

Akari Therapeutics

BioFuture Company Presentation

Rachelle Jacques, President & CEO



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1. Novel Complement + LTB4 inhibitor

Nomacopan is a unique asset inhibiting 2 co-dependent, proinflammatory targets: complement C5 and leukotriene B4 (LTB4)



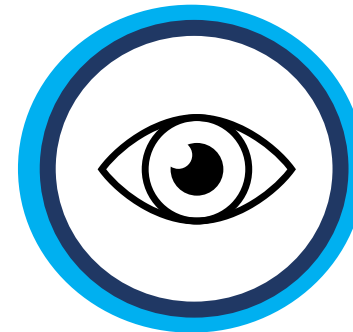
4. HSCT-TMA Phase 3

Phase 3 clinical trial in pediatric hematopoietic stem cell transplant-related thrombotic microangiopathy (HSCT-TMA); no approved therapies and ~80% mortality; FDA Orphan, Fast Track designations; Rare Pediatric Disease designation with potential for Priority Review Voucher upon approval; granted European Commission orphan drug designation; potential for adult indication



2. Broad potential

Potential for use in several diseases; commercial flexibility due to multiple routes of administration (subcutaneous, topical, intravitreal, IV)



5. GA Pre-Clinical

Pre-clinical program investigating PAS-nomacopan in geographic atrophy (GA) with target dose interval of 3 months or longer without increased risk of choroidal neovascularization (CNV) which is associated with complement-only inhibitors approved for GA treatment



3. Robust clinical dataset

Extensive clinical and safety data from multiple clinical trials

Complement Technologies Continue to Garner Significant Investment



8 acquisitions 2017-2022

14 collaborations 2017-2022

Company*	Company Value	Product(s)	Status/Phase	Type	Indications
Astra Zeneca / Alexion	\$39 billion completed acquisition	Soliris®/Ultomiris®	On market	C5	PNH, aHUS, gMG, NMOSD,/PHN, aHUS
Apellis	\$3.85 billion market cap**	Empaveli®/Syfovre®	On market	C3	PNH/GA
Astellas / Iveric	\$5.9 billion completed acquisition	IZERVAY™	NDA approved	C5	GA
Amgen / ChemoCentryx	\$3.7 billion completed acquisition	Tavneos®	On market	C5	ANCA-Vasculitis
UCB / Ra Pharma	\$2.3 billion completed acquisition	zilucoplan	Phase 3	C5	gMG

* A selection of companies with complement therapeutics on market or in development ** As of July 24, 2023

Sources: Needham January 2023 Complement report, company public disclosures. Accessed June 7, 2023.

Nomacopan Is a Novel Dual Action Recombinant Protein Discovered In Ticks

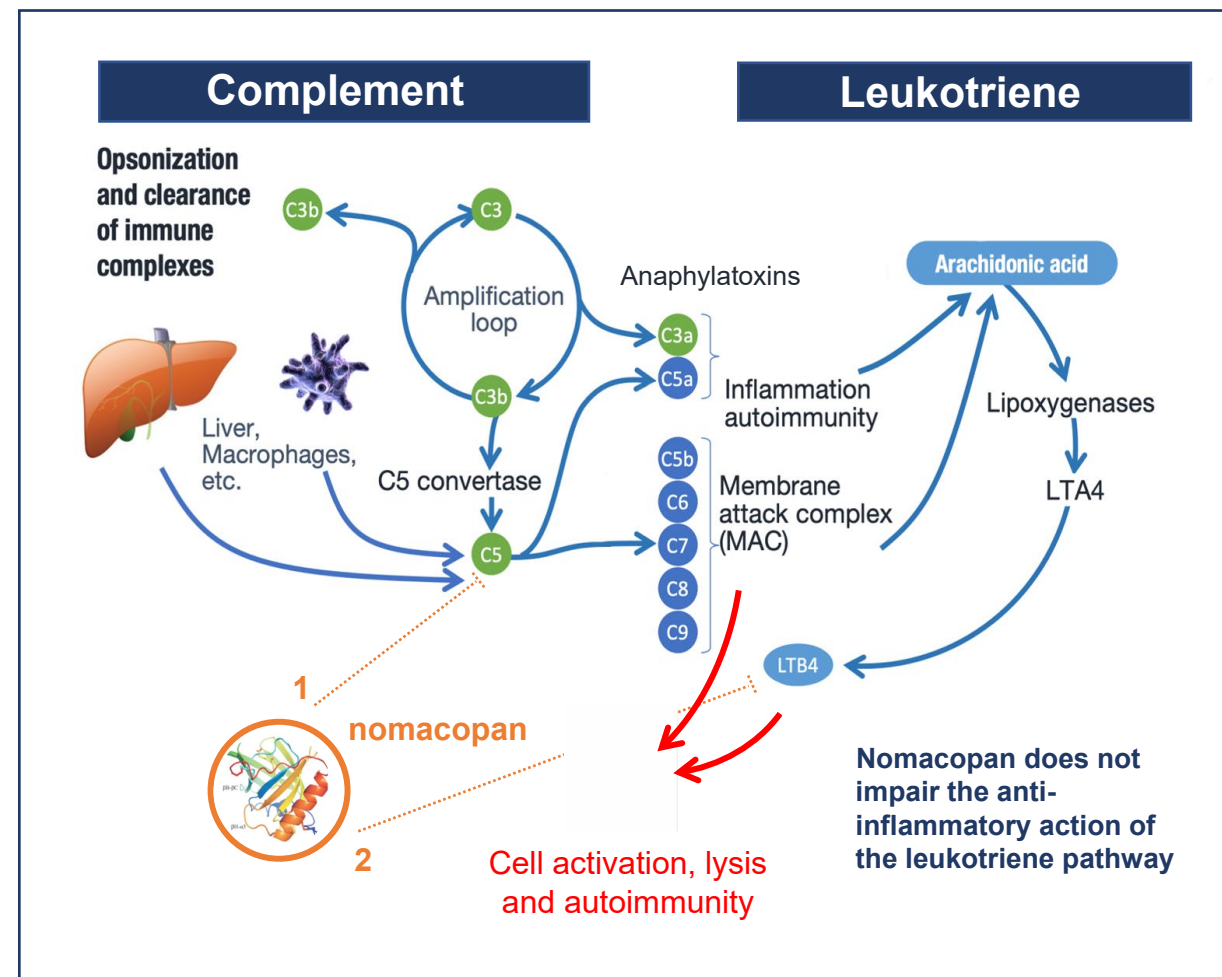


Ticks secrete immunomodulatory proteins that help them control host responses (inflammation, pain, itch and blood flow)

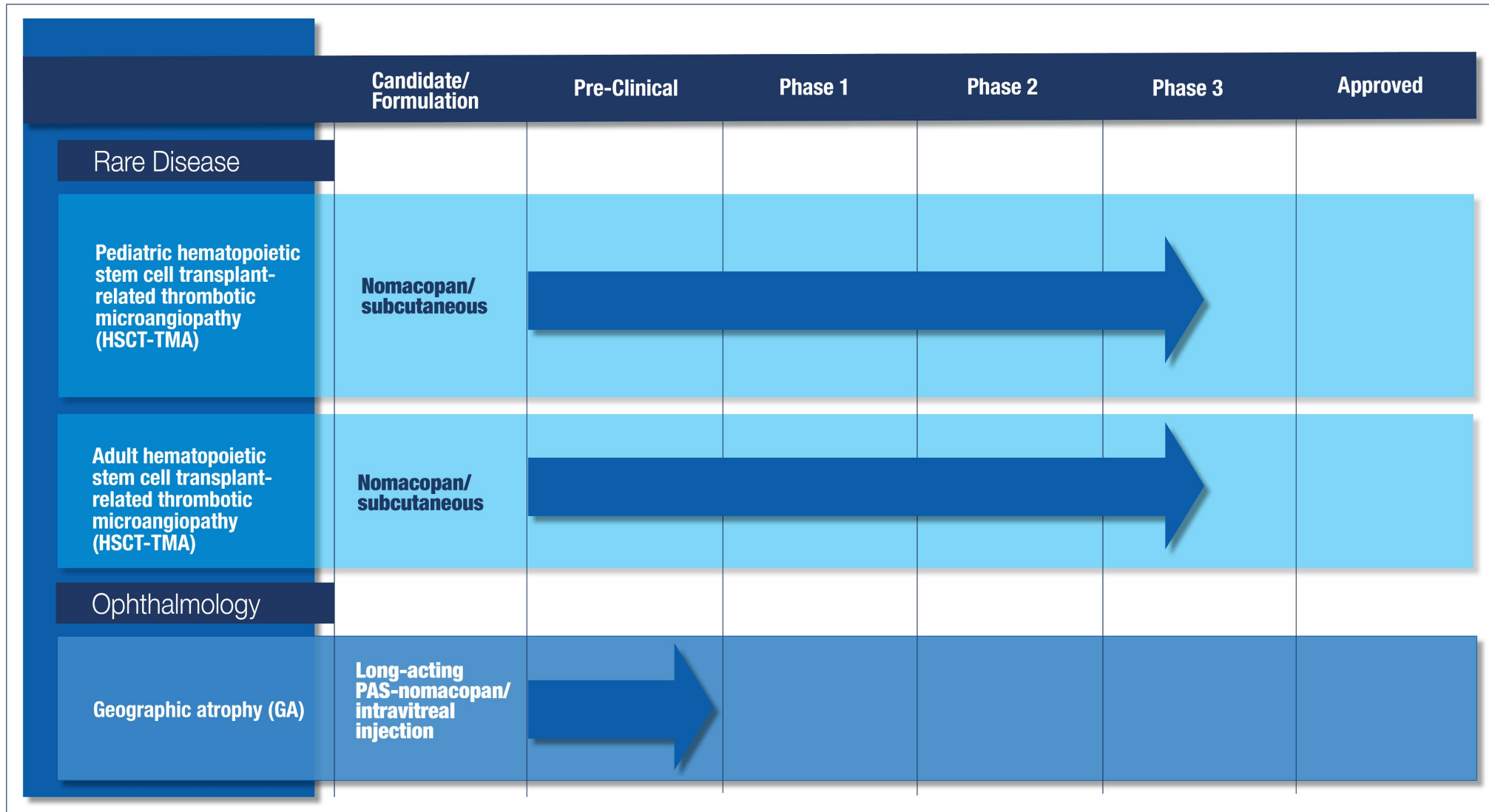
- These are the same responses that may be out of control in certain human autoimmune and inflammatory conditions

Nomacopan inhibits two pathways that can cause damaging inflammation, while preserving important immune functions (such as opsonization)

- C5a, LTB4 and MAC act jointly on neutrophils, macrophages and other cell types that can cause inflammation and damage
- Signaling interplay between C5 and LTB4 may lead to damaging inflammation



The Akari Pipeline Includes Near-Term Potential, Promising Pre-Clinical Program



Previous Areas of Clinical Development, Including PNH and BP, Support Current Development Pathways

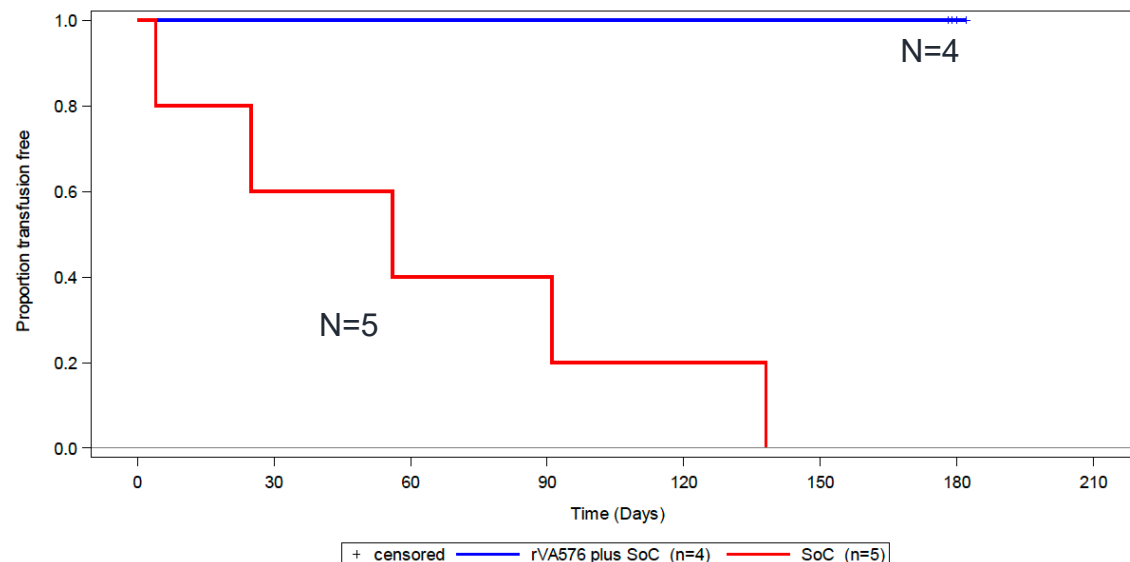


- In addition to current areas of focus, Akari has conducted clinical research in several other areas, including Phase 2/3 clinical trials of subcutaneous nomacopan for treatment of bullous pemphigoid (BP) and paroxysmal nocturnal hemoglobinuria (PNH)
- This research set a solid foundation for the current Phase 3 clinical trial in pediatric HSCT-TMA

- In a Phase 3 study in PNH, 100% of untreated patients were transfusion dependent while 0% of nomacopan patients were transfusion dependent

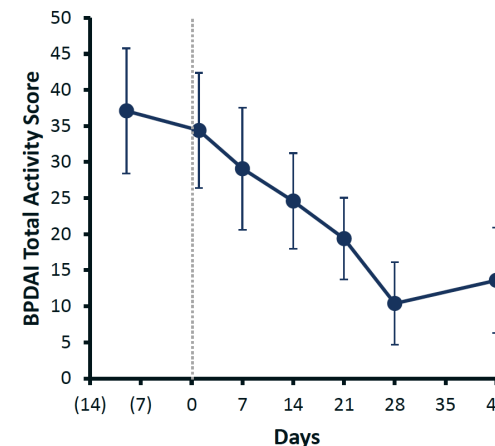
- >32 patient years of nomacopan exposure in PNH in 19 patients

Proportion of PNH patients who were transfusion independent following entry to trial

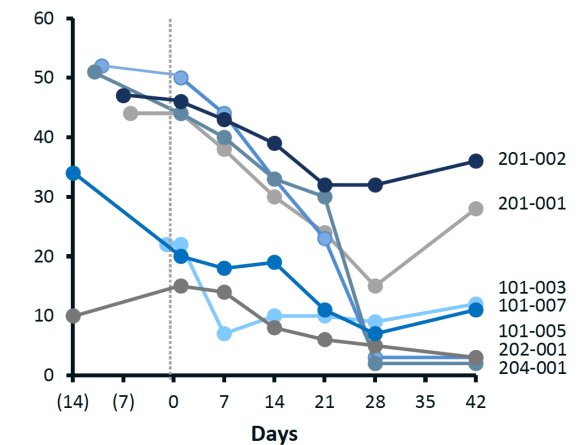


- In clinical studies of nomacopan in BP, 7 of 9 patients responded to nomacopan¹
 - 3 showed >80% reduction in BPDAl by day 42 (BP disease activity)

Mean BPDAl Activity + 90% CI



Individual Patients BPDAl Activity



All prior treatment, including steroids, withdrawn ~one week prior to initiation of treatment with nomacopan. Lesional mometasone was administered to Day 21.

THROMBOTIC MICROANGIOPATHIES (TMAs)



Nomacopan May Be the First Treatment for HSCT-TMA, a Condition with Mortality Up to 80%

- HSCT-TMA is a rare but serious complication of HSCT involving complement activation, inflammation, tissue hypoxia and blood clots, leading to progressive organ damage and death
- Graft versus host disease is commonly present in patients with severe HSCT-TMA¹
- Mortality is 80% across adults and children (severe)²
- No approved treatment options



Nomacopan in HSCT-TMA

1. Complement C5 inhibition efficacy

Nomacopan C5 inhibition supported by clinical PNH research³

2. Simple, fixed dosing

Nomacopan clinical trials are establishing a simple, fixed dose in children; ease of dosing at home or in hospital for adults

3. Rapid onset & offset of action

Rapid onset/offset of action allows complement re-activation when needed

4. LTB4 inhibition may slow GVHD progression

LTB4 is often elevated in patients with GVHD and nomacopan inhibition of LTB4 may slow GVHD progression⁴

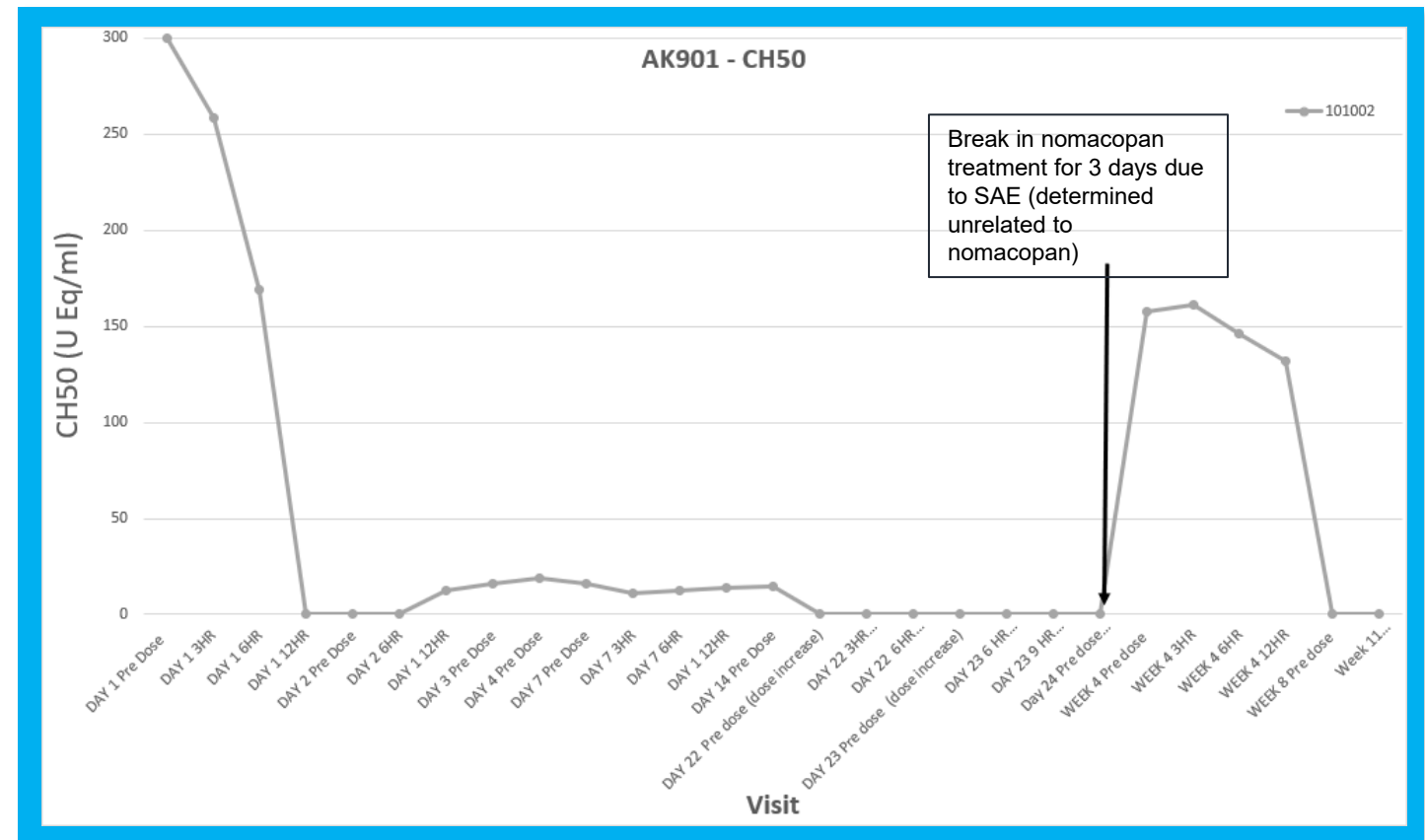
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2. Rosenthal J. Hematopoietic cell transplantation-associated thrombotic microangiopathy: a review of pathophysiology, diagnosis, and treatment. *J Blood Med*. 2016;7:181-186.
3. Schols S, Nunn MA, Mackie I et al. Successful treatment of a PNH patient non-responsive to eculizumab with novel complement C5 inhibitor covers (nomacopan). *Br J Hematol*. 2020; 188: 332-340.
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Clinical Trial Patient Case Study Presented at Two Transplantation and Cellular Therapy Meetings



A patient with severe pediatric HSCT-TMA, which typically involves multi-organ failure and other acute consequences, was discharged home from the hospital following treatment with nomacopan

- 6-year-old male received a cord blood HSCT for relapsed refractory acute myelogenous leukemia (AML)
- Post-transplant acute gut graft-versus-host disease (GVHD)
- TMA at day +66 post-transplant
- Treatment with a single-age, weight-based ablating dose of nomacopan day +74 followed by maintenance dosing for 21 days
- After a 3-day break in treatment for encephalopathy unrelated to nomacopan, treatment continued for a further 46 days until the end of the study with correction of the patient's urine protein creatinine ratio for ≥ 28 days
- Gut pathology and thrombocytopenia resolved
- No adverse events related to nomacopan



GEOGRAPHIC ATROPHY (GA)



Geographic Atrophy (GA)



- Geographic atrophy (GA) manifests as a chronic progressive degeneration of the macula, which occurs during late-stage dry age-related macular degeneration (dAMD) and can lead to irreversible vision loss
- Approximately 5 million people worldwide are affected,^{1,2} with nearly 1 million in the U.S.³
- The first treatments for GA have been approved by the FDA in 2023

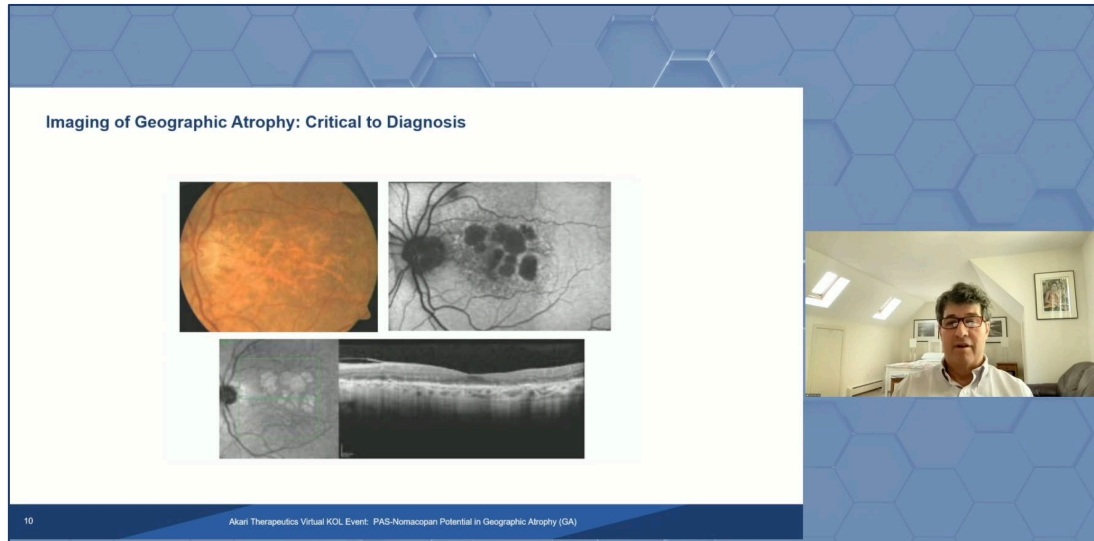
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2. Rudnicka AR, et al. Age and gender variations in age-related macular degeneration prevalence in populations of European ancestry: a meta-analysis. *Ophthalmology*. 2012;119(3):571-580.
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KOL Insights on GA Treatment Landscape and Unmet Needs



The recent key opinion leader event hosted by Akari discussed GA diagnosis, treatment, and significant unmet needs



<https://lifescievents.com/event/akari-event/>

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Despite FDA approvals of the first treatments for GA, there are still significant unmet needs. It's important that we reduce the frequency of therapy, which must be administered through intravitreal injection into the eye. In addition, treating geographic atrophy while preventing choroidal neovascularization from developing is another important unmet need.

Elias Reichel, M.D.
Professor of Ophthalmology
Tufts University School of Medicine

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PAS-Nomacopan May Provide 3 Key Benefits: Complement Inhibition, Fewer Doses & LTB4 Inhibition to Address CNV Risk



PAS-nomacopan in GA

1. Complement C5 inhibition to slow GA progression

Efficacy of complement C3 and C5 inhibition slowing progression of GA lesions is well understood^{1,2}

2. Fewer needle injections into the eye

Frequent needle injections into the back of the eye, a source of fear, discomfort and disruption for patients³; potential for 4 or fewer injections with PAS-nomacopan each year

3. LTB4 inhibition may reduce risk of CNV

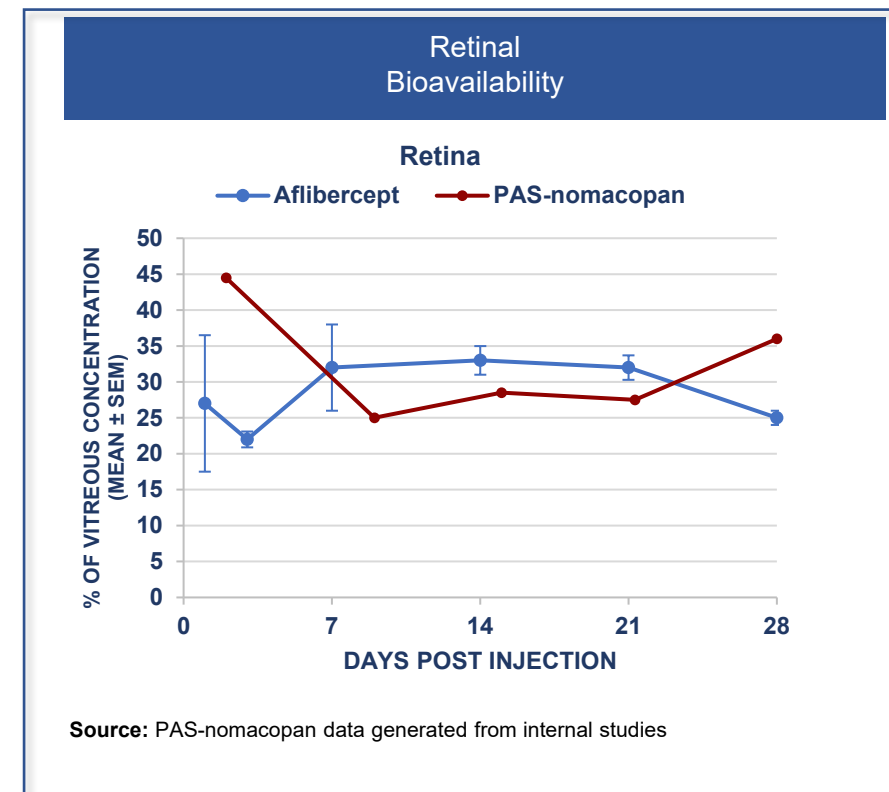
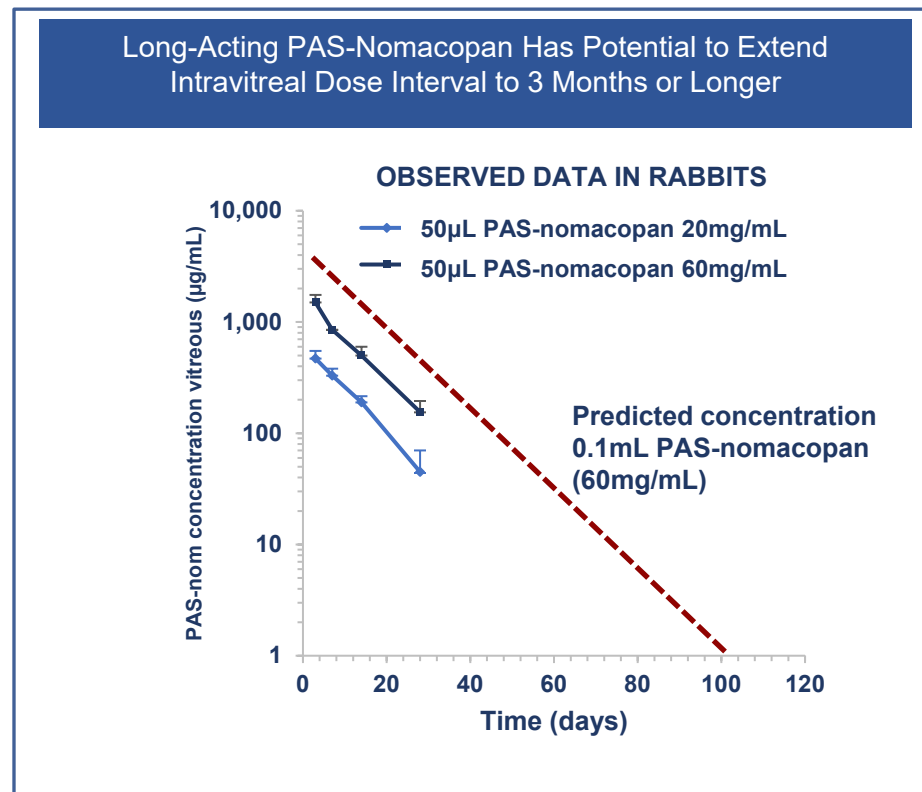
LTB4 inhibition may prevent VEGF-A overexpression, a key driver of sight-threatening CNV,⁴ a safety risk (treated with VEGF inhibitors) associated with complement-only inhibitors approved for GA treatment

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4. Sasaki F, et al., Leukotriene B4 promotes neovascularisation and macrophage recruitment in murine wet-type AMD models. *JCI Insight* 2018; 3: e96902.

Long-Acting PAS-Nomacopan Has Potential for 4 or Fewer Injections Into the Eye Per Year

- PK/PD data show PAS-nomacopan has extended half-life in the eye after intravitreal injection (7.4 to 8.4 days), suggesting the dose interval may be 3 months or longer¹



Reference:

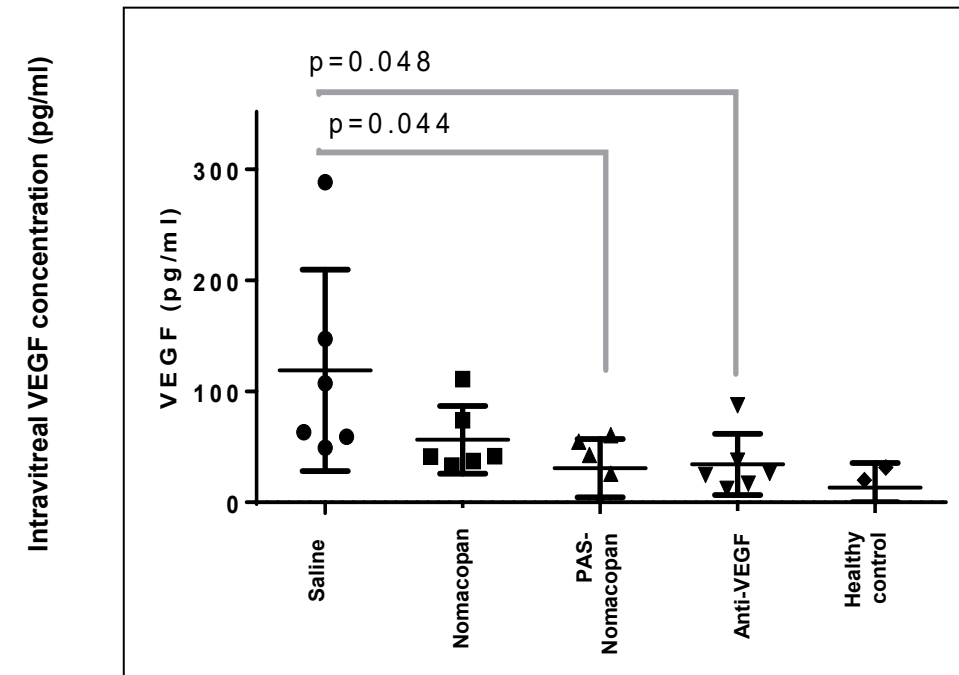
- Weston-Davies, W., et al. Development of long-acting PAS-nomacopan for treatment of GA and other retinal diseases. Poster presentation ARVO, 2022.

PAS-Nomacopan Decreased VEGF Levels As Effectively As An Anti-VEGF Antibody In a Pre-Clinical Model

In a pre-clinical model of severe uveitis, long-acting PAS-nomacopan (single IVI) decreased VEGF levels (VEGF-A is a key driver of CNV) as effectively as anti-VEGF antibody treatment^{1,2}

LTB4 promotes laser induced CNV in a pre-clinical model of wet age related macular degeneration³

Effect of PAS-nomacopan on VEGF levels in a standard pre-clinical model of severe uveitis



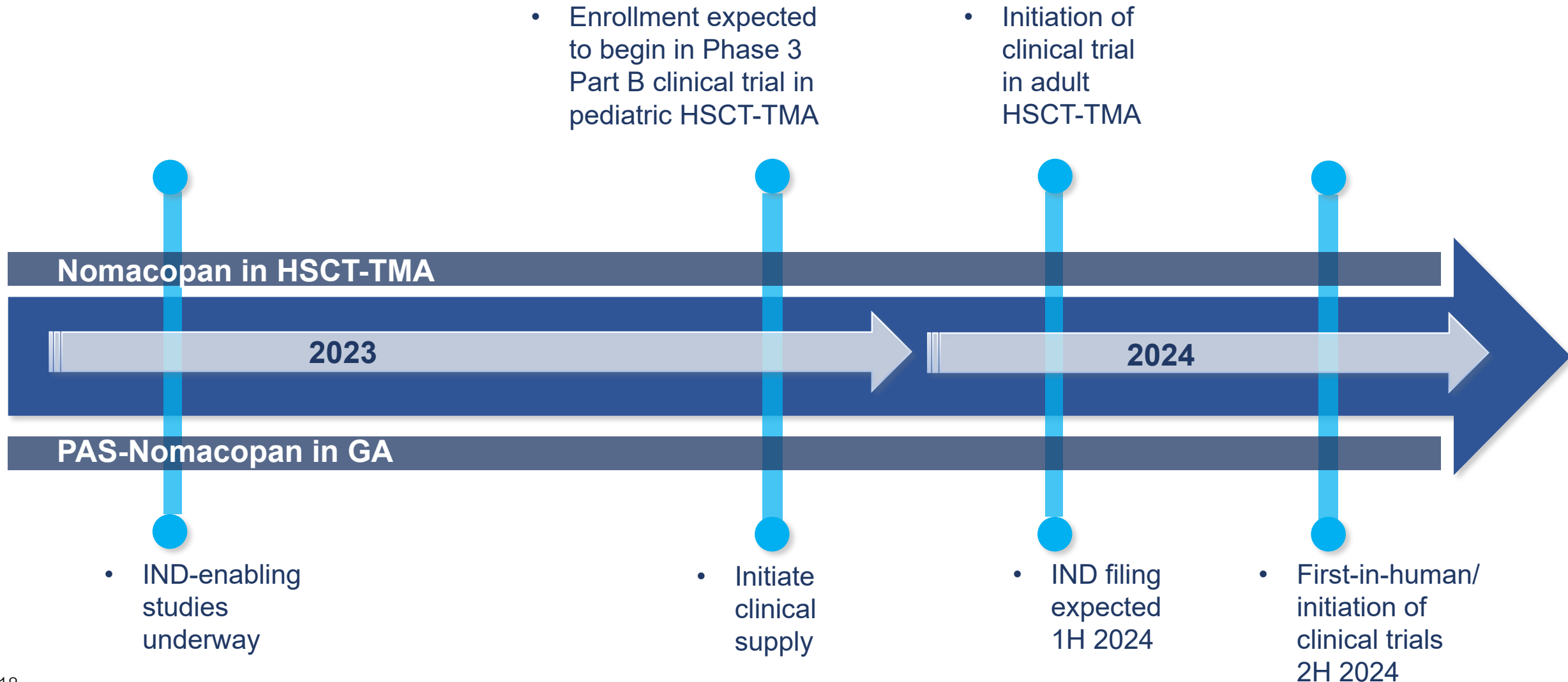
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NEXT STEPS



Next Steps



THANK YOU

