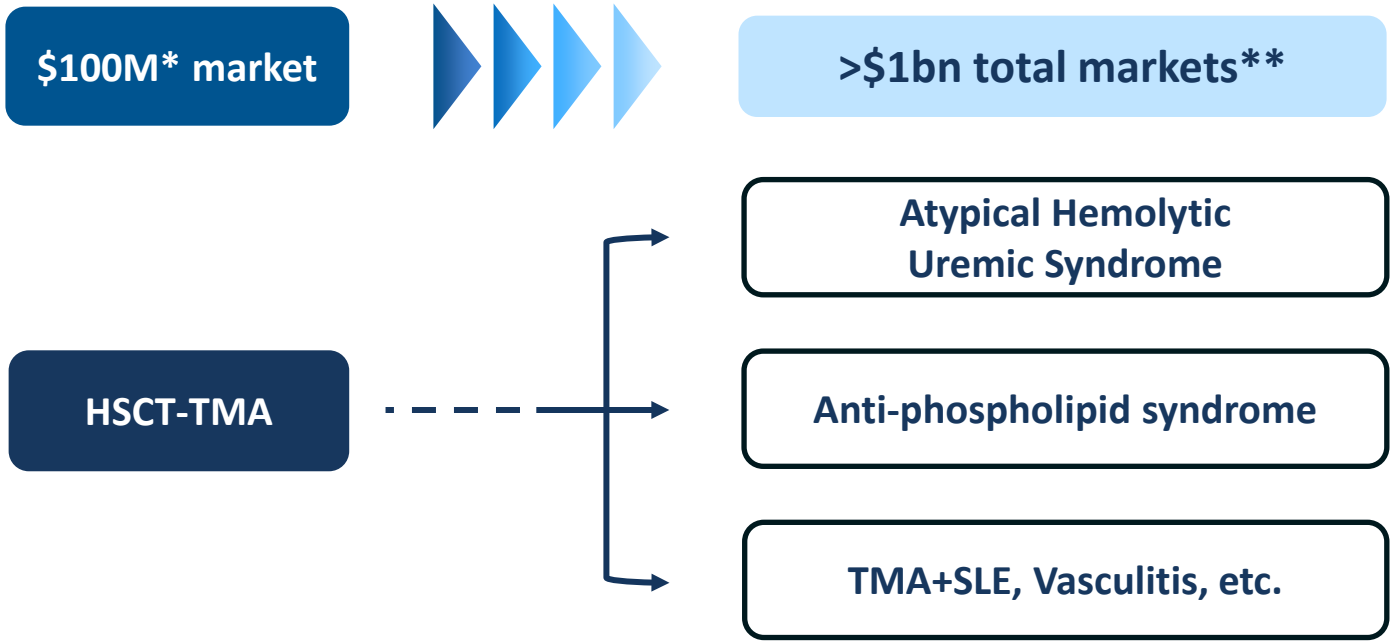
Positive renal & hematological response in TMA-HSCT patients treated with nomacopan

TMA Marker	Days to Resolution (Patient 1)	Days to Resolution (Patient 2)
Red blood cell fragments	60	28
Thrombocytopenia	60	14
Increased LDH	28	14
Proteinuria and/or increased creatinine	28	N/A*
Hypertension	60	14

Data from named patient program presented at the Inborn Errors Working Party (IEWP) meeting, Leiden, The Netherlands, on September 30, 2018
Patient 1: made a complete recovery, Nomacopan discontinued after 7 weeks
Patient 2: despite resolution of TMA markers, patient died at day 63 of complications considered unrelated to treatment with Nomacopan.
** Data up to day 28*

HSCT-TMA: Gateway to related diseases with revenue potential > $1 billion

Success in HSCT-TMA leads to multiple similar-sized follow-up market opportunities



- Eculizumab used off label. Dosing level is higher than that of PNH
- Omeros OMS721: MASP2 inhibitor in Phase 3 inhibits lectin pathway of complement activation; however, the alternative pathway may be a bigger driver of TMA

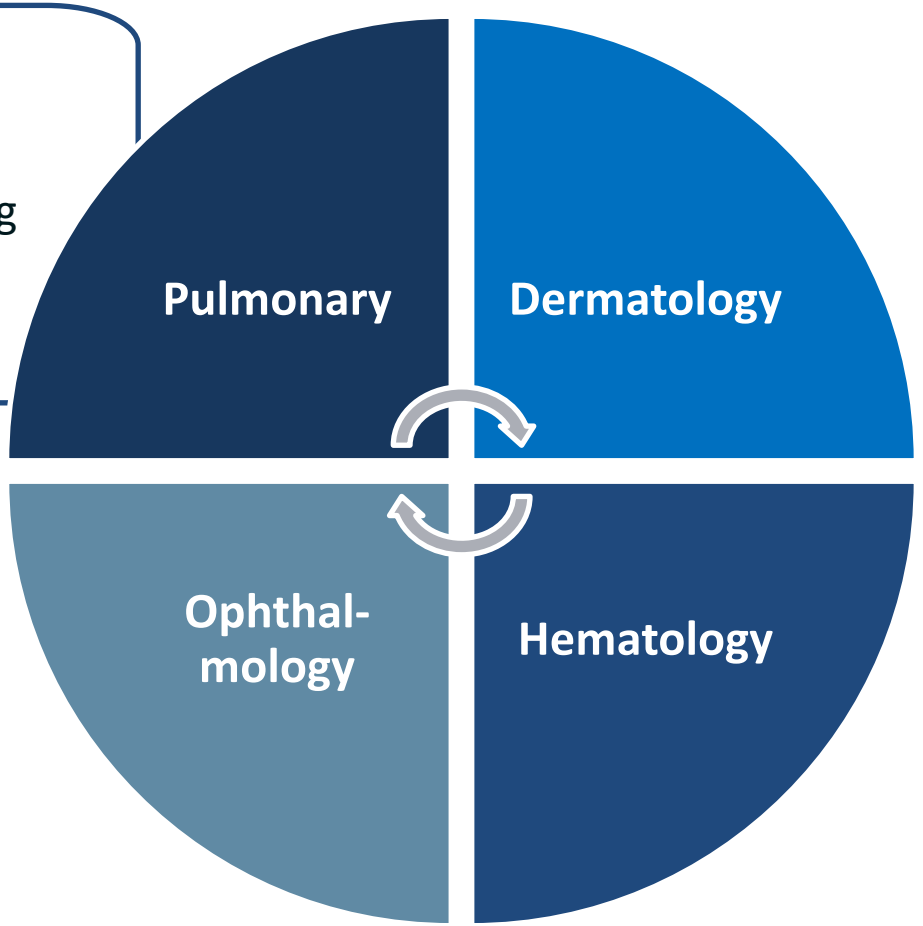
* US and EU5 markets only
** Initial and follow-on indications; company sources

COVID-19 pneumonia: Expansion into conditions with high unmet need, where C5 & LTB4 have pathogenic roles

AKARI THERAPEUTICS

COVID-19 Pneumonia / Lung

- **COVID-19/severe inflammatory lung conditions**
- Multiple inflammatory pathways often implicated underpinning large unmet need
- C5 and LTB4 active in many lung inflammatory diseases



Nomacopan has potential in poorly-treated lung inflammatory conditions, including COVID-19-related pneumonia

- Leukotriene inhibitors Zileuton® & Montelukast® approved in severe asthma
- Preclinical lung models show additive effects of C5 and LTB4 inhibition by nomacopan
- Nebulized nomacopan provides appropriate particle size for deep lung delivery
- Exploring COVID-19-through clinical programs across multiple geographies
- Potential in range of lung disorders, characterised by neutrophil activity or exacerbations initiated by infections

Two primary pathways driving COVID-19 pneumonia

Nomacopan inhibits key COVID-19 pneumonia inflammatory pathways

COVID 19 believed to trigger multiple inflammatory pathways

Nomacopan Inhibition

Complement (C5b9 and C5a)
C5b9 accrues in lung vascular tissue, C5a promotes thrombosis

LTB4 and C5a
drive neutrophil trafficking and cytokine storm in the lung

Lung vascular damage and microthrombi lowered platelets and increased D-dimer

Lung epithelial damage raised neutrophils and cytokines

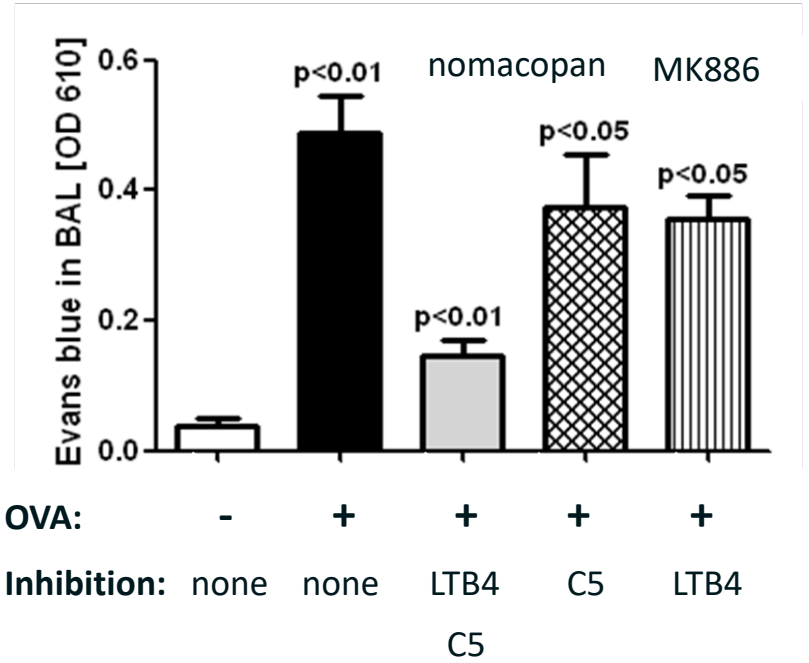
Dramatic reduction in lung perfusion, respiratory distress, microthrombi in lung and other tissues

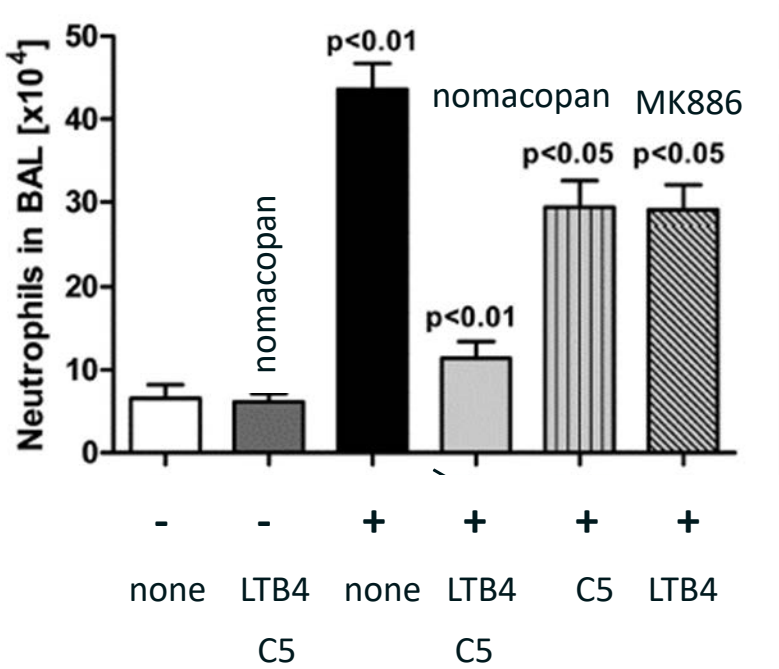
Acute Respiratory Distress

Oxygen support, ventilation, multi organ damage

Nomacopan's dual inhibition of C5 & LTB4 inhibition more effective than inhibiting C5 or LTB4 alone

Lung model of immune-complex alveolitis
Dual inhibition superior to C5 or LTB4 inhibition alone





- *Two forms of Nomacopan one inhibiting C5+LTB4, the other inhibiting C5 only (pre-saturated with LTB4)*
- *LTB4 inhibition only is MK886 a leukotriene inhibitor that inhibits 5-lipoxygenase activator protein (FLAP)*
- *Source : Roversi et al (2013) JBC 288: 18789 - 18802*

Different approaches to inhibiting inflammatory pathways in COVID-19 pneumonia

In trials for COVID pneumonia

Cytokine specific	Complement pathway	Leukotriene pathway	Broad range	Other immune modulators
IL-6 inhibitors GM-CSF inhibitors IFN Gamma inhibitors	C5 inhibitors C5a inhibitors	Montelukast	Dexamethasone	JAK inhibitors BTK inhibitors

Nomacopan inhibits multiple pathways

Standard of care

- **Nomacopan blocks multiple cytokines through inhibition of complement and leukotriene pathways; thrombosis increasingly linked to amplified complement activity (both C5a and C5b9)**
- **Nomacopan inhibits different pathways to remdesivir (anti-viral) and dextromethorphan (SOC); potential to be additive**

Clinical treatment guidelines based on growing understanding of COVID-19 pneumonia

Multiple Pathways	• Anticipated need to inhibit multiple pathways • Complement and cytokines play an important role	Nomacopan inhibits complement and leukotriene pathways
Patient Segmentation	• Timing critical: disease changes dramatically by time on ventilator • Heterogenous patients – biomarker helpful to focus treatment • Need to get patients off treatment quickly once improved, long term immunosuppressant use clinically undesirable	Nomacopan rapid on/off inhibition of C5 and LTB4
Standard of Care Treatment	• SOC changed – dexamethasone and remdesivir improve outcomes in specific patient groups • Long term monitoring important; widespread organ damage	Nomacopan has potential to be additive to SOC
Clinical Trials	• Clinical trials need to be randomized, clinically relevant and with latest SOC	Primary end point normalization of oxygen

Ongoing and planned COVID-19 pneumonia clinical programs

United Kingdom

- Observational biomarker study to identify COVID-19 patients suitable for nomacopan. Data collected on ~50 patients; sample analysis expected Q4 2020
- Ongoing longitudinal study: samples from patients with worsening disease
- Selected by AGILE platform

United States

- Initial proof of principle treatment in patients with COVID-19 pneumonia via expanded access programs
- Proposed multi-center investigator-led randomized study in regulatory submission

Brazil

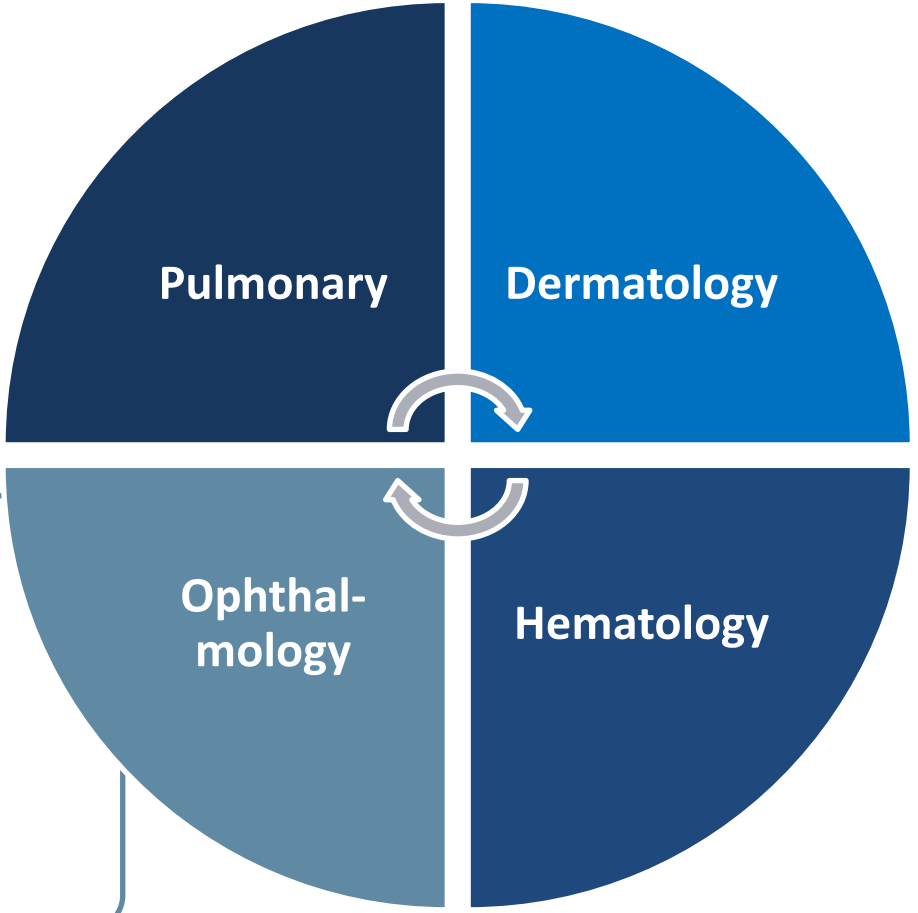
- Recruitment completed into initial proof of principle treatment in patients
- Potential progression to randomized controlled study if review by Data and Safety Monitoring Board (DSMB) is successful

Planned randomized clinical study design: Key considerations

- Randomize patients 2:1
- Patients on supplementary oxygen between 5-20 litres/minute
- Primary end point is time to normalization of oxygen - easily measured using a pulse oximeter
- Nomacopan administered daily sub cutaneous for up to 14 days
- Key secondary end points to include need for intubation and assisted ventilation and survival
- Each individual study powered with circa 60 patients
- Nomacopan additive to current standard of care: dexamethasone and remdesivir where available

COVID-19 programs build on existing clinical experience in the use of nomacopan, including >35 cumulative patient-years of good safety data, and clinical responses across a range of inflammatory conditions in Phase 2 / Phase 3 development

Atopic Keratoconjunctivitis: Topical formulation, first entry into ophthalmic market



Atopic Keratoconjunctivitis (AKC)

Debilitating surface of the eye disease

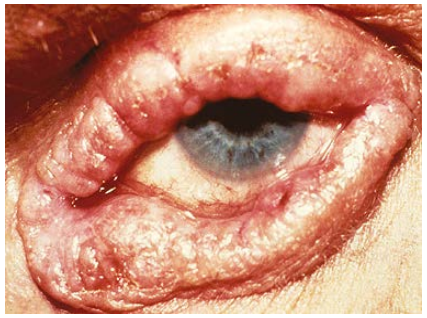
- More severe patients poorly treated with risk of blindness
- C5 and LTB4 active in tissue
- Ongoing Phase 1/2 study

Atopic Keratoconjunctivitis
Large unmet need for severe patients

Unmet Need

Chronic condition can lead to vision loss

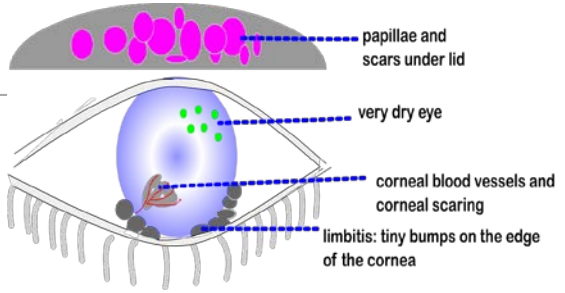
- Need for rapid resolution of both signs and symptoms of the disease



Prevalence

Orphan condition

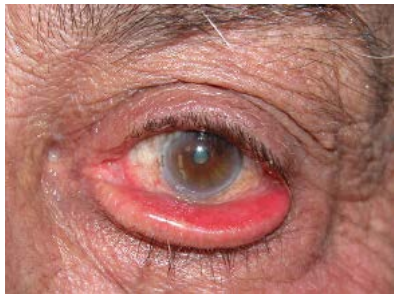
- Prevalence of 160K patients in US & EU



Cause

Severe eye surface inflammation causing infiltration of immune cells (neutrophils & T cells)

- Chronic disease can result in corneal neovascularization, formation of sterile corneal ulcers and blindness



Treatment

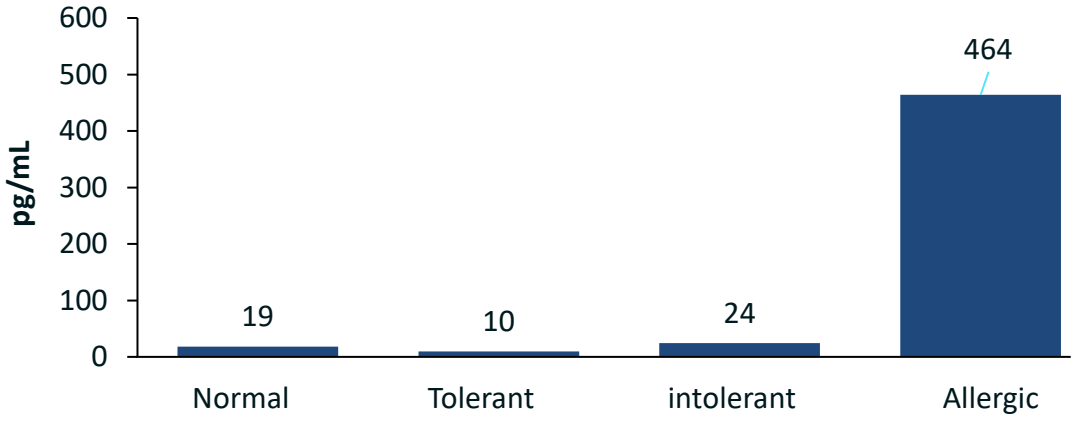
No approved therapies

- Topical drugs, such as steroids or cyclosporine treatments complicated by issues with comfort and side effects of chronic usage

Role of C5 & LTB4 established in eye surface inflammatory conditions

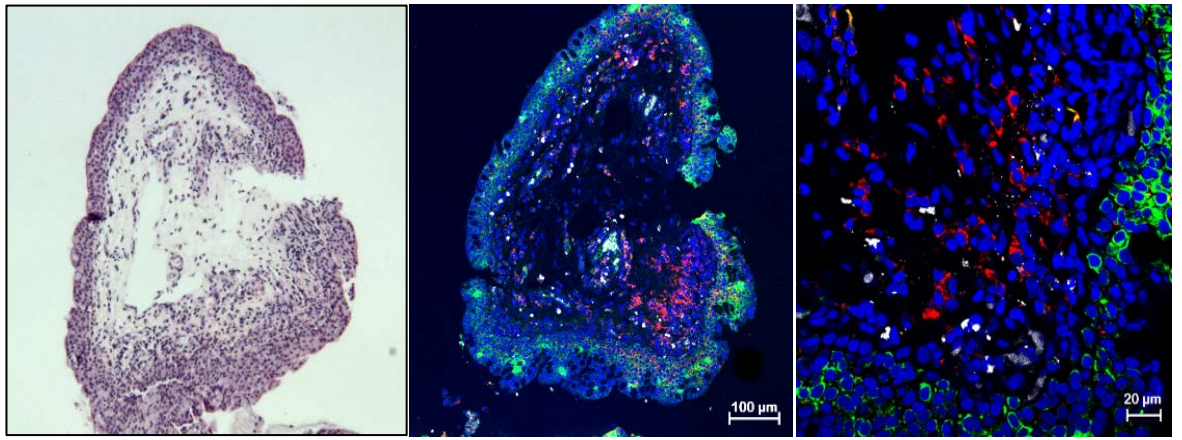
- LTB4 levels elevated in tear fluid
- LTB4 shown to induce mucin secretion by goblet cells[1] which contributes to ocular allergic inflammation[2]
- Inhibition of both LTB4 & C5 has potential to reduce redness, mucous & excess tearing associated with activation of the LTB4 receptor BLT1 & C5a receptors

LTB4 Levels 20X Normal in Patients with Allergic Conjunctivitis[3]



Tear fluid LTB4 in normal subjects, contact lens tolerant and intolerant subjects and allergic conjunctivitis patients (n=5 per group)

Presence of C5a and LTB4 receptor (BLT1R) in biopsies from human keratitis patients[4]



Immunofluorescent and H&E sections of giant papilla from a VKC patient. **C5aR red**, **BLT1R green**, CD4 (T cells) white

Notes:

1. Dartt et al., 2011 J Immunol. 186: 4455-4466
2. Dartt et al., 2014 Curr Opin Allergy Clin Immunol. 14:464-470
3. Professor Mark Wilcox, School of Optometry and Vision Science, University of NSW
4. Professor Virginia Calder (Institute of Ophthalmology, London)

Ophthalmology development programs

Topical program

- Patients had deteriorating moderate to severe AKC despite ≥3 months treatment with cyclosporine t.i.d. ± steroids. Treated topically with nomacopan for 8 weeks in addition to cyclosporine
- Part A : first in man safety study, Part B : randomized study – recruitment disrupted due to COVID
- Interim data from 8 AKC patients from part A and part B (4 active and 4 placebo) showed:
  - No ocular treatment emergent serious adverse events
  - Comfort score measured after each eye drop installation highlighting drug was comfortable and well tolerated
  - In all four efficacy categories (signs, symptoms, visual acuity and tear film break up) nomacopan showed a higher improved mean score than the control group but data set too small to show statistical significance
- Recent IND for topical nomacopan opens up potential to broaden and increase recruitment into the topical program

Back of the eye preclinical program

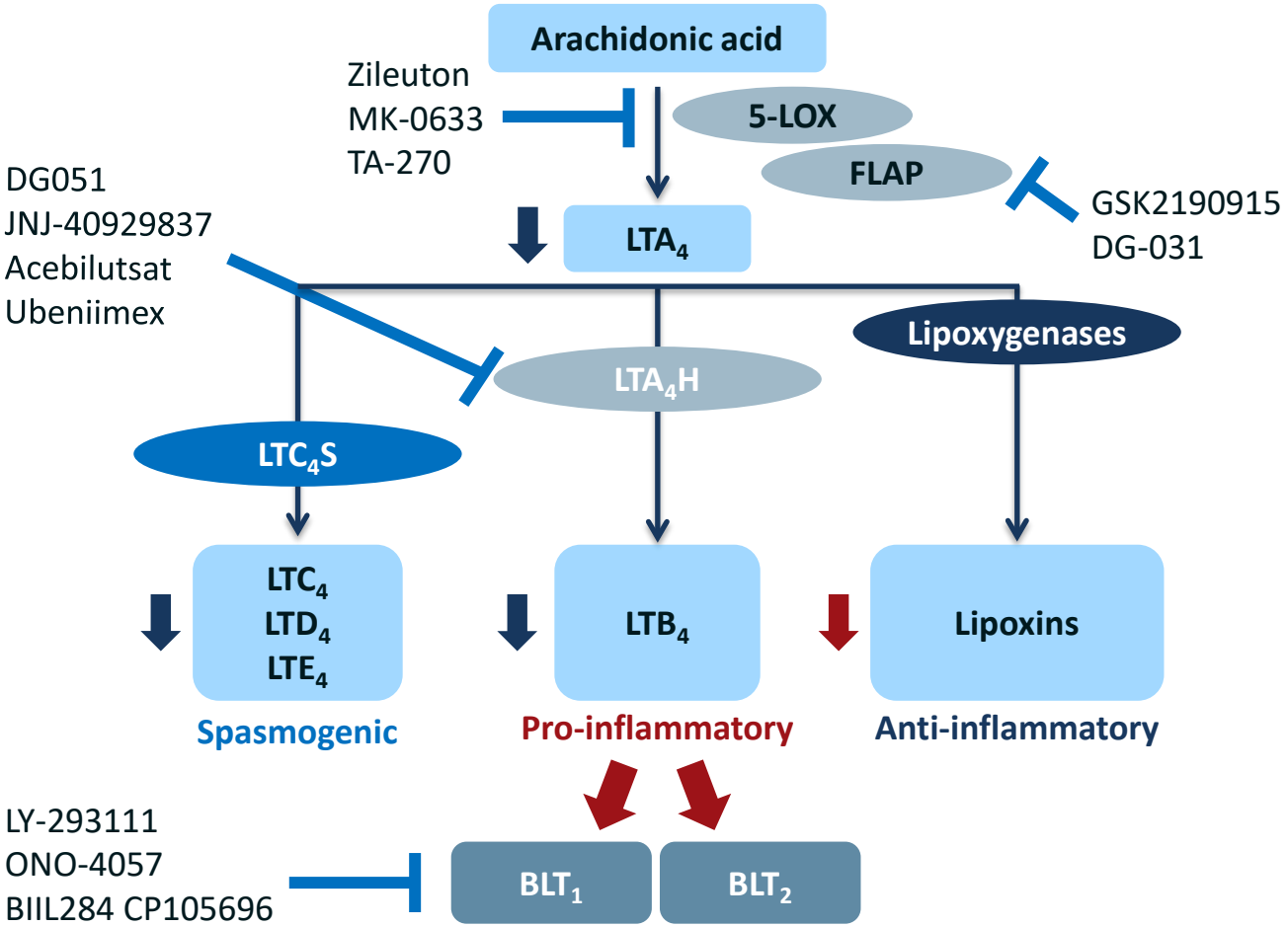
- C5 and LTB4 receptors both identified in retina
- In EAU model, injected PASylated-nomacopan (PAS-nomacopan) significantly reduced inflammation and was comparable to injected dexamethasone
- PAS-nomacopan provides potential long-term residency for delivery to back of the eye

Summary

- Validated therapeutic targets in C5 and LTB4 with recent $1 billion+ acquisitions of companies targeting complement-mediated diseases
- Multiple short-term inflection points
  - **BP**: Phase 3 initiation expected H1 2021
  - **TMA-HSCT**: Pediatric patient recruitment expected to initiate Q4 2020
  - **COVID-19**: Multiple data readouts on COVID -19 pneumonia expected in H2 2020
- Lead indications expected to be gateways to high potential follow-on indications
- Cash at June 30, 2020: $12.7m, excluding $3.4m R&D tax credit received in July
- Circa 33.5m ADS outstanding

Appendix

LTB4 ligand capture
Advantageous and unique MOA



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

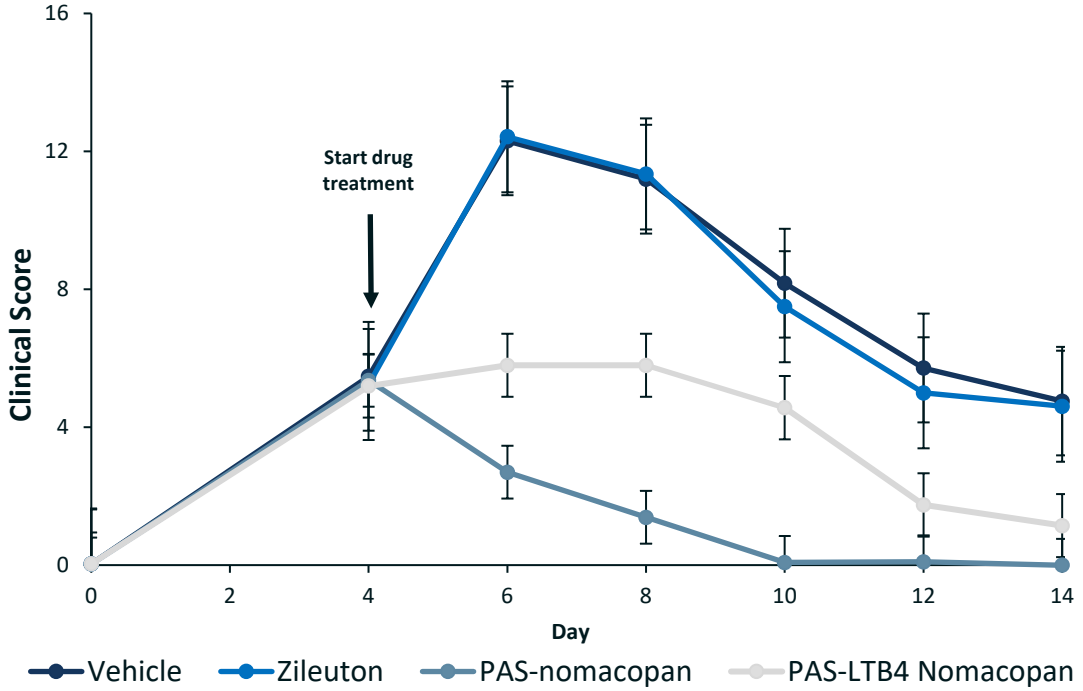
LTA_4H inhibitors

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

Preclinical work demonstrates additional benefit of combined inhibition of C5 and LTB4

Dual action C5+LTB4 (PAS-nomacopan) more effective than inhibition of LTB4 only (PAS-LTB4-nomacopan)

Rheumatoid Arthritis Therapeutic model

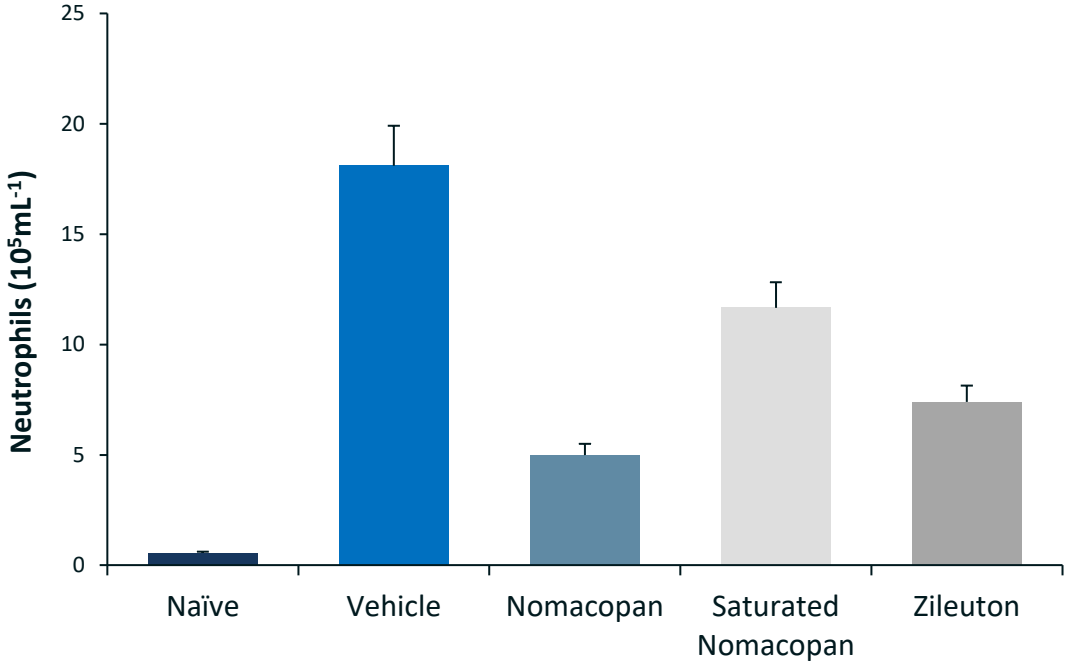


N = 5 mice in each treatment group

Work performed in group of Prof Andrew Luster, Mass Gen Hospital, Boston, USA

Dual action nomacopan more effective than C5-only nomacopan (or Zileuton®) alone

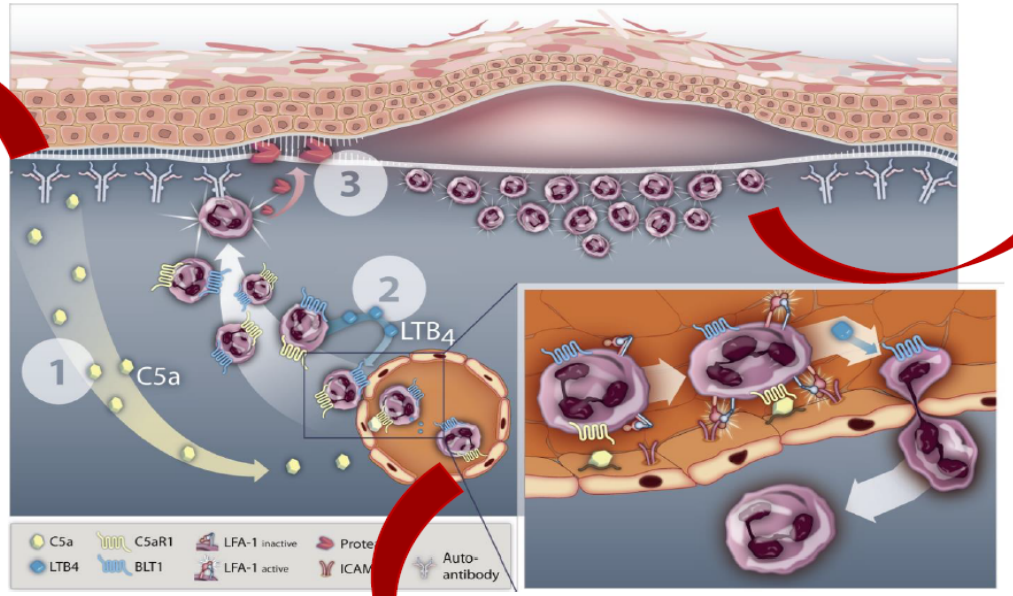
Cell recruitment to Lung Induced by LPS



Mouse model by Pneumolabs

Interaction of C5 & LTB4 in BP 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



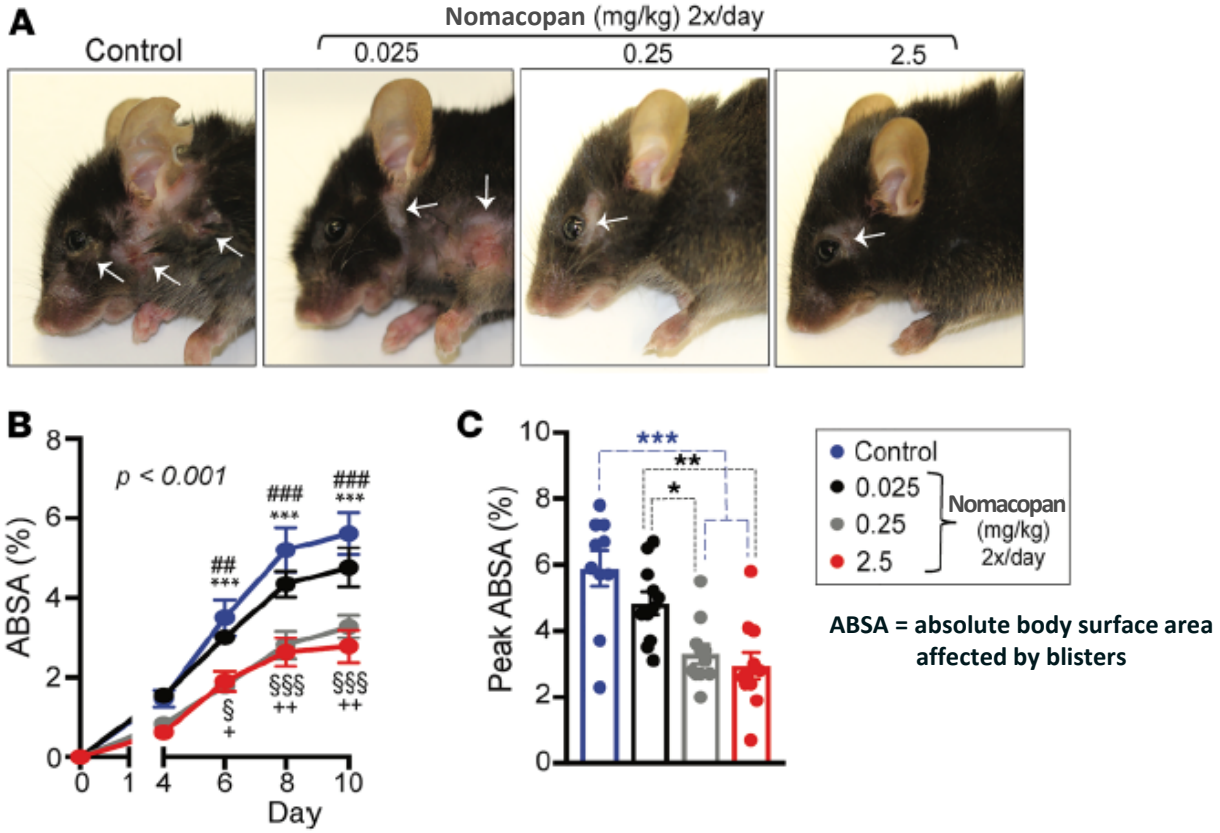
3. Activation of neutrophils at the DEJ by the deposited autoantibodies induces the release of proteases which degrade proteins of the DEJ and compromise dermal-epidermal adhesion.

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)

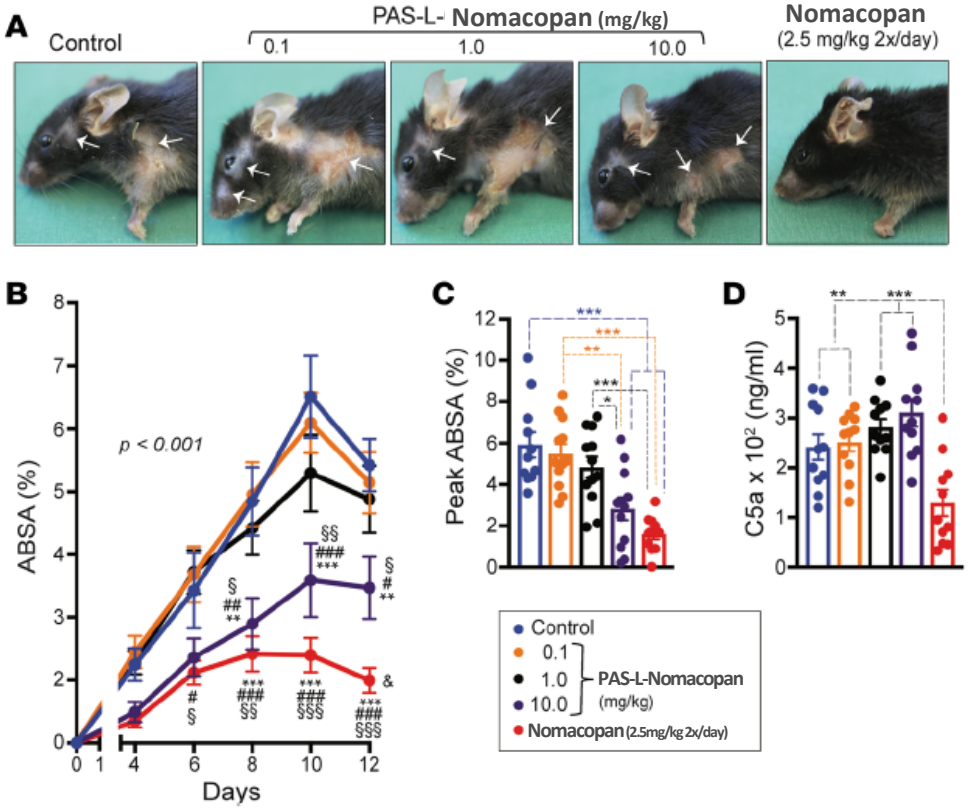
Nomacopan efficacy in BP-like bullosa acquista model

Dose dependent inhibition of blister formation



ABSA = absolute body surface area affected by blisters

Nomacopan that only binds LTB4 is less efficacious



Sezin et al., JCI Insight 4: e128239 (2019)

Combining inhibition of complement and leukotriene pathways to treat inflammatory diseases

AKARI THERAPEUTICS

September 2020