



# CORPORATE PRESENTATION

**AAV + RENAL STRATEGY**

May 2026

# CONTROLLING INFLAMMATION



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We based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements include, without limitation, statements about the following: the success of our future clinical trials for vilobelimab's treatment of other debilitating or life-threatening inflammatory indications, including ARDS; the potential strategic transactions or collaborations, including a potential partnership of izedicopan, or vilobelimab for PG; the success of our future clinical trials for izedicopan, and whether such clinical results will reflect results seen in previously conducted preclinical studies and clinical trials; the timing, progress and results of preclinical studies and clinical trials of vilobelimab, izedicopan and any other product candidates, including for the development of vilobelimab in several indications and other virally induced ARDS, HS and CSU, and statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the trials will become available, the costs of such trials and our research and development programs generally; our interactions with and the receptiveness and approval by regulators regarding the results of clinical trials and potential regulatory approval or authorization pathways, including our BLA submission for GOHIBIC (vilobelimab); the timing and outcome of any discussions or submission of filings for regulatory approval of vilobelimab, izedicopan or any other product candidate, and the timing of and our ability to obtain and maintain full regulatory approval and/or market authorization of vilobelimab or izedicopan for any indication; our ability to leverage our proprietary anti-C5a and anti-C5aR technologies to discover and develop therapies to treat complement-mediated immunological and inflammatory diseases; our ability to protect, maintain and enforce our intellectual property protection for vilobelimab, izedicopan and any other product candidates, and the scope of such protection; whether the FDA or any comparable foreign regulatory authority will accept or agree with the number, design, size, conduct or implementation of our clinical trials, including any proposed primary or secondary endpoints for such trials; the success of our future clinical trials for vilobelimab, izedicopan and any other product candidates and whether such clinical results will reflect results seen in previously conducted preclinical studies and clinical trials; our expectations regarding the size of the patient populations for, the market opportunity for, the medical need for and clinical utility of vilobelimab, izedicopan or any other product candidates, if approved or authorized for commercial use; our manufacturing capabilities and strategy, including the scalability and cost of our manufacturing methods and processes and the optimization of our manufacturing methods and processes, and our ability to continue to rely on our existing third-party manufacturers and our ability to engage additional third-party manufacturers for our planned future clinical trials and for commercial supply of any development candidate in the United States and Europe; our estimates of our expenses, ongoing losses, future revenue, capital requirements and our needs for or ability to obtain additional financing; our ability to defend against liability claims resulting from the testing of our product candidates in the clinic or, if, approved or authorized, any commercial sales; if any of our product candidates obtain regulatory approval or authorization, our ability to comply with and satisfy ongoing drug regulatory obligations and continued regulatory oversight; our ability to comply with enacted and future legislation in seeking marketing approval or commercialization; our future growth and ability to compete, which depends on our retaining key personnel and recruiting additional qualified personnel; our competitive position and the development of and projections relating to our competitors in the development of C5a and C5aR inhibitors and other therapeutic products being developed in similar medical conditions in which vilobelimab, izedicopan or any other of our product candidates is being developed or our industry; and other risk factors discussed under the "ITEM 3. Key information—Risk factors" section of our Annual Report on Form 20-F. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. You should refer to the "ITEM 3. Key information—Risk factors" section of our Annual Report and risks described in our subsequent SEC filings for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. As a result of these factors, we cannot assure you that the forward-looking statements in this presentation or in our Annual Report will prove to be accurate. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. You should, however, review the factors and risks and other information we describe in the reports we will file from time to time with the SEC after the date of this presentation.

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### About InflaRx

InflaRx (Nasdaq: IFRX) is a biopharmaceutical company pioneering anti-inflammatory therapeutics by applying its proprietary anti-C5a and anti-C5aR technologies to discover, develop and commercialize highly potent and specific inhibitors of the complement activation factor C5a and its receptor, C5aR. C5a is a powerful inflammatory mediator involved in the progression of a wide variety of inflammatory diseases. InflaRx's lead program is izecopan (INF904), an orally administered small molecule inhibitor of C5a-induced signaling via the C5a receptor, which has shown promising PK/PD characteristics as well as therapeutic potential in Phase 1 and Phase 2a clinical studies. The company is developing izecopan for the treatment of several inflammatory diseases, including hidradenitis suppurativa (HS). The Company has also developed vilobelimab, a novel, intravenously delivered, first-in-class, anti-C5a monoclonal antibody that selectively binds to free C5a and has demonstrated disease-modifying clinical activity and tolerability in multiple clinical studies.

InflaRx was founded in 2007, and the group has offices and subsidiaries in Jena and Munich, Germany, as well as Ann Arbor, MI, USA. For further information, please visit [www.inflarx.de](http://www.inflarx.de). InflaRx GmbH (Germany) and InflaRx Pharmaceuticals Inc. (USA) are wholly owned subsidiaries of InflaRx N.V. (together, InflaRx).

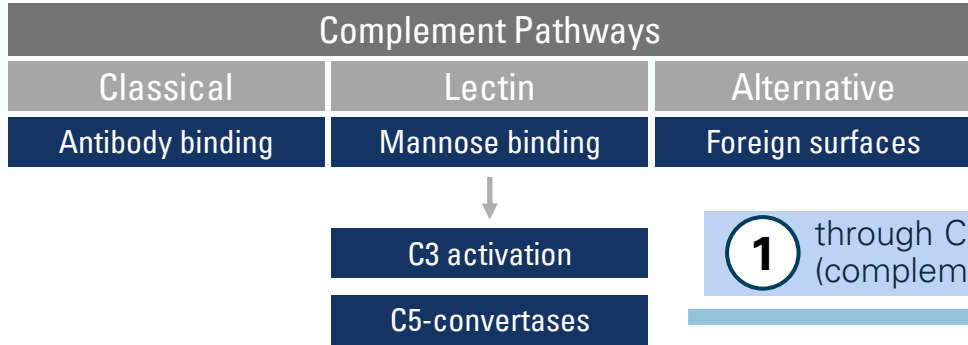
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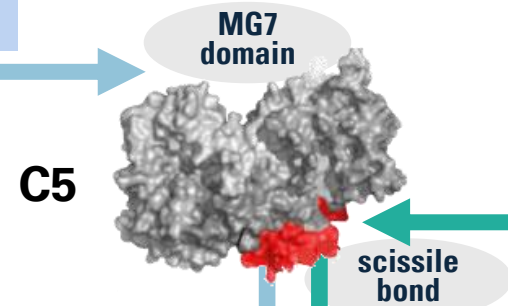
# Izicopan: A next-generation C5aR inhibitor for AAV and broader renal

- **Izicopan is an oral inhibitor of C5a/C5aR, a critical driver of the inflammatory cascade**
  - C5aR has been **validated from a clinical, regulatory and commercial perspective in AAV**
  - Further validation in AAV provided by **promising clinical data with C5a antibodies vilobelimab and BDB-001**
- AAV market growth and regulatory scrutiny related to the marketed comparator, avacopan, **has provided InflaRx a clear and present opportunity** with its next generation C5aR inhibitor, izicopan
- By improving upon the significant limitations of the marketed comparator, **izicopan has potential best-in-class properties**
  - Faster onset of action and higher target coverage leading to potentially differentiated efficacy
  - Cleaner safety profile with low risk of liver toxicity and drug-drug interactions
  - More convenient dosing with the potential for lower pill burden and once-daily dosing
- Given its class-leading properties izicopan has the **potential to improve upon the ~\$1.3B peak sales estimate\*** of avacopan
- Izicopan could also address significant unmet needs and large commercial markets across broader I&I, including **renal indications such as aHUS, IgAN, C3 glomerulopathy, and others**
- **Strong IP position** and a team with proven track record of delivering clinical and regulatory successes

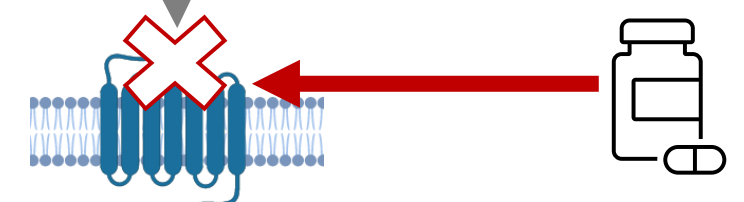
# Izicopan prevents binding of C5a to C5aR1



① through C5 convertases (complement mediated)



② through enzymatic cleavage at scissile bond (thrombin, trypsin, elastase, etc.)



## Advantages of blocking C5aR with izicopan

- Blocking C5 or further upstream (e.g., with eculizumab and related antibodies) **does not adequately inhibit C5a/C5aR1 signaling**
- A small molecule oral compound should have better tissue penetration and better ability to control C5a/C5aR1 signaling at the site of inflammation
- C5aR1 is selectively expressed on various immune and tissue cells, and blocking C5aR1 will not be impacted by increasing C5a generation

**C5aR1**

**izicopan**

# Izicopan's "triple threat" for a potential best-in-class agent in AAV

**Superior PK/PD profile** in Phase 1 and Phase 2 studies compared to reported data from marketed comparator avacopan \*

- **~10-fold higher AUC<sub>last</sub> and ~3-fold higher C<sub>max</sub>** (Phase 1)
- **Significantly increased blocking activity** >90% blocking of C5a activity
- **Faster achievement** of therapeutic exposure - within the first week vs 13 weeks for avacopan

## Improved safety profile

- **No signals of safety concern** (>180 humans exposed, clean GLP toxicology studies)
- **No time dependent CYP3A4 inhibition** (IC<sub>50</sub> > 100 μM) as measured via Ki-based TDI study

## Dosing advantages

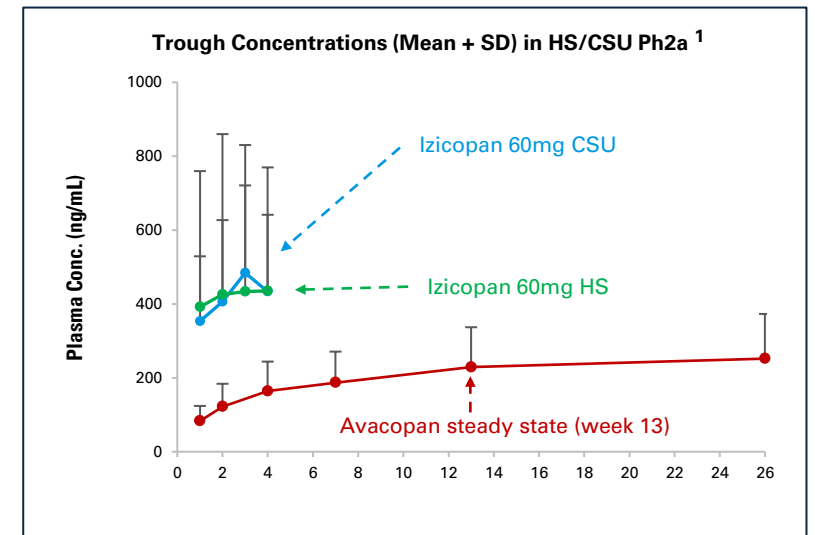
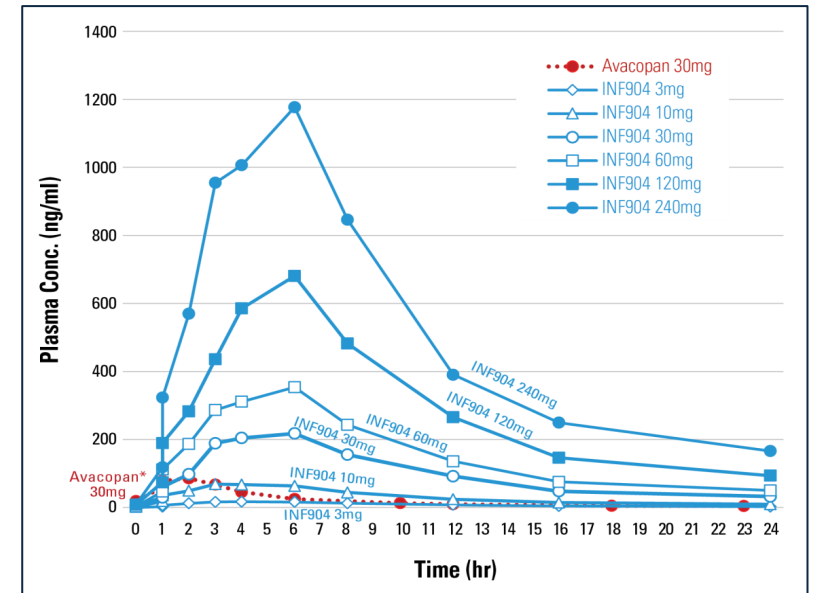
- 30mg per capsule (vs 10mg for avacopan) **and potential for once-daily dosing**

## Izicopan potential advantages

Faster onset of action + higher target coverage + differentiated efficacy  
 Cleaner safety profile with low risk of liver toxicity and drug-drug interactions  
 More convenient dosing, with lower pill burden and QD potential

\*InflaRx data on file: PK Results From Single Ascending Dose (SAD) Phase 1 study – note: Avacopan data (Becker et al, 2016, PLoS One) are superimposed in graph for orientation. Avacopan was not included as a comparator in INF904 Phase I study. PD Results from multiple ascending dose (MAD) Phase 1 study.

**1: Preliminary PK results of pooled patients:** 10 - 11 HS patients (60mg bid) and 10 -11 CSU patients (60mg bid). Steady state plasma levels of avacopan (NDA filing for ANCA-associated vasculitis, 75-100 patients) are reached by 13 weeks and the accumulation is approximately 4-fold.



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**ANCA-associated vasculitis (AAV)**

# ANCA-associated vasculitis (AAV)

## Clinical features

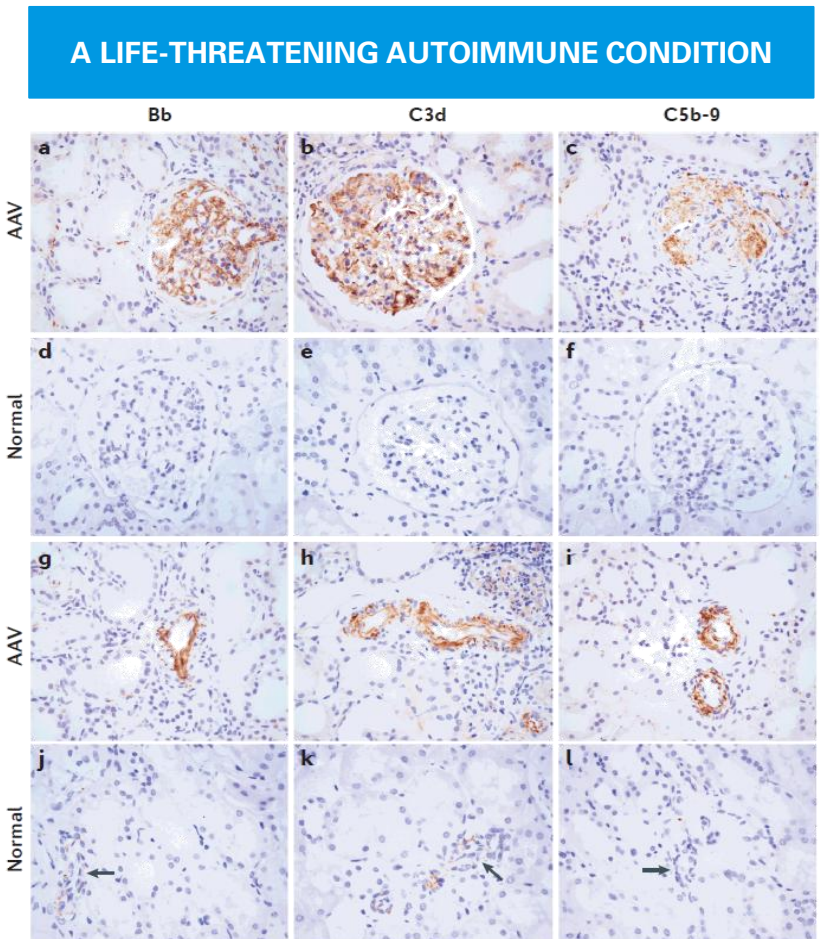
- Rare, life-threatening autoimmune disease, characterized by necrotizing vasculitis
- Life-threatening flare phases affect organs, leading to potentially fatal organ dysfunction and failure
- Predominantly affecting small vessels associated with anti-neutrophil cytoplasmic antibodies (ANCA) leading to complement activation

## Prevalence

- Orphan drug market
- Roughly 60K - 120K in US (2021 estimate) – increasing likely due to advanced diagnosis
- Roughly 75K patients in Europe
- In China, microscopic polyangiitis (MPA; p-ANCA/MPO; 80-90%) is more common than GPA (granulomatosis with polyangiitis; c-ANCA/PR3) vs western countries with ~60% p-ANCA (less severe form)
- Renal function is commonly impaired with prevalence in MPA > GPA

## Current treatment & medical need

- Induction of remission critical during flare phases
  - Induction treatment differs from maintenance therapy and consists of high dose corticosteroids plus either cyclophosphamide or rituximab
- Induction of remission therapy has significant side effects



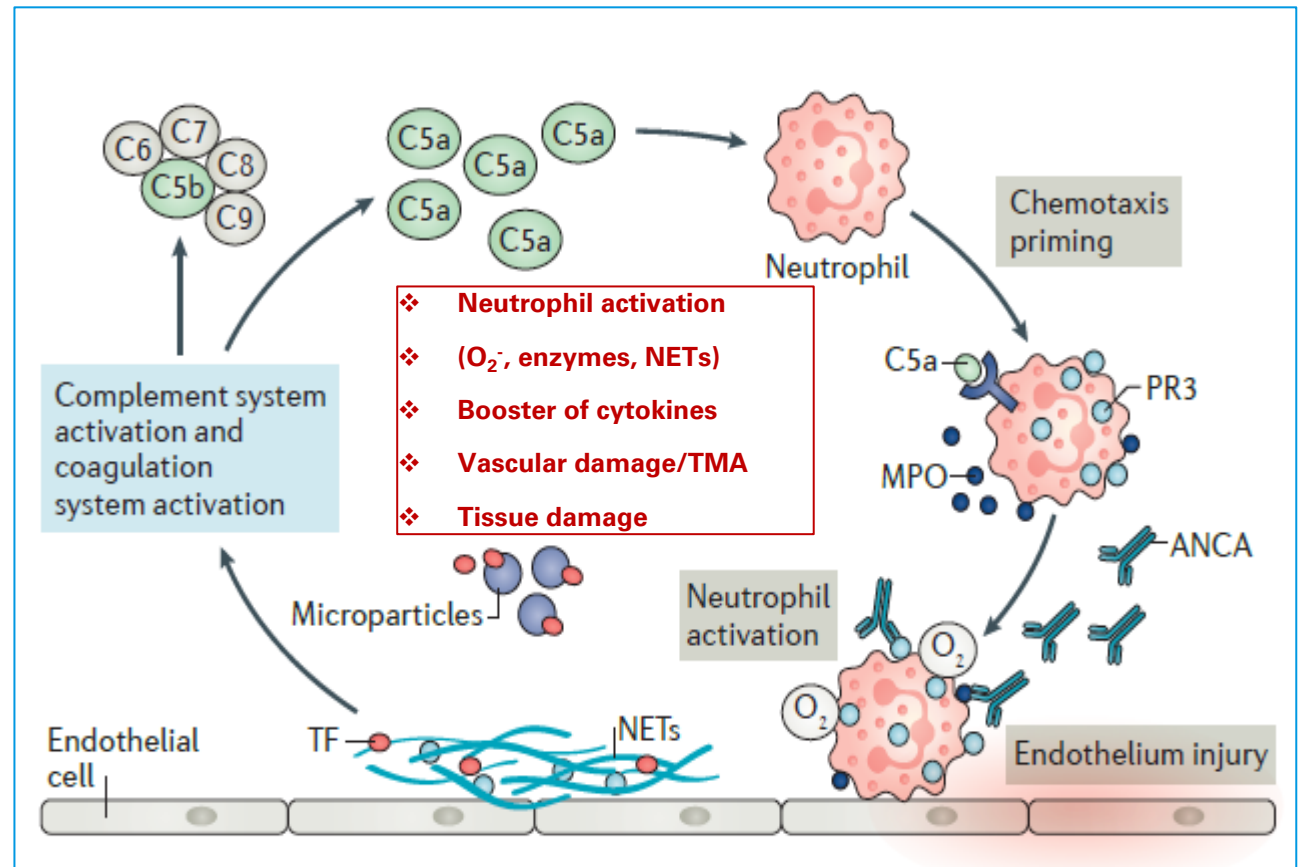
Expression of complement activation products in renal samples from patients with AAV. Immuno-histochemistry staining of Bb, C3d and C5b-9 in the glomerulus (a-f) and small vessels (g-l).

# The key role of C5a/C5aR in AAV pathophysiology

## C5a-driven vicious cycle in ANCA

- ANCAs trigger complement activation/C5a generation, leading to neutrophil activation
- ANCAs can activate primed neutrophils to undergo respiratory burst and degranulation, as well as NETosis
- Neutrophil activation can lead to endothelial cell injury, NETosis and tissue damage, enhancing complement activation and C5a production
- Forming a vicious cycle: ANCA/C5a – neutrophil activation – vascular injury and NETosis – C5a generation

## Proposed model for the interaction of ANCA, neutrophils and complement activation in the pathogenesis of AAV



Chen et al. Nat Rev Nephrol 2017, 13(6):359

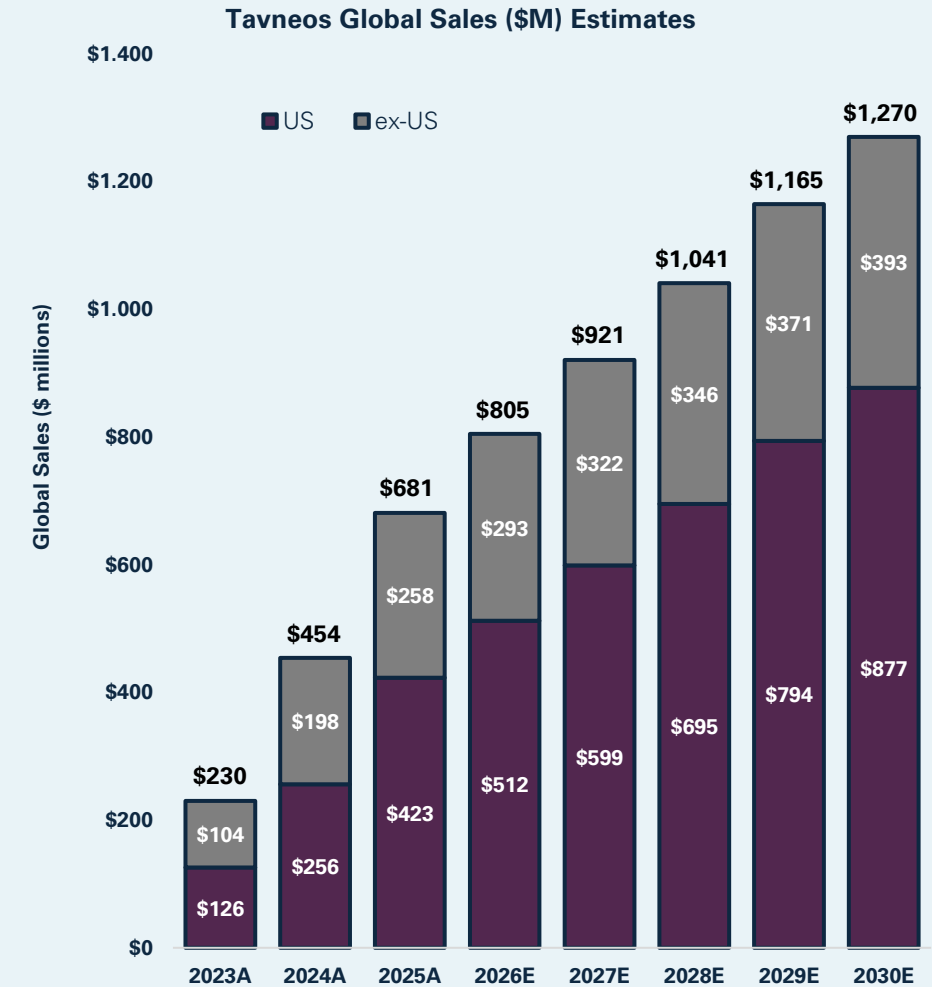
# Izicopan in AAV – A proven large market opportunity

- Market for C5aR inhibitor **avacopan (marketed as Tavneos) estimated to be ~\$1.3B\***
- **MoA has been established and accepted** to drive organ dysfunction in AAV
- With avacopan under regulatory scrutiny, a safer drug with faster onset and more convenient dosing **could significantly expand this opportunity**

## What US physicians think\*\*

- C5aR inhibition is typically **initiated during major flares**
- Treatment duration varies between 6 and 48 months
- C5aR inhibition is mainly used by physicians for:
  - **Glucocorticoid reduction**
  - **Renal function preservation**
- Avacopan tox signals **are an issue for physicians**
- “Product X” with an improved tox profile, faster onset of action and once-daily dosing could capture **strong share of new AAV patient starts, and promote switching from avacopan:**
  - Survey: “Product X” share of new patient starts could be 55% vs 15% for avacopan
  - Survey: 45% of current avacopan patients could switch to “Product X”

**C5aR inhibition is a well established and accepted MoA in AAV  
Izicopan’s profile could significantly expand the market >\$1.3bn**



\* **March 2026:** Guggenheim Securities, market research, Yatin Suneja – Figures and estimates by Guggenheim Securities, FactSet, Evaluate Pharma.

\*\* **April 2026:** LifeSci Capital, market research, Sam Slutsky – Survey of 21 US physicians.

**Note:** Ex-US Tavneos sales include sales booked by Amgen ex-US marketing partners.

# Izicopan in AAV – Capturing the opportunity

## Goal: 'Rock the Boat' Scenario

- **Steroid-reducing / rapid taper label**
  - Avacopan label does not state steroid-sparing
- **Demonstrate early benefit (potentially label relevant)**
  - Early reduction of proteinuria (w4)
  - Improve eGFR (w26 / w52)
  - Improve time to remission (BVAS-0)
- **Clean label (no liver tox)**
- **Lower capsule intake or once-daily dosing**

*“Steroids have much more toxicity than just infection. Steroids are incredible medicines - they help control these conditions, but used long-term and high dose cumulative use of these medications are extraordinarily toxic to the body, so you want to lower their use to zero, if possible.” – interview # 2*

## Key Development Improvements

### Overall Goal

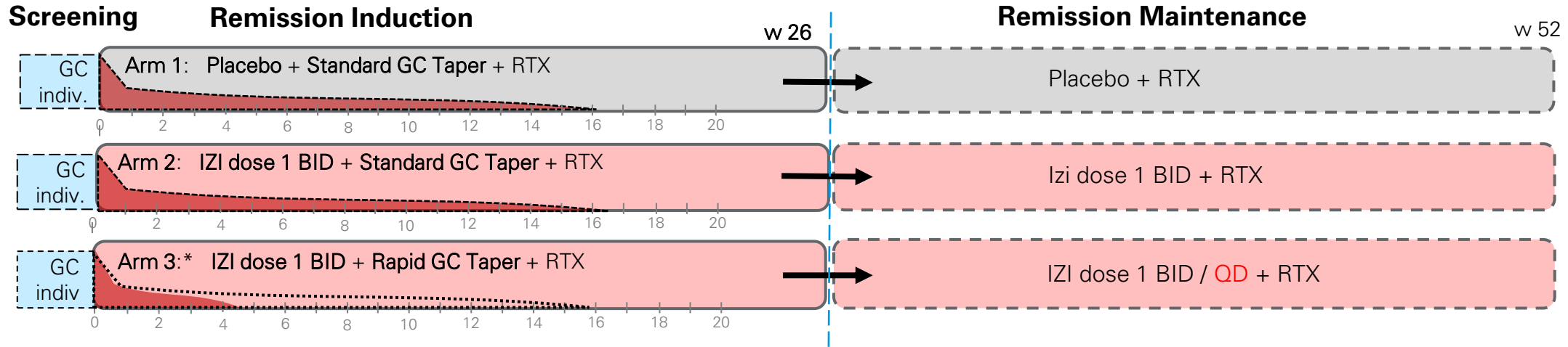
Increase signal delta to placebo especially during early major flare phase while demonstrating a rapid steroid tapering / reduction

### Study Design Aspects

- Enrolling fast = get patients on izicopan early in the flare
  - No mandatory GC tapering before initiation of dosing
- Enrich for / allow patients with severe renal impairment
- Fix SOC remission induction treatment to rituximab
- Aggressive rapid steroid taper in treatment arm(s) tested versus standard steroid tapering in placebo arm

**Development improvements to focus on izicopan advantages**

# Izicopan AAV Phase 2 trial – Base case / current planning stage



Phase 2 over 12 mos with unblinded analysis for primary endpoint at wk 26 (6 mos), GC tapering according to SOC (PEXIVAS), izicopan arm rapid GC tapering within 4-6 wks

\* Possibility to add an additional dosing arm with same GC tapering regimen switching to QD earlier – will depend on regulatory discussions

n = approximately 30-50 per arm

## Endpoint analyses

### Primary: Safety

- TEAEs, SAEs, TRAEs, infections + descriptive BVAS-0 non-inferiority week 26

### Secondary efficacy focus

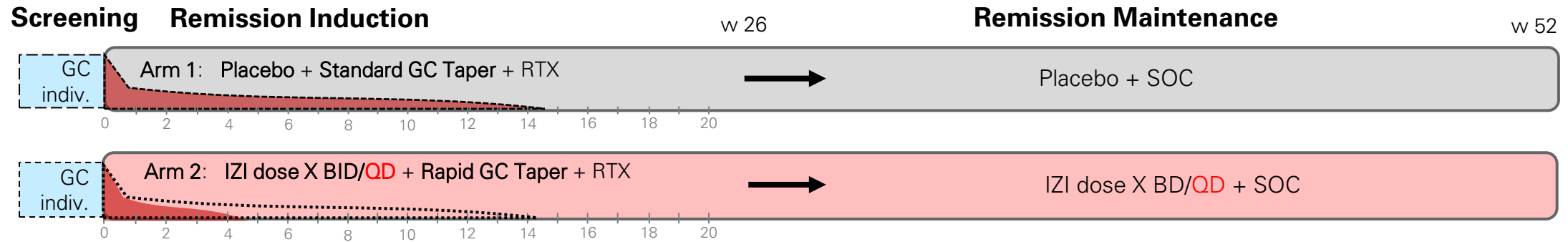
- Early Proteinuria reduction: UACR delta  $\geq 30\%$  to placebo at Wk 4 ( $\geq 20\%$  at w 2)
- eGFR week 26 / 52
- Time to BVAS-0 (clinical remission) + # of patients with BVAS-0 per early time points

### Secondary other

- Pharmacokinetics (PK)
- Time in clinical remission 12 mos
- GC infections / toxicity
- Urine NGAL / MCP-1, other biomarkers

**BVAS** [Birmingham Vasculitis Assessment Score]. **CYC** [cyclophosphamide]. **GC** [glucocorticoids]. **IZI** [izicopan]. **RTX** [rituximab]. **SOC** [standard of care maintenance]. **NGAL** [neutrophil gelatinase-associated lipocalin]. **MCP-1** [monocyte chemoattractant protein-1]. **TEAEs** [treatment emergent adverse events]. **SAEs** [serious adverse events]. **TRAEs** [treatment-related adverse events].

# Izicopan AAV Phase 3 trial – Base case / current planning stage



Phase 3 over 12 mos with unblinded analysis including for primary endpoint, GC tapering according to SOC (PEXIVAS), izicopan arm rapid GC tapering within 4-6 wks

n = approximately 150 - 170 per arm, depending on final endpoint choice and powering

## Endpoint Analyses Scenario I

- **Primary endpoint\***
  - Non-inferiority BVAS-0 (w26 + w52)+
  - Superiority eGFR (w26 / 52) or time to BVAS-0
- **Secondary endpoints**
  - Early proteinuria reduction: UACR (w4)
  - Safety : TEAEs, SAEs, TRAEs,
  - Time in clinical remission 12 mos
  - GC related infections / toxicity
  - QOL

Choice of primary will depend on outcome of phase II and interaction with FDA

## Endpoint Analyses Scenario II

- **Primary endpoint\***
  - Superiority eGFR week 26 / 52 or time to BVAS-0
- **Secondary endpoints:**
  - Safety: TEAEs, SAEs, TRAEs, + BVAS non-inferiority week 26 / week 52
  - Early proteinuria reduction: UACR (w4)
  - Time in clinical remission 12 mos
  - GC related infections / toxicity
  - QOL

\* Primary endpoint efficacy will depend on Phase 2 results; potential alternatives include absolute BVAS reduction, composite measures (BVAS + renal outcomes)

BVAS [Birmingham Vasculitis Assessment Score]. CYC [cyclophosphamide]. GC [glucocorticoids]. IZI [izicopan]. RTX [rituximab].

# Izicopan in AAV – Exploring potential for expedited development

Concurrent with AAV planning and in accordance with the fluid regulatory environment for avacopan, **InflaRx is evaluating the feasibility of an expedited clinical and regulatory path for izicopan in AAV**

## Options for expedited clinical and regulatory path could include

- Use of a “seamless” trial strategy for a “one-shot” Phase 2 - 3 registrational trial approach
- Seamless trial strategy could explore 2 doses in its first phase, including once-daily dosing, transitioning to a second phase focusing on one dosing regimen in the Phase 3 part
- Potential to reduce time to the commercial market by 6 to 12 months

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**Renal indications**  
**Development opportunities**

# Potential izicopan renal disease PoC basket studies

- A strategy to conduct studies in regions where InflaRx can rapidly generate data, including China, **for a strategic advantage in indications such as IgAN, aHUS, and C3G**

- **Large patient populations, centralized nephrology networks**, and strong expertise in complement-mediated kidney disease trials
- Strong potential for **rapid recruitment and efficient proof-of-concept generation**

## ▪ aHUS

- Compelling biology with strong evidence for C5a/neutrophil-driven endothelial injury
- Fast POC with clear, **regulator-accepted TMA response (biomarker) endpoint with rapid efficacy readout**
- Izicopan: differentiated safety with no vaccination, low infection risk, oral therapy
- Monotherapy potential or as add-on / rescue to anti-C5

## ▪ IgAN

- **Accelerated approval via biomarker surrogate (proteinuria), with eGFR stabilization as confirmatory endpoint**
- Autoimmune disease with immune complex-driven pathology, where C5a/C5aR1 is a clearly defined key disease mechanism.
- Aligned with growing adoption of complement therapies in this kidney disease
- Izicopan: no vaccination required, and low infection risk compared with other complement inhibitor such as iptacopan.

## ▪ C3G

- **Accelerated approval pathway based on biomarker surrogate (proteinuria), with eGFR stabilization as supportive endpoint.**
- Strong proof-of-concept data from avacopan support C5a/C5aR1 as a validated therapeutic target pathway.
- Aligned with growing adoption of complement therapies in this kidney disease
- Izicopan could have oral convenience, no vaccination requirement and low infection risk compared with pegcetacoplan.

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## **Renal indications**

**aHUS (atypical Hemolytic Uremic Syndrome)**

# A new paradigm for aHUS: C5a likely a key driver for TMA

## aHUS is a potentially life-threatening condition that causes small blood clots and organ damage

- Caused by genetic abnormalities that result in chronic uncontrolled complement activation, leading to complement-mediated **TMA (thrombotic microangiopathy)** in small blood vessels throughout the body.
- **Prevalence:** aHUS alliance Global Action estimates a prevalence rate of 6.5 per million in US, over 2,000 patients in US; rising due to more sensitive diagnostic tests. (FutureMarketInsights)
- **Treatment:** Anti C5 Abs Soliris and Ultomiris
- **Primary endpoint:** complete TMA response\*. Soliris registration trial (N=20 and N=17); Ultomiris single-arm trial (N=56). TMA improvements can be detected within days to weeks.

Avacopan PoC ex vivo data suggest that the C5a/C5aR1 pathway is essential for TMA formation in aHUS patients, consistent with in-house InflaRx data

### \* Criteria for complete TMA response

Platelet count normalization ( $\geq 150 \times 10^9/l$ ), LDH normalization ( $\leq 246$  U/l), and 25% or better improvement in serum creatinine from baseline.

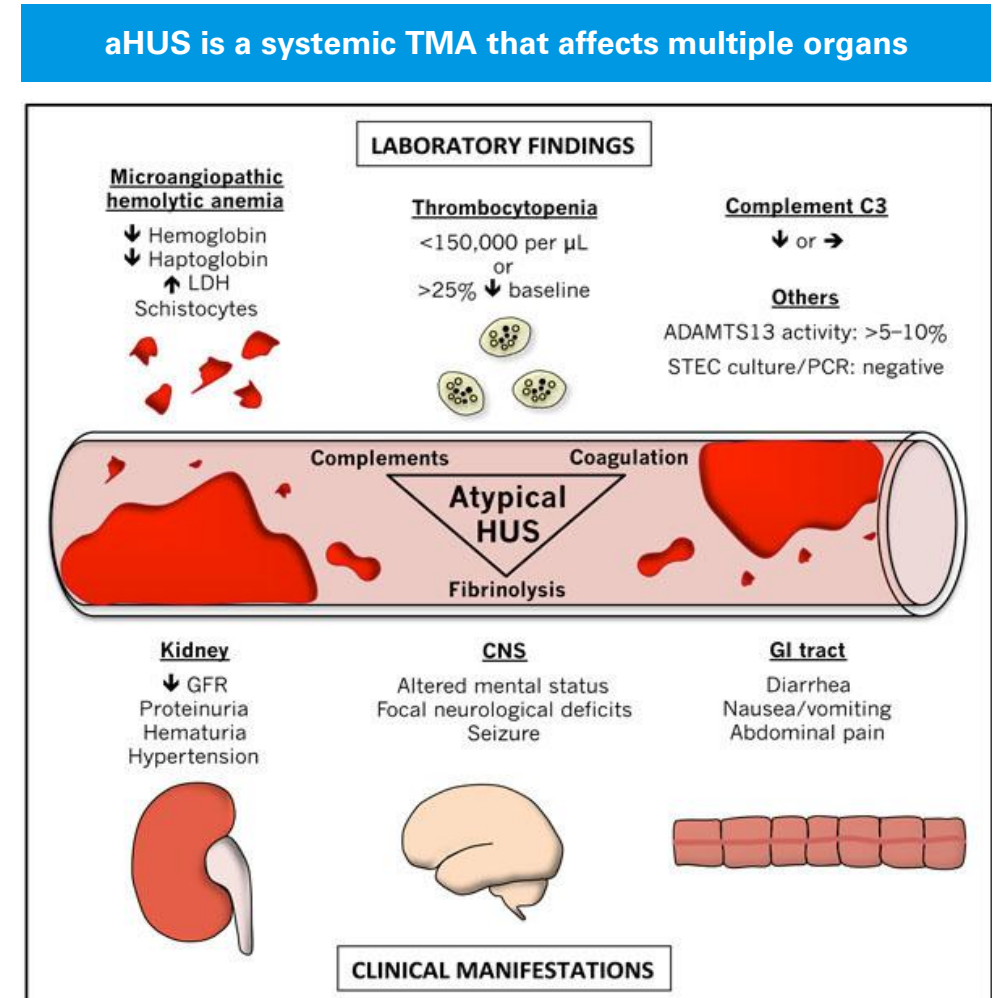


Figure source: Grepmed

# aHUS: Ex vivo PoC with avacopan

## Ex vivo findings in aHUS patients treated with avacopan (CCX168, n = 5)

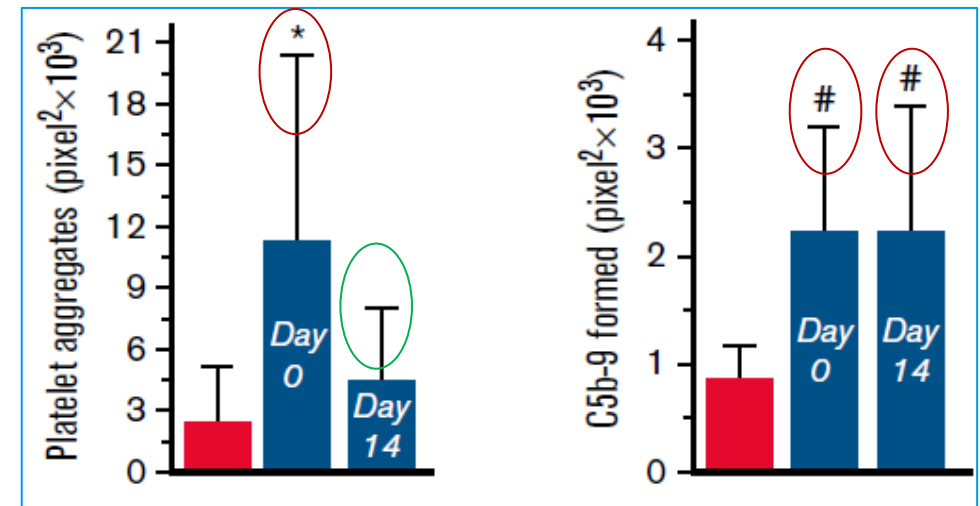
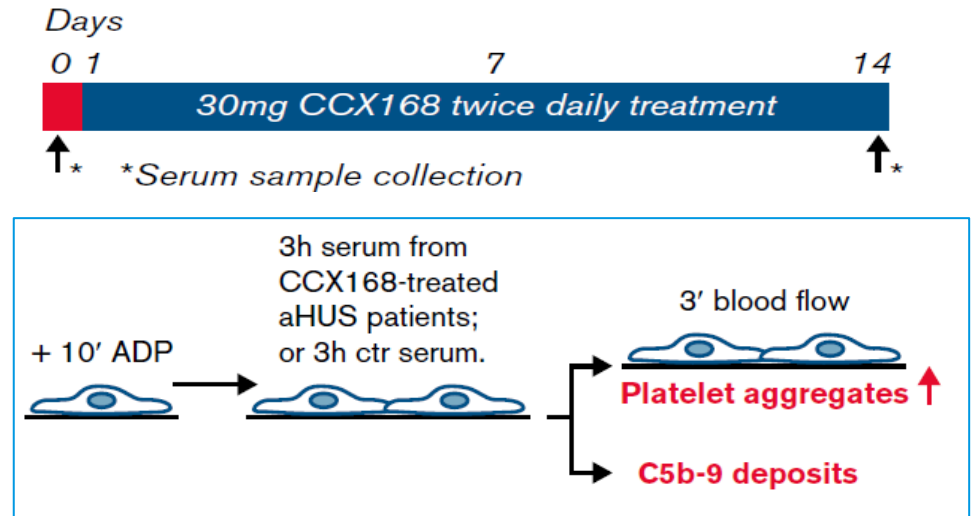
- **Serum from Day 0:** Lead to strong platelet aggregates and C5b-9 deposition
- **Serum from Day 14 after CCX168 treatment:** Platelet aggregates were almost reduced to baseline level, while C5b-9 deposition was not impacted, suggesting C5a/C5aR1 axis but not C5b-9 playing a critical role in platelet aggregation in aHUS

InflaRx study using the same in-vitro model demonstrate that both izicopan and vilobelimab could effectively reduce thrombus formation induced by aHUS serum.

## Suggesting a new pathogenesis for aHUS

- I. C5a → direct EC injury → thrombogenicity
- II. C5a/C5aR1 - neutrophil → enhancing EC injury

**Versus the classic paradigm of MAC (C5b-9) playing the dominant role in EC injury in aHUS**



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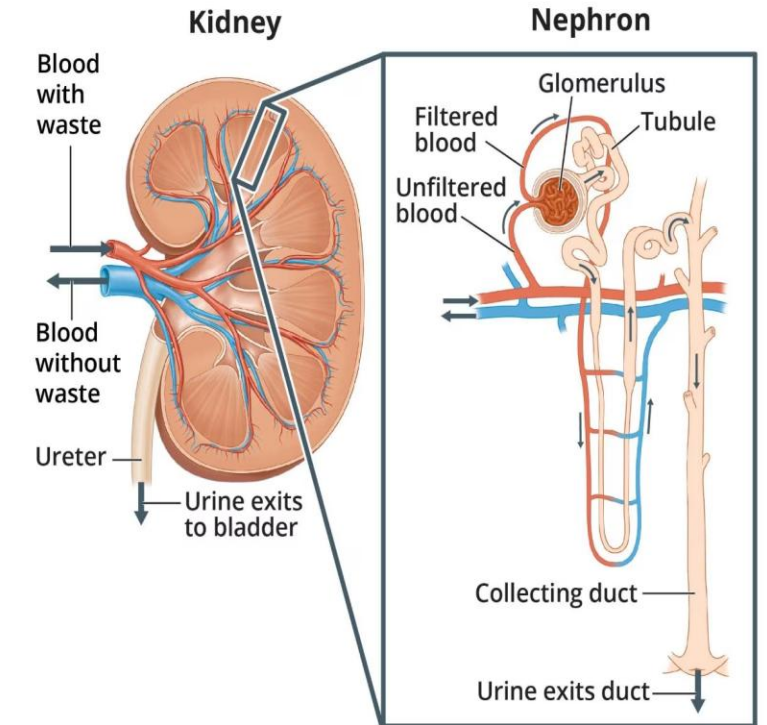
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**Renal indications**  
**IgA nephropathy (IgAN)**

# IgAN: An autoimmune condition with complement activation

## IgAN is an autoimmune condition in which IgA deposits in the glomeruli of the kidneys, impacting filtration

- **Prevalence<sup>5</sup>**: US: ~85k; EU5: ~180k; China: ~800K; Japan: ~85k
- **IgAN is the most common cause of primary glomerulonephritis (GN)<sup>3</sup>**
  - It may also occur in association with other conditions, including lupus nephritis and thrombotic microangiopathy.
- **Disease course and symptoms**
  - Typically, slow-progressing; may ultimately lead to acute kidney injury and chronic kidney disease, including end-stage renal disease (ESRD)
  - Approximately 25% of patients develop ESRD over the disease course<sup>1,2</sup>
- **Complement activation is a key driver of kidney inflammation and injury in IgAN**, highlighting an unmet need for a safe and effective complement inhibitor to control complement-driven damage<sup>4</sup>
- **Iptacopan, an oral factor B inhibitor, has achieved regulatory approval**
- **Ultomiris (ravulizumab), an anti-C5 antibody, has recently demonstrated statistically significant reductions in proteinuria, meeting the primary endpoint in Phase 3 clinical studies**



Source: NIDDK

# Avacopan – Blockade of C5aR1 “PoC” in Patients with IgAN

## Avacopan treatment

- Attenuated kidney injury  
Urinary Proteinuria – uPCR ↓
- Reduced inflammation  
Urinary MCP-1/creatinine ↓

## Proposed MOA

Inhibition of C5a/neutrophil-mediated endothelial injury and downstream inflammatory activation in the kidney



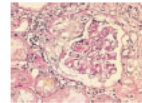
## C5a receptor inhibitor avacopan in IgA nephropathy – an open-label pilot study

This study evaluates the safety and efficacy of avacopan in patients with IgAN with persistent proteinuria despite RASi blockage

### Methods

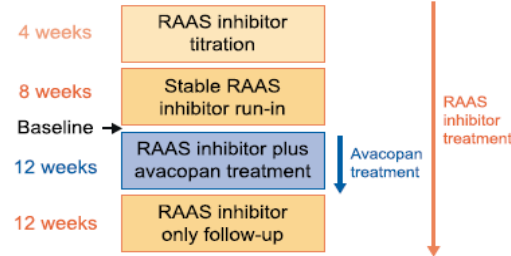
#### Open-label pilot trial

- ✓ UPCR > 1g/g
- ✓ eGFR > 60 mL/min/1.73 m<sup>2</sup>



OR

- ✓ eGFR > 45 mL/min/1.73 m<sup>2</sup> (if eGFR has not declined > 10 mL/min/1.73 m<sup>2</sup> in 24w)



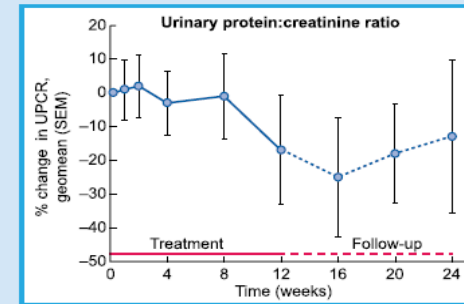
### Results



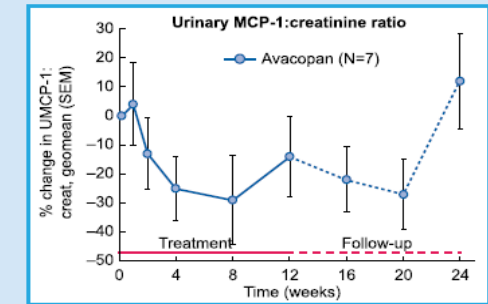
Run-in period of 8 w  
UPCR > 1g/g



Avacopan  
30 mg × 2 day



Improvement in UPCR during treatment



Urinary MCP-1: creatinine decreased 30%

⚠ 1 event: unstable angina – unrelated to avacopan

**Conclusion:** This short-term trial showed an improvement in the slope of UPCR in 6 out of 7 patients, with ~ 50% improvement in 3 out of 7 patients with IgAN. Longer avacopan treatment duration may be indicated for maximal benefit.

Bruchfeld, A. et al.  
Clinical Kidney Journal (2021)  
annette.bruchfeld@liu.se  
@CKJsocial

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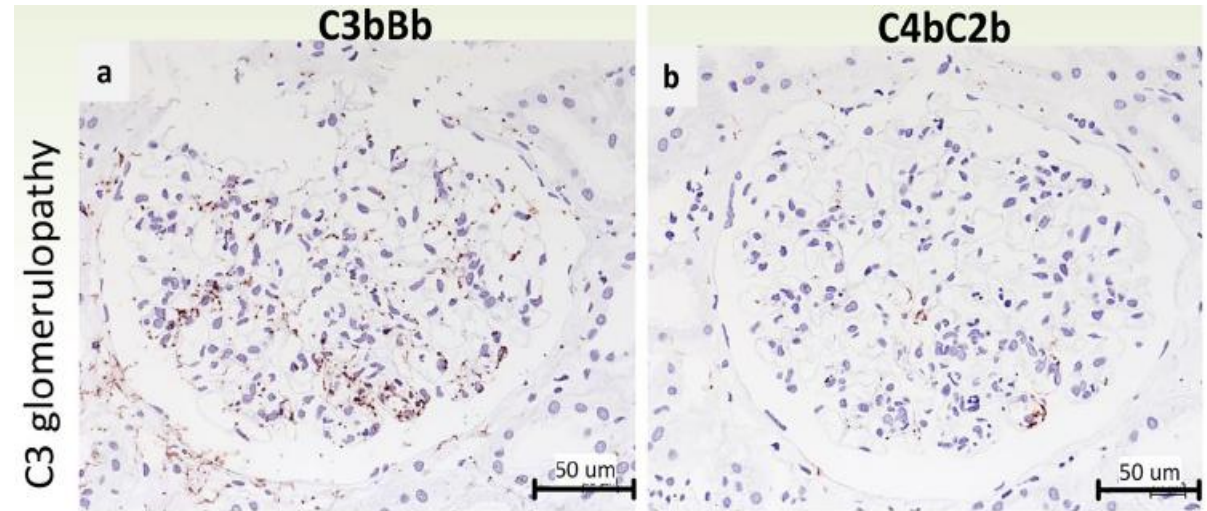
*infla***Rx**

**Renal indications**  
**C3 glomerulopathy (C3G)**

# Complement activation in C3G

**C3G is a rare immune disease characterized by complement dysregulation that undermines the ability of the kidneys to perform many vital functions**

- **A life-threatening kidney disease;** half of all patients with C3G ultimately have kidney failure; Kidney transplant does not cure disease; relapse is common
- **Prevalence<sup>1</sup>:** US ~10,000 cases; China ~32,000
- FDA approval of pegcetacoplan (2025) in C3G/IC-MPGN **set a disease-specific precedent**
  - **Proteinuria can be a primary endpoint** supported by eGFR stability and mechanistic complement biomarkers.



## **Alternative vs classical complement pathway activation in C3G**

A predominant activation of the alternative complement pathway in C3 glomerulopathy as evidenced by C3bBb staining

Zipfel et al. Cell and Tissue Research (2021) 385

# Avacopan Phase 2 data in C3G

## Promising results from the avacopan Accolade Phase 2 trial

N = 22 for each group

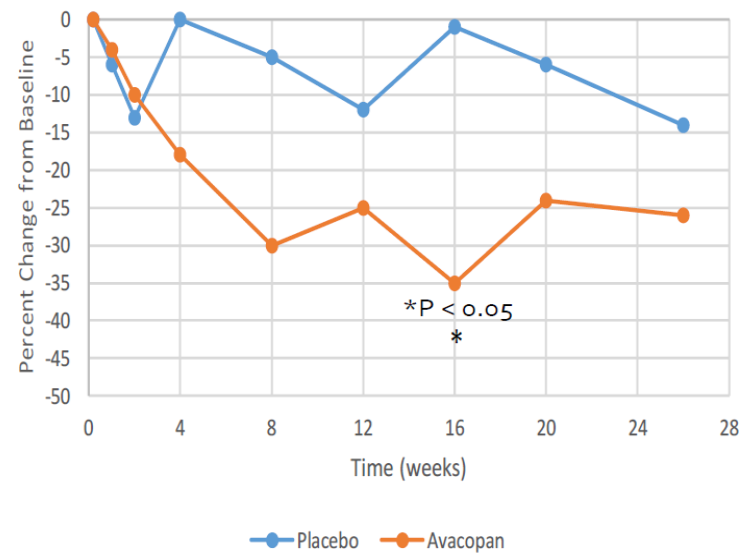
### Safety

- Adverse event incidence similar between the two groups

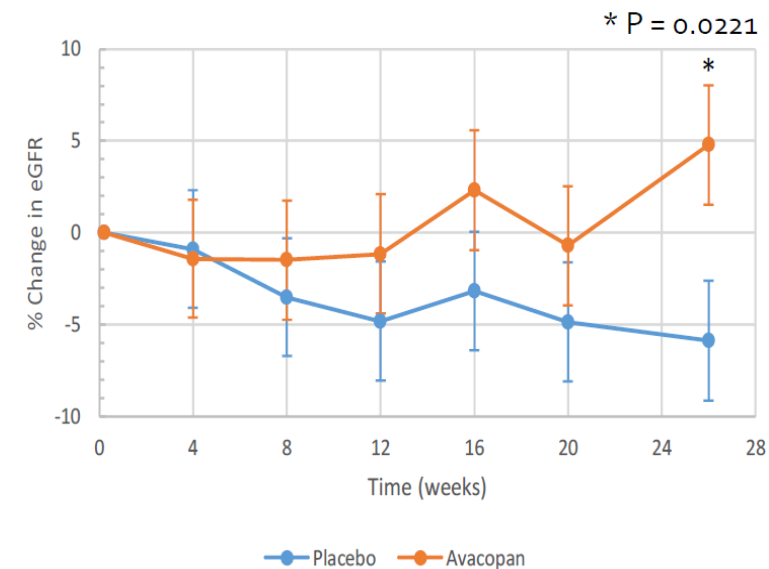
### Efficacy

- Rapid and sustained reduction of proteinuria
- Improved kidney function (eGFR) at Week 26 after treatment ( $P < 0.05$ )
- Improved histological index score for disease chronicity ( $P < 0.05$ )

Improvement from Baseline in UPCR



Improvement from Baseline in eGFR in all Patients



Chemocentryx Corp Presentation 2020-Dec (Accolade Trial)

# Potential izicopan renal disease PoC basket studies

**Izicopan has a differentiated safety and convenience profile versus other complement inhibitors**, including fast onset, oral administration, no vaccination requirement, and no increased infection risk, with **potential to drive improved physician adoption, patient acceptance, and treatment persistence**

- **Fast PoC execution**
  - Streamlined regulatory pathways for rare diseases, unmet needs, and strong KOL engagement support rapid enrollment
- **Cost efficiency**
  - Lower clinical trial costs can improve capital efficiency and enable larger, faster PoC studies within the same budgets
- **Established clinical expertise and network**
  - Strong investigator networks including key opinion leaders and city centers such as Beijing University Hospital, and population centers, support efficient recruitment and high-quality trial execution
- **Clear endpoint readouts**
  - Primary readouts based on endpoint such as proteinuria reduction (UPCR), eGFR stabilization and optional biomarker profiling to confirm mechanism

**Fast, focused, Phase 2 PoC studies: Smaller sizes, optimized for early go/no-go decision in these rare renal indications**

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**Hidradenitis suppurativa (HS)**

# FDA interactions indicate a viable path forward for izicopan in HS

Phase 2a data indicate izicopan has **biologic-like activity** within just 4 weeks of treatment, with AN count reduction and HiSCR in line with successful Phase 3 comparators, **fast and deep reduction in dT, and significant improvement in pain (NRS30)**

## Outcome of FDA interactions

- FDA has acknowledged the importance of draining tunnels (dT) as a major contributor to HS disease burden
- FDA supportive of development of a new endpoint in HS, the modified Hidradenitis clinical response score (mHiSCR) which, depending on validation work in a Phase 2b trial, could be used as primary endpoint in pivotal trials.
- mHiSCR incorporates reduction of dT by requiring on overall 50% abscess, nodule and dT (ANdT) count reduction from baseline and separately, a 50% dT reduction from baseline as key criteria (next to no increase in abscesses and no new dT development from baseline)
- InflaRx believes mHiSCR may be suitable to meaningfully control placebo response rates in HS while catering to izicopan's MoA
- Phase 2b study could provide additional insight into the clinical utility of izicopan in HS, help validate mHiSCR and dT reduction as a label relevant endpoints and establish a dose for Phase 3
- HS remains a large market opportunity for izicopan: Currently further development is only envisioned in collaboration with a partner

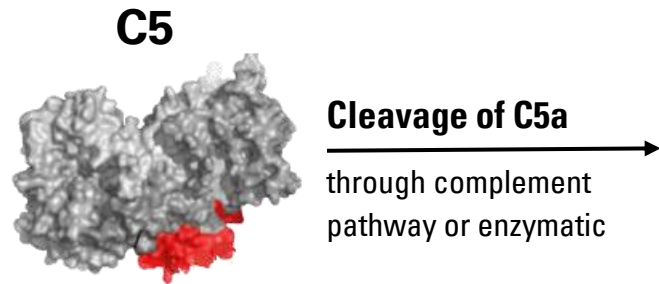
**Izicopan shows promise to be a safe oral agent with biologic-like activity and a differentiated new mechanism of action and a market potential that could exceed \$1.5B per year<sup>1</sup>**

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INFLAMMATION

*infla***Rx**

**Appendix**

# C5a/C5aR are validated targets promoting inflammation



## Targeting strong pro-inflammatory mechanisms

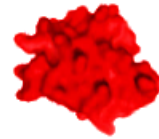
**vilobelimab**

intravenous mAb

**izicopan**

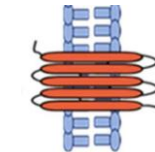
oral small molecule

**C5a**



strong amplifier of inflammation

**C5aR**



expressed on many immune cells and upregulated in many tissues under disease conditions

### Anaphylatoxin C5a is upstream of the cytokine network

- Induces histamine release – can lead to anaphylactic reactions
- Boosting effect on various pro-inflammatory cytokines from various immune cells (IL-17, IL-6, IL-8, IL-1 and others)
- Drives TH1 and TH17 T-cell differentiation

### Strong activator of neutrophils and macrophages

- Chemotaxis of neutrophils / macrophages / monocytes into tissue
- O<sub>2</sub> radical generation + granular enzyme release from neutrophils
- NETosis induction (neutrophil extracellular traps)

### Essential role in many inflammatory conditions

- Acute and chronic inflammation and other conditions
- Over 6,000 publications on role in numerous diseases

# InflaRx Pipeline: Targeting the C5a–C5aR1 axis to control inflammation

|               | INDICATION   | PRECLIN                                | PHASE 1 | PHASE 2 | PHASE 3 | MARKET | STATUS & MILESTONES  |
|---------------|--|--|---------|---------|---------|--------|--|
| I&I           | <b>izicopan</b><br><i>Oral C5aR inhibitor</i>      | <b>ANCA-associated vasculitis</b>      | ▶       |         |         |        | Phase 2b planning ongoing  |
|               |  | <b>other renal indications</b>         | ▶       |         |         |        | Additional renal indications such as aHUS, IgAN, C3G, and others               |
|               |  | <b>HS + CSU</b>                        | ▶       |         |         |        | Topline Phase 2a reported  |
|               |  | <b>broader I&amp;I</b>                 | ▶       |         |         |        | Additional indications in immuno-dermatology, hematology, neurology and others |
| CRITICAL CARE | <b>Gohibic vilobelimab</b><br><i>C5a inhibitor</i> | <b>critical COVID-19</b>               | ▶       |         |         |        | US EUA granted*  |
|               |  | <b>SARS-CoV-2-induced ARDS</b>         | ▶       |         |         |        | Approved by European Commission*   |
|               |  | <b>broader ARDS</b>                    | ▶       |         |         |        | Phase 2 "Just Breathe" ASPR/BARDA clinical platform study                      |
| DERM          | <b>vilobelimab</b><br><i>C5a inhibitor</i>         | <b>pyoderma gangrenosum</b>            | ▶       |         |         |        | Phase 3 reported**   |
| OTHER         | <b>IFX002</b><br><i>C5a inhibitor</i>              | <b>vilobelimab life-cycle approach</b> | ▶       |         |         |        | For optimized use in chronic inflammatory indications                          |

\*Commercial partnering and distribution options in the US and EU being considered.

\*\* Phase 3 stopped early for futility at interim analysis, FDA interaction considered.

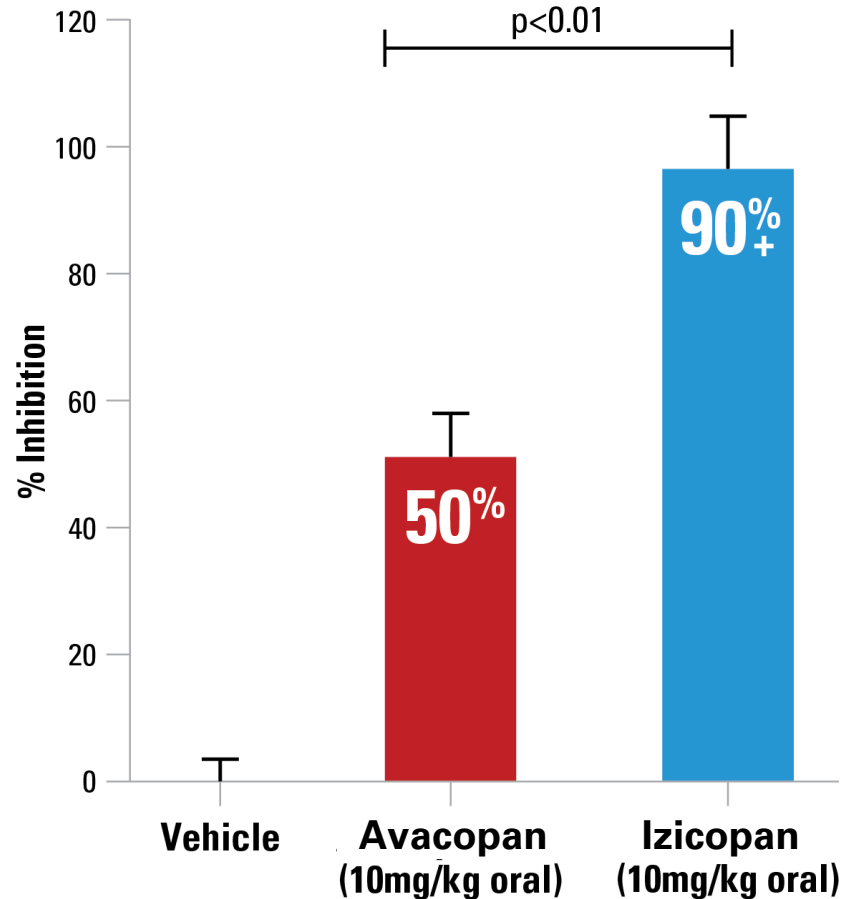
aHUS [atypical hemolytic uremic syndrome]. IgAN [IgA nephropathy]. C3G [anti-C3 glomerulopathy].

# Izicopan's improved chemistry, metabolic & safety features

| Feature   | Avacopan  | Izicopan  | Key differentiation for izicopan   |
|---|---|---|--|
| <b>Medicinal chemistry</b>                          | Used as a lead compound series for the development of izicopan  | Further structure-activity optimization performed   | Izicopan <b>has improved PK/PD profiling in humans and improved safety features</b> (e.g. metabolic stability and CYP inhibition)  |
| <b>Chirality</b>                                    | 2 chiral centers  | 3 chiral centers  | The extra stereocenter in izicopan <b>provides additional conformational control, significantly improving physiochemical properties and druggability</b>   |
| <b>Solid-state form</b>                             | Crystalline   | Amorphous   | The amorphous form of izicopan supports <b>faster absorption and quicker attainment of therapeutic exposure</b><br>Izicopan therapeutic exposure reached in days to one week, vs 13 weeks for avacopan   |
| <b>CYP inhibition</b>                               | Time dependent inhibitor of CYP3A4  | Ki/Kinact assay demonstrates:<br>No inhibition of CYP3A4 (IC50 >100 µM)<br>No time dependent inhibition (TDI)   | <b>Avacopan CYP3A4 inhibition raises risk of drug–drug interactions</b> and may slow clearance of co-medications (incl. steroids), potentially contributing to liver toxicity. This is <b>not a concern with izicopan</b>  |
| <b>Metabolic stability</b>                          | Lower stability and high CYP-mediated turnover in human liver microsome (HLM) and human hepatocyte (HH)   | Very high stability and very low CYP-mediated turnover in HLM and HH:   | <b>Izicopan demonstrates high metabolic stability</b> , with very low intrinsic clearance and long half-lives in both HLM and HH, compared with avacopan, suggesting a substantially reduced risk of reactive metabolite formation.  |
| <b>GSH-trapping in vitro (reactive metabolites)</b> | Rapid and high-level of formation of multiple structurally diverse thiol conjugates, indicating extensive oxidative bioactivation via multiple pathways | Minimal formation of thiol conjugates, with levels remaining consistently low throughout the incubation, supporting a low oxidative bioactivation profile | Total reactive conjugate signal for <b>avacopan exceeding 100-fold higher than izicopan at early time points</b> (5 and 10 minutes), consistent with rapid initial bioactivation. This elevated reactive metabolite burden persisted over time, with <b>avacopan remaining more than 10-fold higher than izicopan at 20 and 40 min</b> |

# Izicopan shows ~2x the inhibitory effect in vivo compared to avacopan

## Inhibition of in vivo neutrophil activation by izicopan compared to avacopan-like molecule\*



Plasma concentration sampled at **8 hours**:

Izicopan = **538 ng/mL**

Avacopan-like molecule = **119 ng/mL**

APPROXIMATELY **2X** izicopan doubled the in vivo inhibitory effect at comparable dose when tested head-to-head with avacopan.

The **strongly improved PK features of izicopan** (plasma exposure) may drive the ability to increase efficacy in vivo.

**Experiment:** Challenge of rodents with C5a leads to neutrophil activation and consequent adherence (sticking) of neutrophils to the endothelial cell wall of vessels = mimicking a neutropenia (vehicle). This effect can be completely inhibited when C5aR activation is blocked.

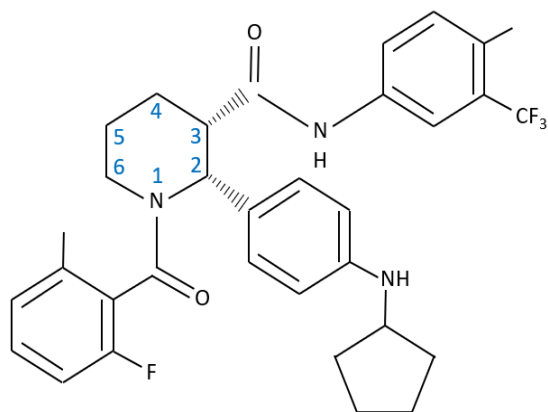
**Note:** Izicopan dosing within this experiment exerts an approximately 4.5-fold higher plasma level 8 h after dosing when compared to the identical dosing with avacopan\*.

Source: InflaRx data on file.

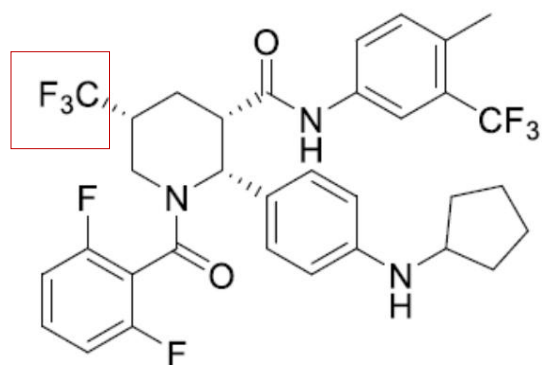
\*Avacopan synthesized based on the published structure and publicly available data.

# Izicopan design: Optimized avacopan backbone structure

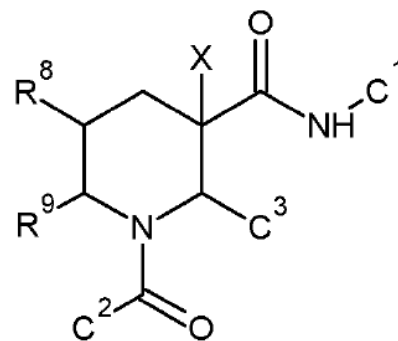
avacopan



izicopan



## Strong IP positions in INF904



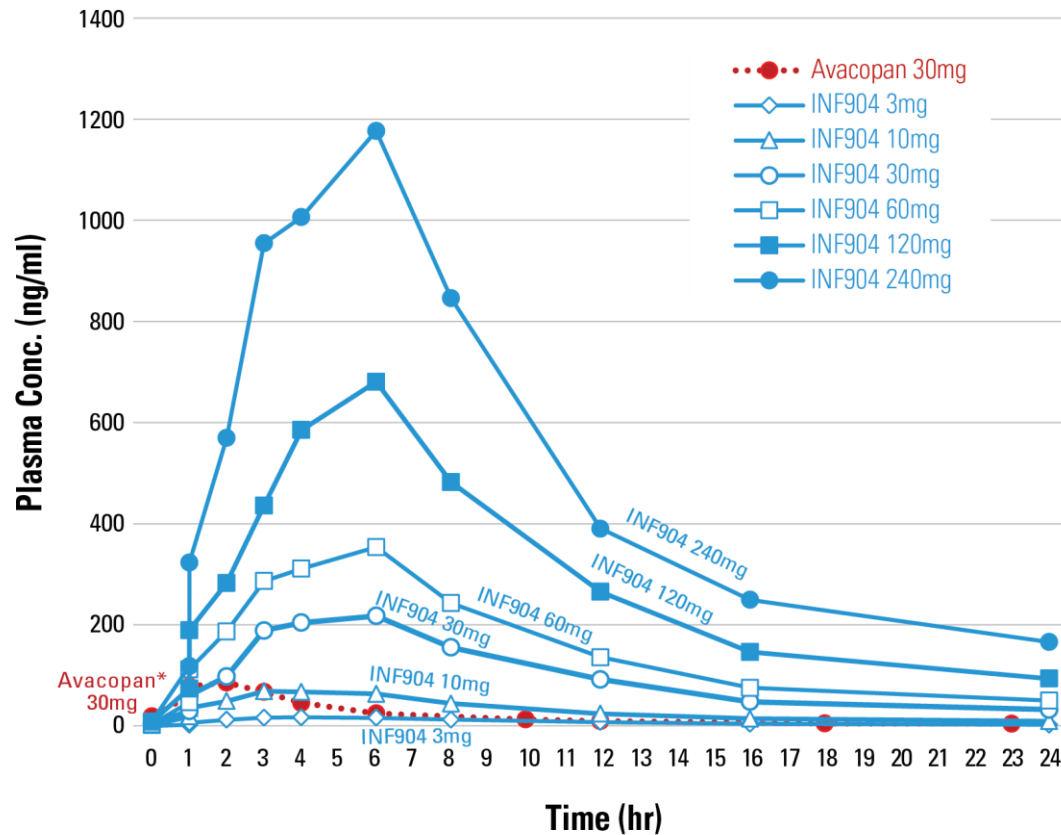
Markush Structure

Li et al. US patent No. 11,149,009 (2021.10)

Among ~100 compounds synthesized with modifications to avacopan core structure in positions C3, R8 and/or R9, izicopan was selected and showed desired blocking activities and PK profile in animals.

| Property | Avacopan | Izicopan |
|----------|----------|----------|
| MW       | 581.67   | 653.23   |
| cLogP    | 8.19     | 8.15     |

# PK results from single ascending dose (SAD) Phase 1



| Parameter    | Unit    | Dose  | INF904 | Avacopan* |
|--------------|---------|-------|--------|-----------|
| $AUC_{inf}$  | h.ng/ml | 3 mg  | 285    | 25        |
|              |         | 10 mg | 1264   | 130       |
|              |         | 30 mg | 5956   | 628       |
| $AUC_{last}$ | h.ng/ml | 3 mg  | 254    | 23        |
|              |         | 10 mg | 1117   | 122       |
|              |         | 30 mg | 5197   | 557       |
| $C_{max}$    | ng/ml   | 3 mg  | 21.5   | 9         |
|              |         | 10 mg | 74.8   | 25        |
|              |         | 30 mg | 289    | 79        |
| $t_{max}$    | hr      | 3 mg  | 3.5    | 1.2       |
|              |         | 10 mg | 4      | 1.7       |
|              |         | 30 mg | 5.01   | 1.7       |

In comparison to published data for avacopan, izedipron is approximately **3-fold higher in  $C_{max}$**  and **10-fold higher in systemic exposure ( $AUC_{last}$ )** for comparable doses (3, 10, 30 mg)

Source: Bekker et al. 2016, PLoS One; 11(10): e0164646

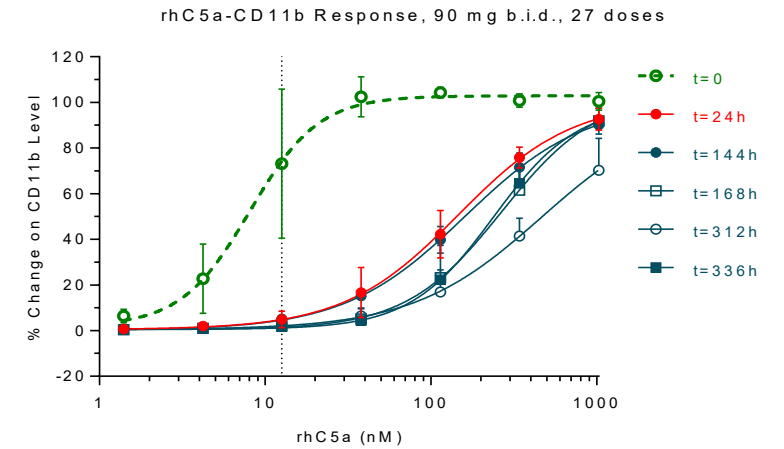
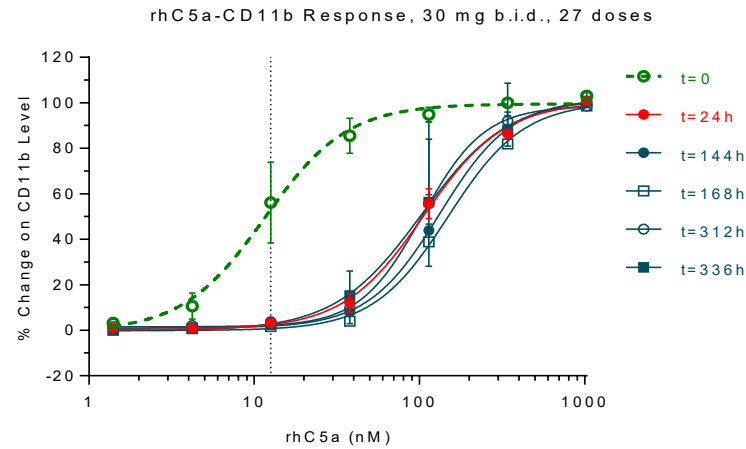
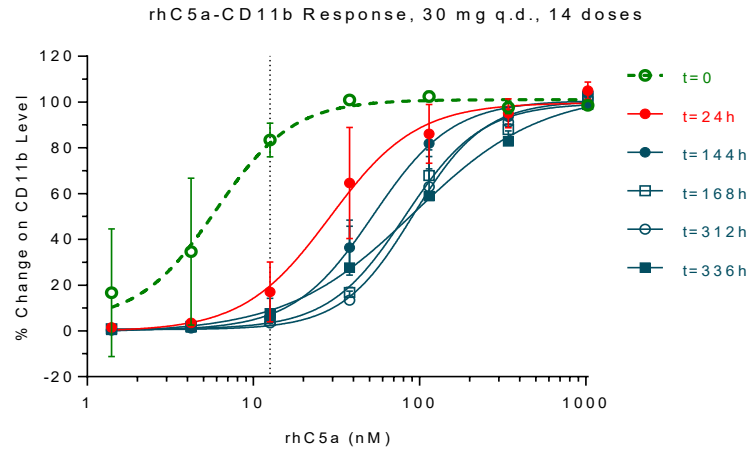
\*Please note: Avacopan data taken from Bekker et al. 2016, PLoS One; 11(10): e0164646 are superimposed in graph for orientation. Avacopan was not included as a comparator in INF904 Phase I study.

# C5a-mediated CD11b upregulation on neutrophils ex vivo

## IZICOPAN 30 MG QD

## IZICOPAN 30 MG BID

## IZICOPAN 90 MG BID



### Upon stimulation with 12.6 nM rhC5a (levels observed in disease state)

|                       | Upon stimulation with 12.6 nM rhC5a (levels observed in disease state) |       |       |               |       |       |               |       |       |                |       |       |                |       |       |
|-----------------------|--|-------|-------|---------------|-------|-------|---------------|-------|-------|----------------|-------|-------|----------------|-------|-------|
|                       | 24 h   |       |       | 144 h (Day 6) |       |       | 168 h (Day 7) |       |       | 312 h (Day 13) |       |       | 336 h (Day 14) |       |       |
|                       | 30QD   | 30BID | 90BID | 30QD          | 30BID | 90BID | 30QD          | 30BID | 90BID | 30QD           | 30BID | 90BID | 30QD           | 30BID | 90BID |
| Blockade (%)          | 80   | 94    | 90    | 93            | 95    | 94    | 95            | 97    | 97    | 96             | 92    | 97    | 90             | 95    | 97    |
| EC <sub>50</sub> (nM) | 35.6   | 106.2 | 145.6 | 52.4          | 134.7 | 160   | 74.2          | 149.0 | 268.2 | 92.4           | 126.3 | 465.7 | 94.6           | 110.9 | 238   |

### PD MAD results confirm strong 90%+ C5a inhibition at C5a levels found in human diseases

- This is **differentiated from reported avacopan results** which have shown approximately 50% inhibition at a lower challenge of 10nM C5a (7-day dosing – trough)\*\*

\*EC<sub>50</sub> (nM) is the half maximal effective C5a concentration \*\* Bekker et al. 2016, PLoSOne; 11(10): e0164646

# C5aR proof-of-concept in AAV, other renal diseases, and broader I&I

## nephrology

avacopan

- ANCA-associated vasculitis (AAV)
- Atypical hemolytic uremic syndrome (aHUS)
- Immunoglobulin A nephropathy (IgAN)
- Anti-C3 glomerulopathy (C3G)

## immuno-dermatology

izicopan

- Hidradenitis suppurativa
- Chronic spontaneous urticaria

respiratory

neurology

gynecology

### Clinical POC for C5aR inhibitor

**AAV:** Approved

**C3G:** Phase 2 (n=22)

**IgAN:** Phase 2a (n=7)

**aHUS:** Ex-vivo (n=5)

### Phase 2a completed

Option to develop with partner

**Strong preclinical POC demonstrated with C5aR inhibition**


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