Novartis Renal Portfolio Investor Event

Virtual, October 28, 2024

NOVARTIS | Reimagining Medicine

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Participants

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Development

Agenda

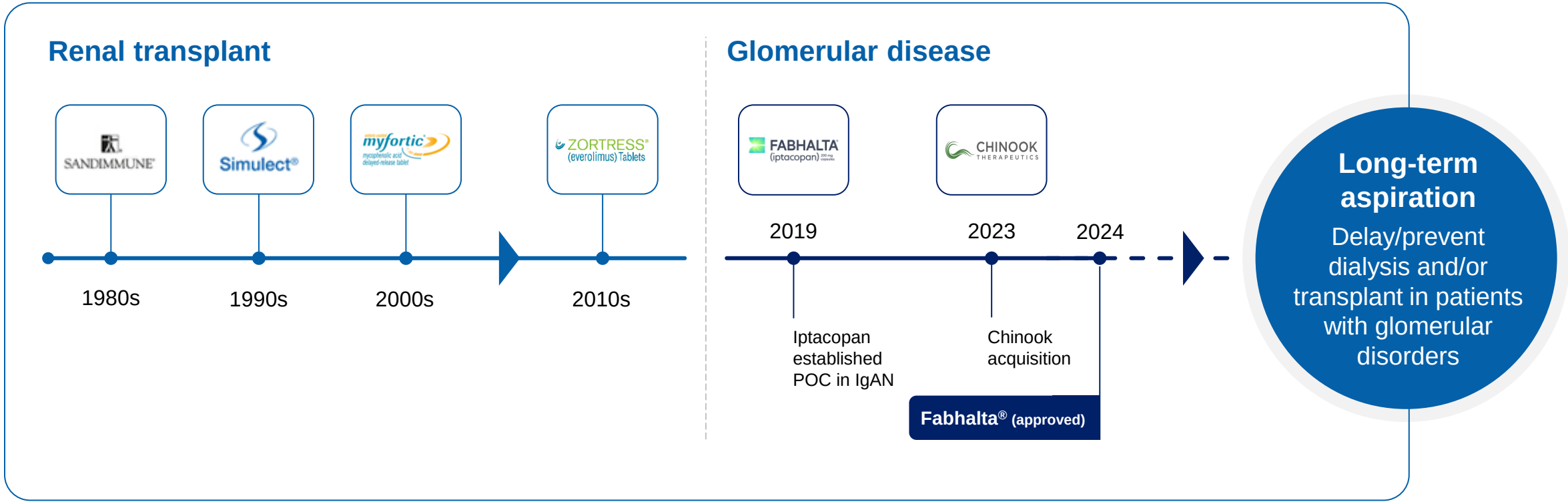
1 **Novartis aspiration in renal diseases**

2 Building launch capabilities to scale across the renal portfolio

3 Advancing a comprehensive renal pipeline

4 Q&A

Building on our legacy in renal transplant, we are on a mission to help transform the kidney disease landscape...



Iptacopan is the INN (international non-proprietary name) of Fabhalta for unapproved indications.

... by building a comprehensive renal pipeline

Select pipeline assets

Expected submission		
2024 - 2026	**2027 - 2030**	**2031+**
Fabhalta | IgAN	**Ianalumab** | LN	**Atrasentan** | FSGS
Atrasentan | IgAN	**Iptacopan** | IC-MPGN	**Iptacopan** | AAV
Iptacopan | C3G	**Iptacopan** | aHUS	**Iptacopan** | LN
	Zigakibart | IgAN	**OJR520** | Late CKD
		TIN816 | AKI
		UFJ776 | AKI
		YTB323 | srLN
		Other early targets | Alport FSGS ADPKD Late CKD
		Borealis collaboration | Several undisclosed early-stage targets

Iptacopan is the INN (international non-proprietary name) of Fabhalta for unapproved indications.

Our initial focus is on glomerular diseases that represent significant unmet need with risk of progression to kidney failure

IgAN	C3G	LN	IC-MPGN	aHUS	AAV	FSGS	Alport's
Up to 50% patients with persistent proteinuria progress to kidney failure within 10-20y of diagnosis	~50% patients progress to kidney failure within 10y High recurrence rate post kidney transplant	Remission achieved in only 30-50% of patients 10-20% of patients develop kidney failure within 10y	~50% patients progress to kidney failure within 10y High recurrence post kidney transplant	Untreated, ~50% of patients progress to kidney failure within 1y of diagnosis	Renal remission achieved in only 50% of patients with current therapies	~50% patients progress to kidney failure within 10y High recurrence post kidney transplant	Males often develop kidney failure and hearing loss before age 30 20% of females progress to kidney failure by age 60
~523k[1,6]	**~22k**[2,6]	**~455k**[3,6]	**19k**[4,6]	**18k**[4,6]	**~102k**[4,6]	**~494k**[1,6]	**~820k**[5,6]
Fabhalta (Approved)[7]	**Iptacopan** (Filings on track)	**Iptacopan** (Ph2 ongoing)	**Iptacopan** (Ph3 ongoing)	**Iptacopan** (Ph3 ongoing)	**Iptacopan** (Ph2 ongoing)	**Atrasentan** (Ph2 ongoing)	**3 pipeline projects**
Atrasentan (Submitted)		**Ianalumab** (Ph3 ongoing)					
Zigakibart (Ph3 ongoing)		**YTB323** (Ph1/2 ongoing)					

For references see page 44 in Appendix. Iptacopan is the INN (international non-proprietary name) of Fabhalta for unapproved indications.

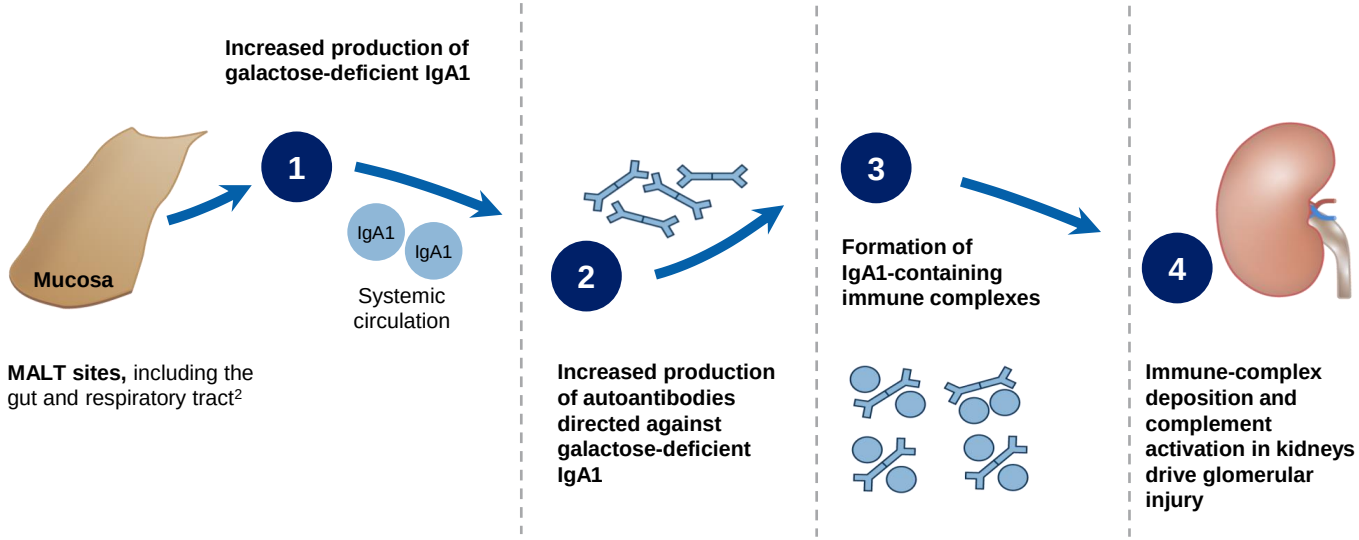
IgAN is a heterogeneous disease presenting with a variety of clinical manifestations, phenotypes, and speeds of progression

Disease background and unmet need

Prevalence

US	185k[1]
Global[2]	523k[1]
Clinical manifestations	Varies from asymptomatic microscopic hematuria to more severe sustained proteinuria, hypertension, and rapid deterioration of kidney function[4-6]
Diagnosis	Kidney biopsy is the gold standard
Current management	Focused on optimized supportive care to slow disease progression
Disease progression	Up to 50% of patients with persistent proteinuria progress to kidney failure within 10-20 years of diagnosis[7-13]

Disease pathophysiology[3]

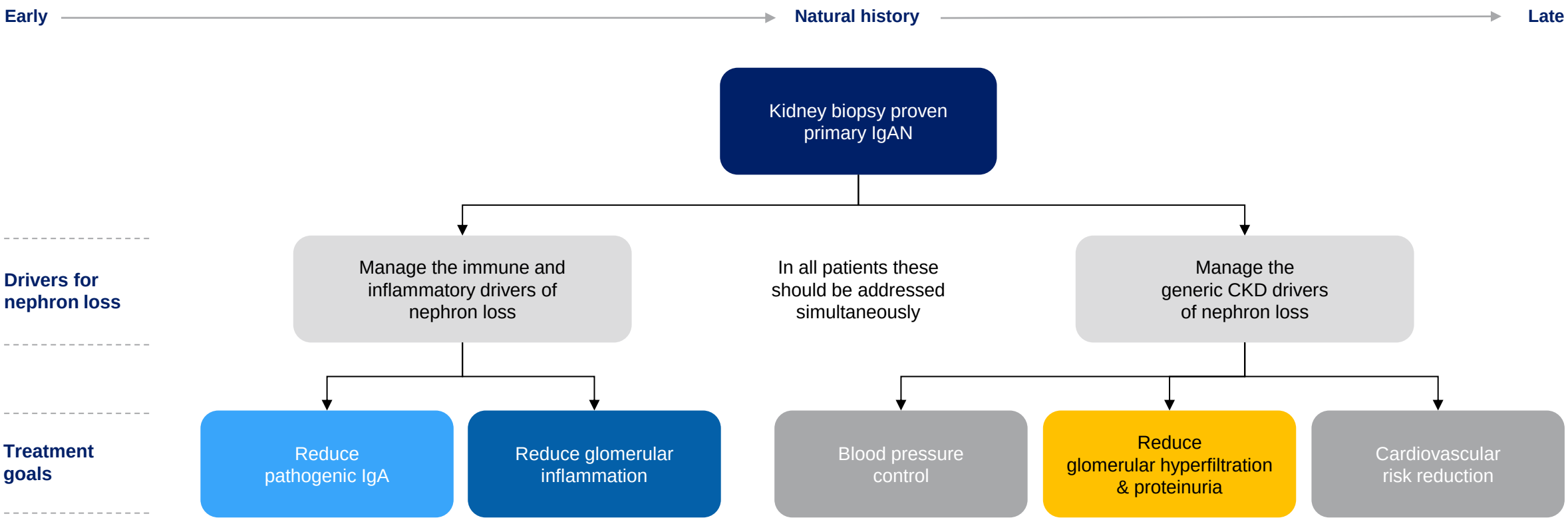


For references 3-13 see page 42 in Appendix. 1. Diagnosed lifetime prevalent cases of IgAN, DRG estimates 2023. 2. Includes prevalence estimates of 7 largest mature pharmaceutical markets (USA, France, Germany, Italy, Spain, UK, and Japan).

Treatment goals in IgAN reflect this heterogeneity

IgAN

Disease progression



Adapted from *When to treat autoimmunity and when to treat CKD in IgAN,* Barrat J, ERA Congress, May 2024.

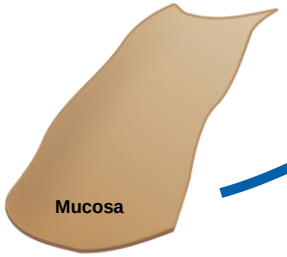
Our broad portfolio allows us to target distinct steps in IgAN pathophysiology and potentially address multiple treatment goals

IgAN

Zigakibart

APRIL leads to increased production of pathogenic Gd-IgA1[4]

Reduces pathogenic IgA

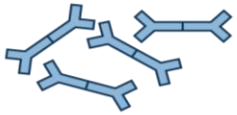


MALT sites, including the gut and respiratory tract[2]

1

Increased production of galactose-deficient IgA1

Systemic circulation

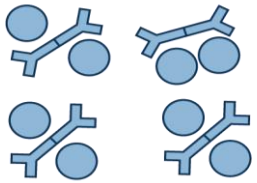


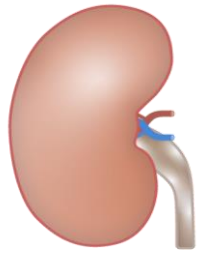
2

Increased production of autoantibodies directed against galactose-deficient IgA1

3

Formation of IgA1-containing immune complexes





4

Immune-complex deposition and complement activation in kidneys drive glomerular injury

Atrasentan

Reduces glomerular hyperfiltration & proteinuria

ET_A receptor activation drives mesangial cell activation, kidney inflammation & fibrosis, and proteinuria[5,6]

Fabhalta

May result in glomerular injury and tubulointerstitial scarring[1,3]

Reduces glomerular inflammation

For references see page 42 in Appendix.

Fabhalta approved as a first-in-class, oral factor B inhibitor that inhibits the effect of the alternative pathway

IgAN

Accelerated approval received from the FDA

Granted based on positive UPCR data from the interim analysis at 9 months of APPLAUSE Ph3

Study continues to evaluate whether Fabhalta slows disease progression as measured by eGFR decline over 24 months

Study completion data expected in 2025

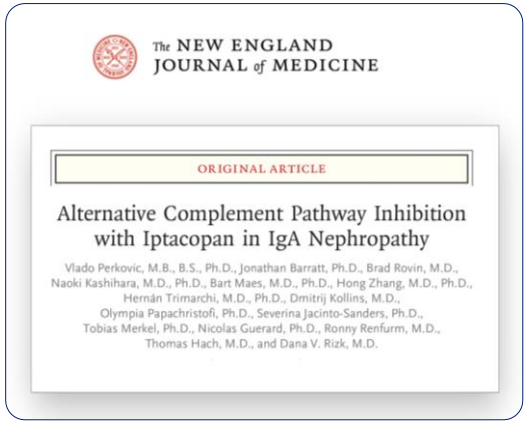
New data at ASN

Biomarker data showing inhibition of systemic and intrarenal activation of AP in IgAN patients at month 9[1]

Ph3 APPLAUSE-IgAN data from subcohort with baseline eGFR 20 to <30 mL/min showing 34.5% proteinuria reduction (at month 9) with a favorable safety profile[2]

ASN
American Society of Nephrology

NEJM publication[3]


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Alternative Complement Pathway Inhibition with Iptacopan in IgA Nephropathy

Vlado Perkovic, M.B., B.S., Ph.D., Jonathan Barratt, Ph.D., Brad Rovin, M.D., Naoki Kashihara, M.D., Ph.D., Bart Maes, M.D., Ph.D., Hong Zhang, M.D., Ph.D., Hernán Trimarchi, M.D., Ph.D., Dmitrij Kollins, M.D., Olympia Papachristofi, Ph.D., Severina Jacinto-Sanders, Ph.D., Tobias Merkel, Ph.D., Nicolas Guerard, Ph.D., Ronny Renfurm, M.D., Thomas Hach, M.D., and Dana V. Rizk, M.D.

Fabhalta launch in IgAN will serve as a blueprint for future renal launches, and give us insights for future development programs

For references see page 42 in Appendix. Iptacopan is the INN (international non-proprietary name) of Fabhalta for unapproved indications.

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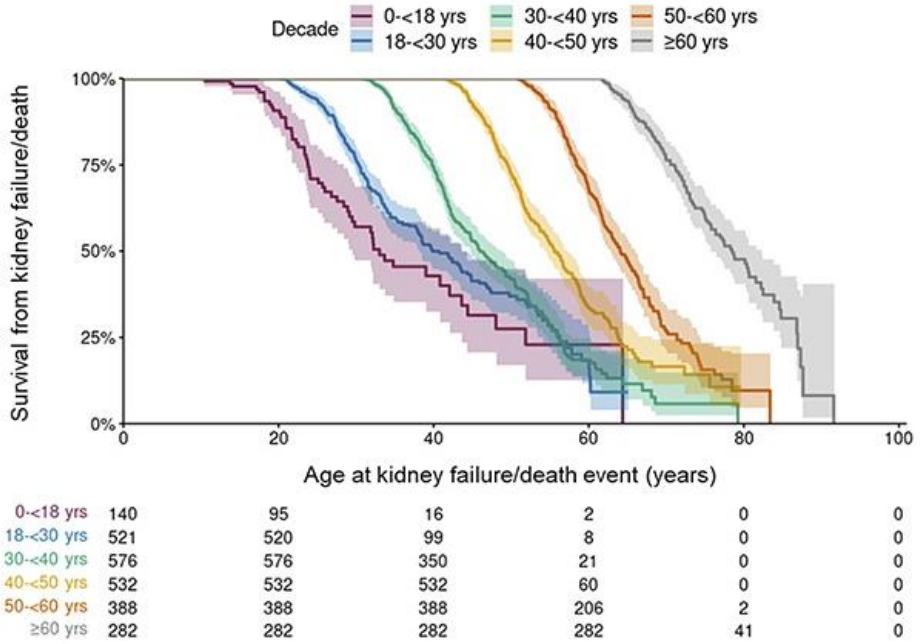
As the most common glomerular disease, IgAN is the ideal entry point for our renal portfolio

IgAN key dimensions in US

- **Incidence: 7-21 per million,** with 3:1 ratio of men:women in Caucasians and 1:1 in Asians
- Affects **younger adults** (20-30 years) more than older adults (>65 years of age)[1]
- 2024 draft KDIGO clinical practice guideline for the management of IgAN has added a new **preferred threshold for proteinuria of 0.3g/d,** while maintaining the recommended threshold of 0.5g/d

Up to 50% of patients with persistent proteinuria progress to kidney failure within 10 to 20 years of diagnosis[1-7]

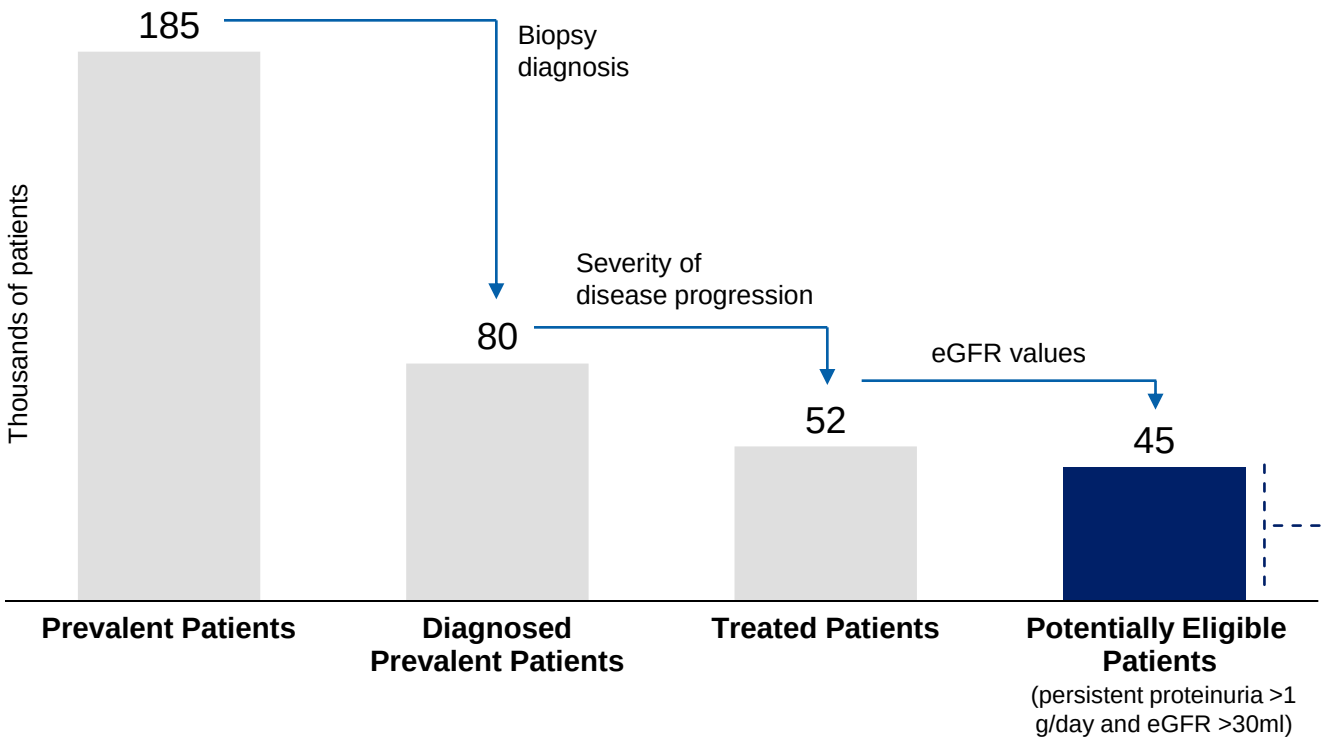
Time to kidney failure/death event from RADAR, a UK retrospective cohort[3]



For references see page 43 in Appendix.

There are ~45k US IgAN patients potentially eligible for Novartis medicines

IgAN patient opportunity (2024)[1]



Current treatment landscape[2]

- ~80% of patients treated with supportive care (mix of RASi, SGLT2i, periodic steroid use);
- IgAN is a combination therapy market: ~60% of patients treated with >1 therapy
- Combination therapy expected to grow as new therapies are approved
- ~40% of patients use steroids on annual basis
- <15% utilization of newer IgAN therapies

Candidates for Novartis medicines[3]

- **Atrasentan**: 100% of eligible patients
- **Fabhalta**: 15-30% of eligible patients with persistent proteinuria and glomerular inflammation phenotype

1. Data for year 2024. Sources include CDA, Clarivate, Opti-Brand PMR, Adelphi, Novartis. Epidemiology numbers include patients without access 2. Sources include earnings calls, Komodo claims (Open claims; Coverage 60%-70%; Timeframe: Oct'2015 – Jun'2024), secondary and primary research reports; Veeva claims (open claims; coverage 70-80%; timeframe: Jan 2017 – Dec 2023). 3. Novartis internal estimates based on proprietary market research. Treated includes ACEi, ARBs, SGLT2i, corticosteroids, non-steroidal immunosuppressants, anti-CD20s, anti-c5s, anti-platelet agents, diuretics, statins, NSAIDs, alternative medicine.

Nephrologists want multiple treatment options for IgAN patients, which supports co-positioning

Atrasentan

Patients with proteinuria despite RASI +/- SGLT2i

- Potential to address a **broad population** of patients who have **persistent proteinuria**
- **"Foundational" ETA therapy** added to supportive care for IgAN patients with persistent proteinuria
- **Seamless addition** to supportive care doesn't require discontinuation or adjustment of background therapy

Potential candidates for atrasentan **100%** **of IgAN eligible patients**

~45k patients in the US

Fabhalta

Patients with persistent proteinuria and glomerular inflammation

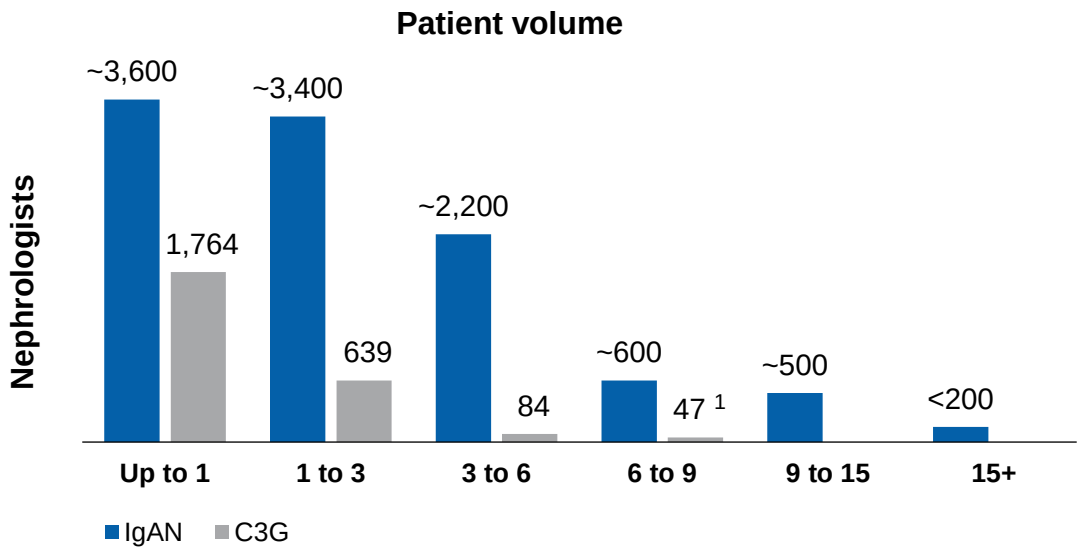
- A different approach to managing patients with **persistent proteinuria and glomerular inflammation**
- **Unique in addressing complement activation,** which is thought to contribute to the pathogenesis of IgAN
- The **first and only treatment to target the alternative complement pathway** in IgAN

Potential candidates for Fabhalta **15-30%** **of IgAN eligible patients**

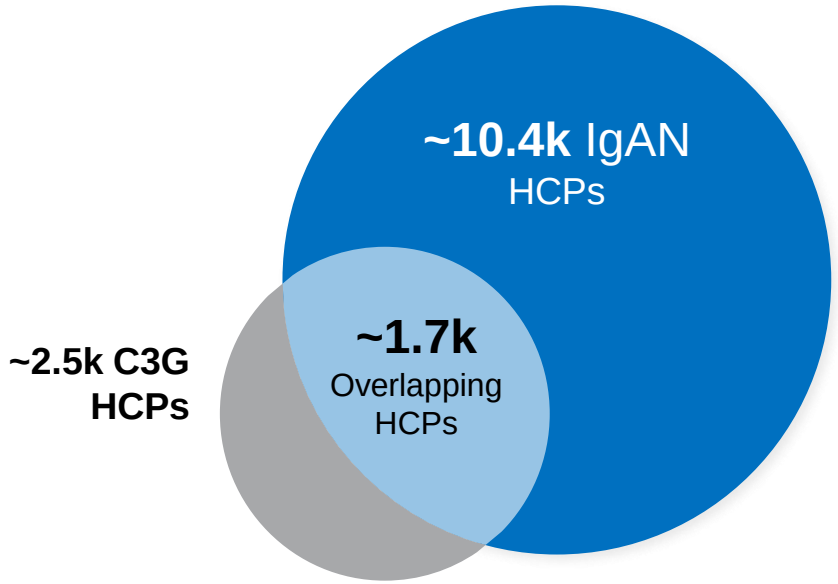
~7-14k patients in the US

Having a renal portfolio makes each future launch more effective and efficient

2/3 of Nephrologists manage <3 IgAN and ~1 C3G patient



2/3 of Nephrologists treating C3G overlap with IgAN HCPs

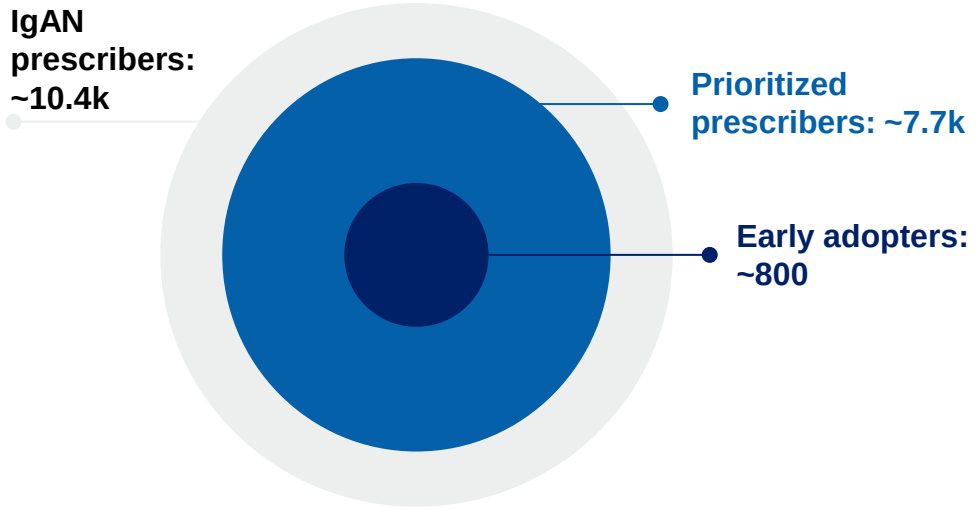


We deployed a robust Renal footprint early with IgAN to build a solid foundation for the portfolio, with an integrated customer facing team (+100 FTEs), and strong Medical and Patient Support presence on the field

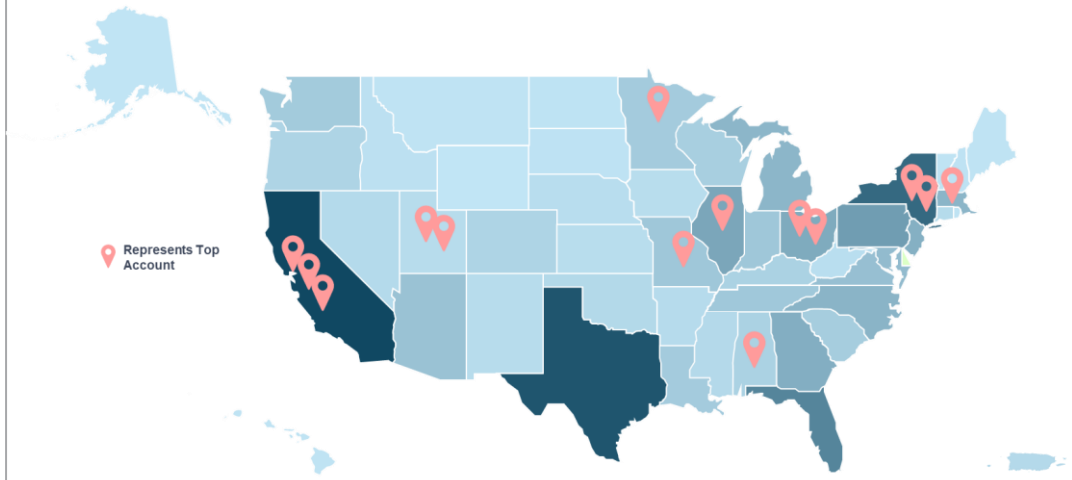
1. Covers 6+. No additional segmentation due to small #Nephrologists.

Our current renal footprint covers >70% of all IgAN HCPs with an initial focus on ~800 early adopters and 14 top accounts

US IgAN prescriber population[1]



Localization of top 14 accounts across the country[1]



Early insights from Fabhalta launch in IgAN

- Strong engagement with 100% of top accounts
- +90% of top accounts with at least 1 REMS certified HCPs
- Majority of new patients coming from top accounts

1. Novartis internal market research and claims analysis.

We have deployed advanced analytics to reach HCPs and patients more effectively...

Optimizing our patient reach

Leverage novel AI machine learning models

To predict IgAN cases and link to nephrologists/accounts

Validate the results

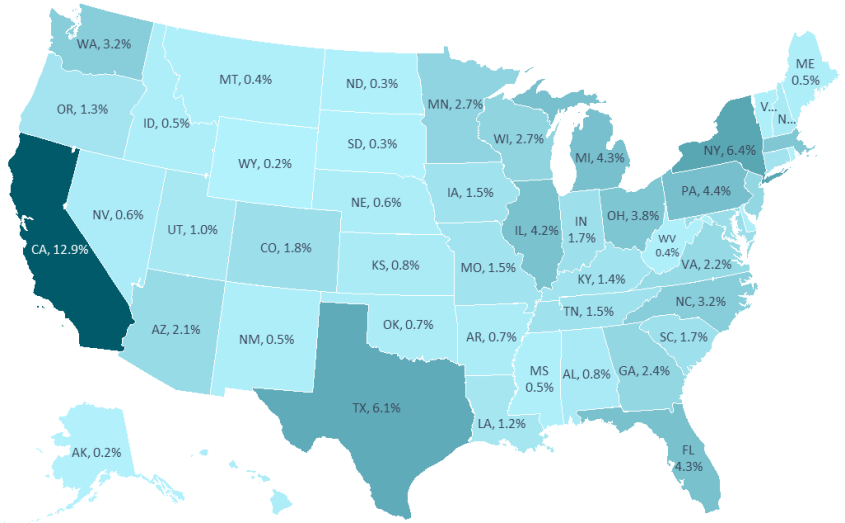
Field team validates point of care, increasing efficiency and impact

Confirm high accuracy

Predictions validated with 84% accuracy

Significantly larger proportion of IgAN cases identified through AI/ML model vs. using ICD codes

Geographical distribution of IgAN cases



CA + NY + TX account for **25% of predicted IgAN cases**, while **top 10 states** cover **+50%**

... and implemented DTC capabilities to more effectively reach the right IgAN patient, at the right moment, through the right channel

1. Reaching relevant audiences	Aggregated datasets to reduce audience and refine composition for more effective reach
2. Engaging at high relevancy moments	Engage via content placed in office waiting room sign-in applications, and intersected experiences between rep-delivered and digital content
3. Connecting through multiple channels	Media mix model and ML algorithms for social media to reach more relevant audiences and optimize engagement level

Novartis proprietary data + **Customized solutions**

88% reduction in audience size, enhancing content relevancy to patients with IgAN, resulting in more effective conversations with their HCP

We established a strong Market Access foundation in PNH that enables patient access and coverage across future indications

Payers increasingly suppress coverage to new specialty drugs; mitigation requires scale and a flexible distribution model

Maximizing coverage across indications

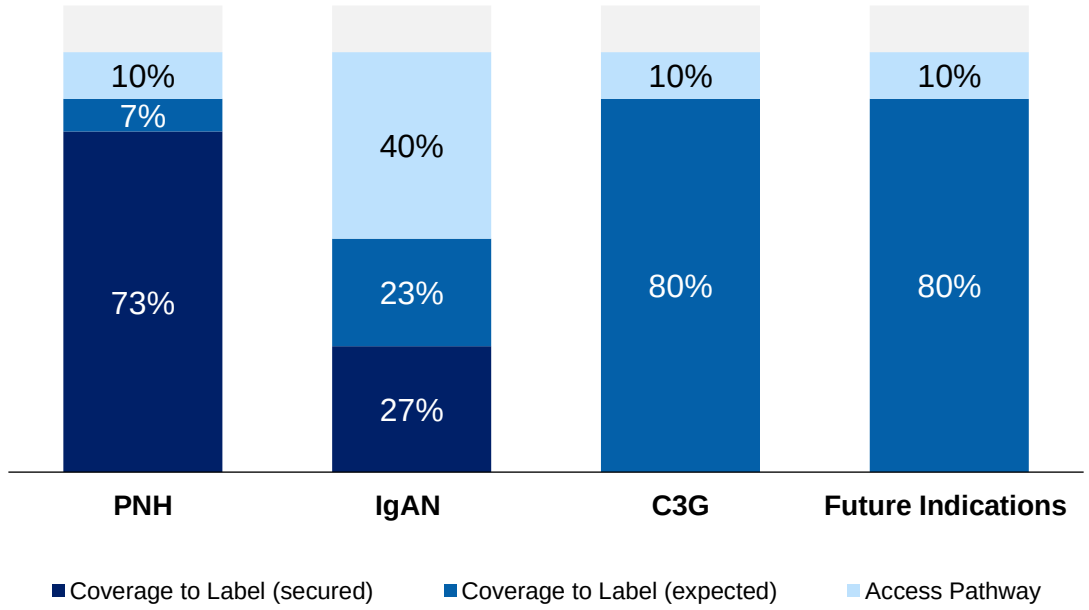
- PNH coverage success established strong foundation, with >70% coverage-to-label within 8 months
- Pathway to coverage for ~90% of Fabhalta patients
- Coverage-to-label strategy enabled speed and quality of coverage for Fabhalta IgAN and will support future indications

Distribution network with vendors who have proven capabilities in rare diseases

- Ability to manage REMS reporting
- Effectiveness and ease of onboarding patients
- Assistance to patients and HCPs around navigating coverage and educational support

Fabhalta commercial coverage (Oct'24)[1,2]

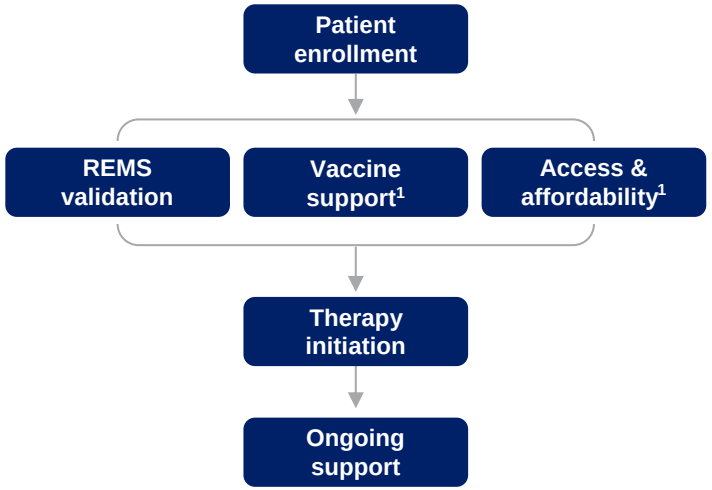
Estimated % lives covered; >60 days post IgAN launch



1. Novartis internal data for PNH and IgAN. 2. Fabhalta (iptacopan) not approved for C3G and other future indications. Estimates of % lives covered for these indications represent expectations based on internal analysis and market research.

We are leveraging insights from the PNH launch to provide best-in-class patient and physician support program

Patient support minimizes friction so patients and HCPs can focus elsewhere



A best-in-class program designed to scale across indications

- Industry-leading **bridge support** offering to help accelerate onboarding
- Covers **REMS/Vaccine support**
- **Dedicated patient navigators** guide patients throughout their journey
- **Omnichannel** engagement
- **SP distribution network** designed to better serve patient needs

Delivering results for IgAN patients today

- **$0 Commercial Copay Offer[2]**
- **12-month bridge support[2]**
- **~15 days Time to Dispense[3]**
- **80% priority accounts with Patient Support engagement[3]**

By running this program fully internally (dedicated resources, with Novartis-owned tech stack and 1st party data) we are continuously bringing learnings and have flexibility to allocate resources to scale quickly

1. For eligible patients. 2. Limitations apply. See full terms and conditions. 3. Novartis Patient Support Fabhalta Launch Performance Reports through October 15, 2024.

We are compounding capabilities to support all future renal launches

Portfolio synergies

1. **Co-positioning** of multiple MoAs to address heterogenous disease
2. **Go-to-market synergies** across a broad renal portfolio, making launches more effective
3. **Long company legacy** in rare/ultra-rare spaces, with proven successes across TAs

Capabilities across patient journey

4. **Effective DTC** to reach the right patient, at the right moment, through the right channel
5. **Payer strategy** enabling affordable patient access for products with multiple indications
6. **Robust patient support program** ready to be scaled across indications/products

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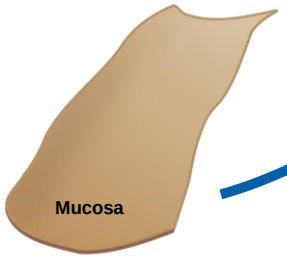
In addition to Fabhalta, atrasentan and zigakibart target distinct components of IgAN pathophysiology

IgAN

APRIL leads to increased production of pathogenic Gd-IgA1[4]

Zigakibart

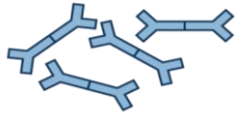


MALT sites, including the gut and respiratory tract[2]

1

Increased production of galactose-deficient IgA1

Systemic circulation

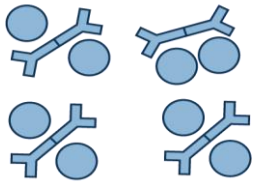


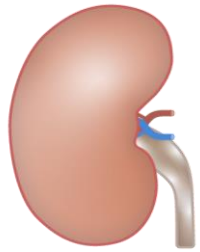
2

Increased production of autoantibodies directed against galactose-deficient IgA1

3

Formation of IgA1-containing immune complexes





4

Immune-complex deposition and complement activation in kidneys drive glomerular injury

Atrasentan

ET_A receptor activation drives mesangial cell activation, kidney inflammation & fibrosis, and proteinuria[5,6]

May result in glomerular injury and tubulointerstitial scarring[1,3]

Fabhalta

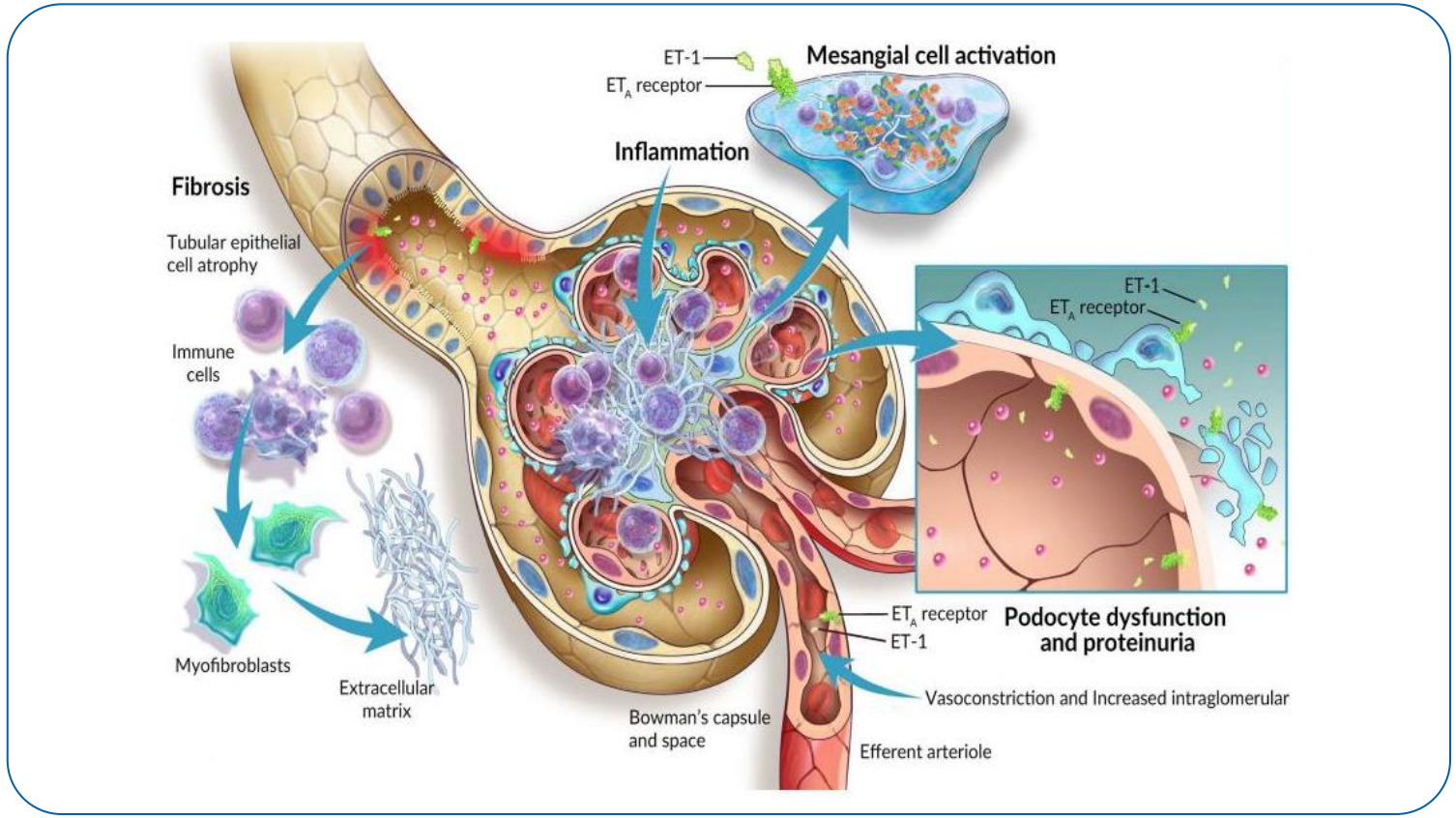
For references see page 43 in Appendix.

Atrasentan: Selective and potent endothelin A receptor antagonist with the potential to be a foundational therapy in IgAN

IgAN

Atrasentan MoA
Oral small molecule

- ET-1 & ET_A receptors are typically elevated in IgAN patients[1-4]
- By preventing the binding of ET_1, atrasentan reduces mesangial cell activation, kidney fibrosis and inflammation, glomerular pressure, and proteinuria[5]
- Permits independent RASi optimization and can therefore be seamlessly added to supportive care
- Well-characterized safety profile (SONAR dataset of >5k patients with diabetic kidney disease)[6,7]

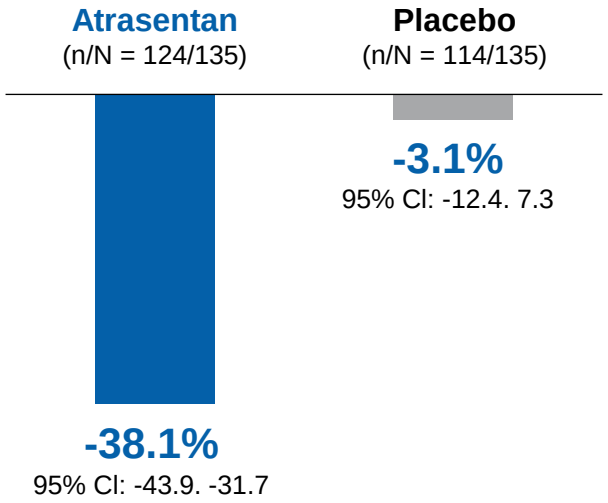


For references see page 43 in Appendix.

Atrasentan: Ph3 ALIGN data forms the basis for our regulatory submissions

IgAN

Proteinuria reduction in IgAN patients at week 36[1]

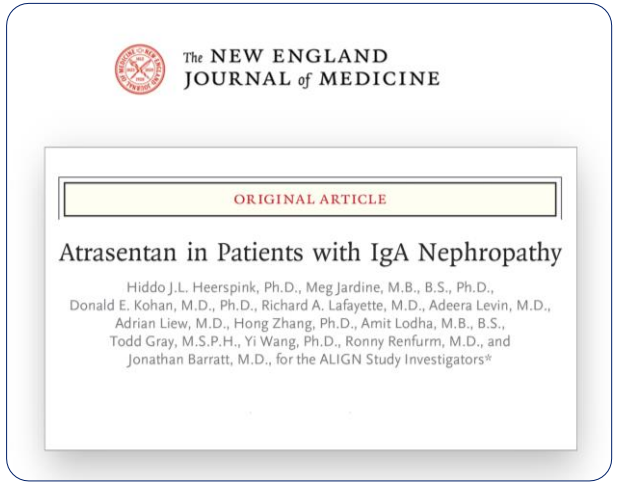


Exploratory subgroup analysis data at ASN

- Statistically significant and clinically meaningful proteinuria reduction relative to placebo of 36.1% at 36 weeks[1]
- Reductions observed in all subgroups, regardless of baseline demographic or disease characteristics[2]
- Exploratory SGLT2i subgroup consistent with overall population, with a proteinuria reduction of 37%[2]

ASN American Society of Nephrology

NEJM publication[3]



Submitted to FDA in H1 2024; study continues in blinded fashion to final analysis in 2026

For references see page 44 in Appendix

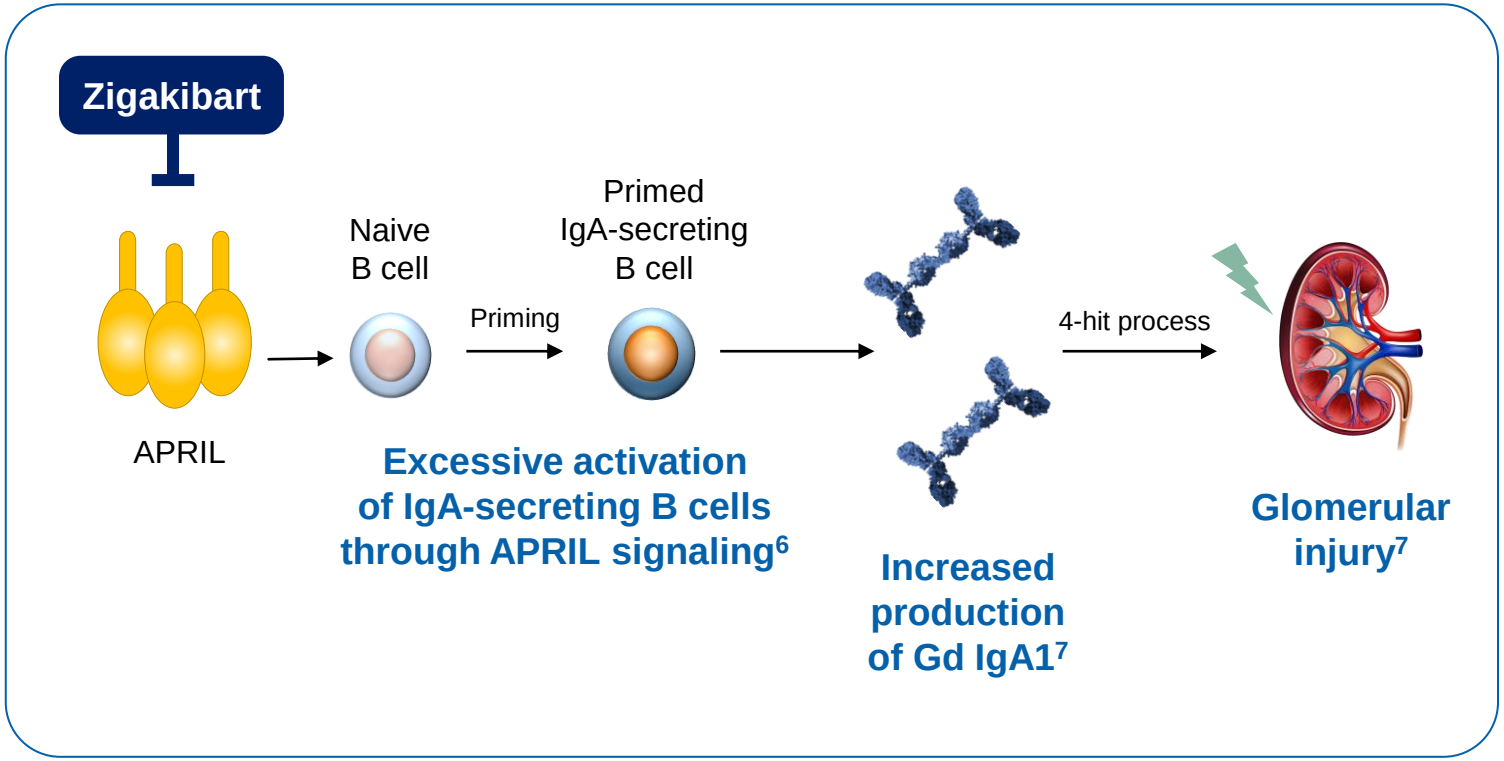
Zigakibart: Potentially disease-modifying treatment by binding and blocking APRIL (a proliferation-inducing ligand)

IgAN

Zigakibart MoA

Novel humanized monoclonal antibody administered subcutaneously

- Patients with IgAN have higher circulating levels of APRIL than healthy individuals[1]
- APRIL is a TNF superfamily cytokine that drives IgA class switching and survival of IgA-secreting plasma cells in IgAN, leading to elevated Gd-IgA1 and immune complex deposition in the mesangium[1-3]
- Blocking APRIL decreases gd-IgA1 and prevents formation of pathogenic immune complexes[3]
- Well-tolerated safety profile in Ph1/2 study[4, 5]

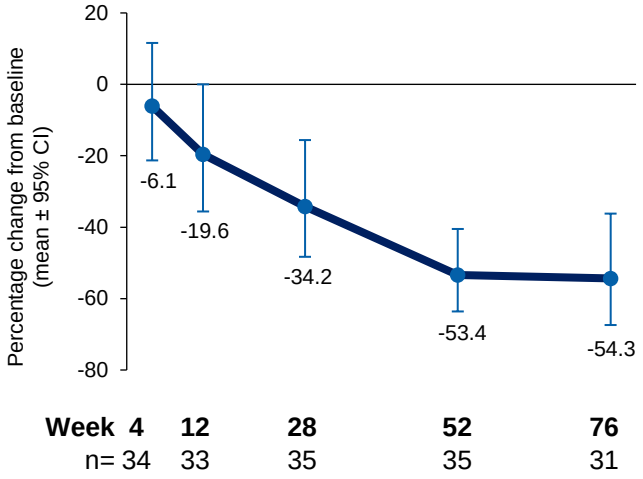


For references see page 44 in Appendix.

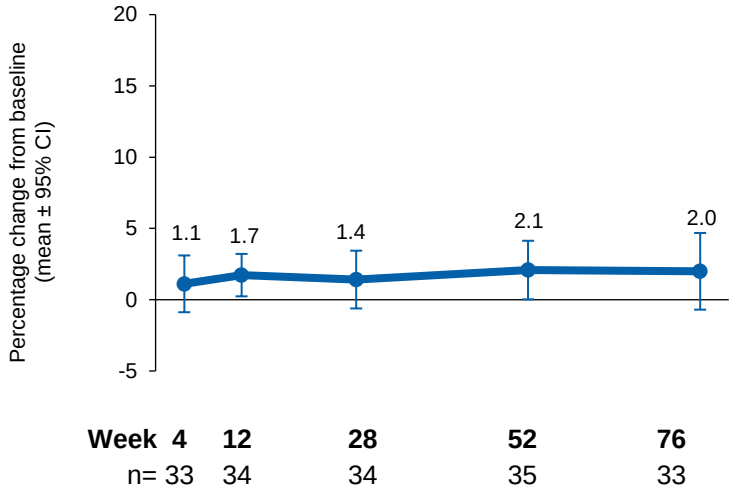
Zigakibart: Ph2 updates showed clinically meaningful persistent eGFR stabilization and sustained reduction in UPCR at week 76

IgAN

Clinically meaningful reduction in proteinuria[1]



eGFR stabilization over 76 weeks[1]



- Rapid and sustained reduction in proteinuria
- Clinically meaningful eGFR stabilization through 76 weeks
- Continues to be well-tolerated with no AEs leading to study drug discontinuation or deaths

1. Barratt J, et al. J Am Soc Nephrol. 2024;35:718 [Abstract FR-PO856].

Zigakibart: Ongoing Ph3 BEYOND study currently recruiting, with readout expected in 2026

IgAN

Key patient characteristics

- Adult patients with biopsy-confirmed IgAN (within 10 yrs)
- Proteinuria ≥1g/day AND ≥ 0.7g/g
- Stable, on an optimized dose of RASi or RAS intolerant (stable SGLT2i and/or ERA/MRA allowed)

Objectives

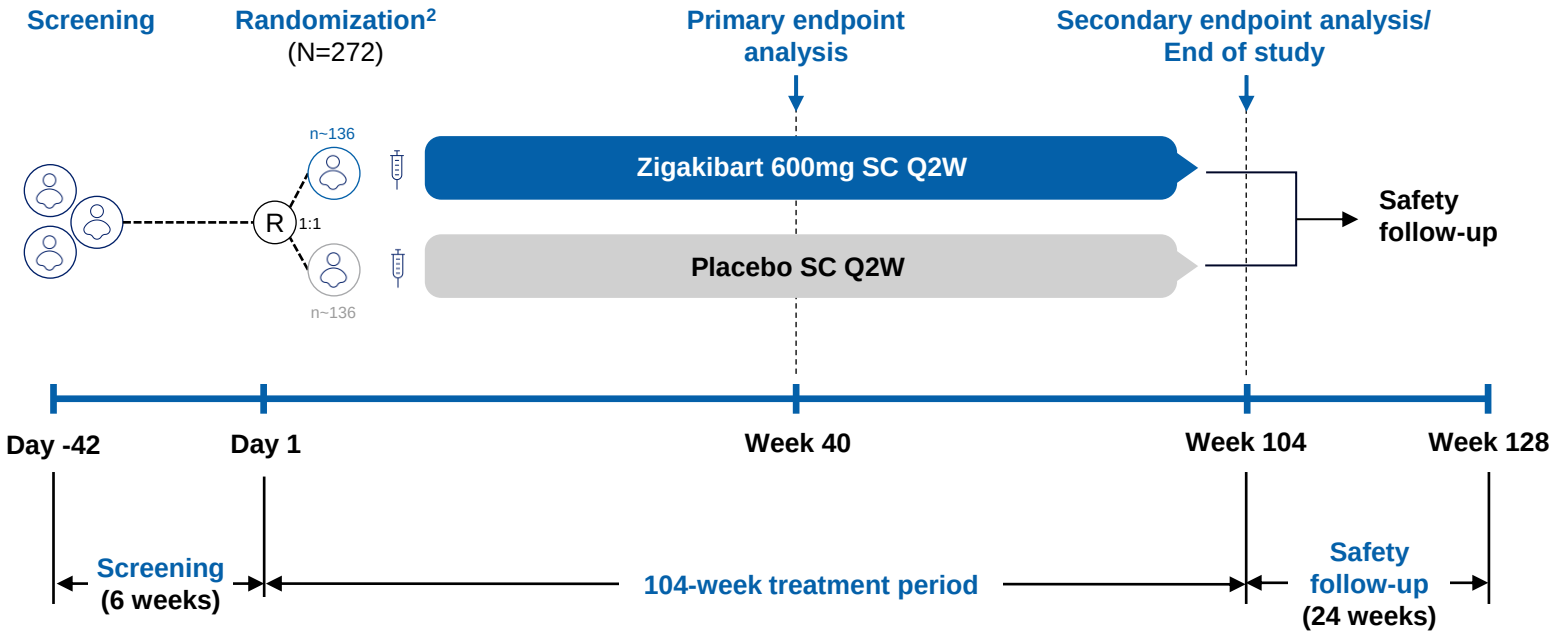
Primary

Evaluate the change in proteinuria (UPCR) from baseline to week 40

Secondary

Evaluate the change in eGFR from baseline to week 104

Study design[1]



1. https://clinicaltrials.gov/study/NCT05852938. 2. Up to 20 additional patients with eGFR ≥20 to <30mL/min/1.73m2 will be enrolled in an exploratory cohort (not included in the primary analysis) for a total N=292.

Beyond IgAN, we are pursuing a range of glomerular diseases

Focus today

IgAN	C3G	LN	IC-MPGN	aHUS	AAV	FSGS	Alport's
Up to 50% patients with persistent proteinuria progress to kidney failure within 10-20y of diagnosis	~50% patients progress to kidney failure within 10y High recurrence rate post kidney transplant	Remission achieved in only 30-50% of patients 10-20% of patients develop kidney failure within 10y	~50% patients progress to kidney failure within 10y High recurrence post kidney transplant	Untreated, ~50% of patients progress to kidney failure within 1y of diagnosis	Renal remission achieved in only 50% of patients with current therapies	~50% patients progress to kidney failure within 10y High recurrence post kidney transplant	Males often develop kidney failure and hearing loss before age 30 20% of females develop kidney failure by age 60
~523k[1,6]	**~22k**[2,6]	**~455k**[3,6]	**19k**[4,6]	**18k**[4,6]	**~102k**[4,6]	**~494k**[1,6]	**~820k**[5,6]
Fabhalta (Approved)[7]	**Iptacopan** (Filings on track)	**Iptacopan** (Ph2 ongoing)	**Iptacopan** (Ph3 ongoing)	**Iptacopan** (Ph3 ongoing)	**Iptacopan** (Ph2 ongoing)	**Atrasentan** (Ph2 ongoing)	**3 pipeline projects**
Atrasentan (Submitted)		**Ianalumab** (Ph3 ongoing)					
Zigakibart (Ph3 ongoing)		**YTB323** (Ph1/2 ongoing)					

For references see page 44 in Appendix. Iptacopan is the INN (international non-proprietary name) of Fabhalta for unapproved indications.

C3G is an ultra-rare, severe form of primary glomerulonephritis commonly diagnosed in adolescents/young adults

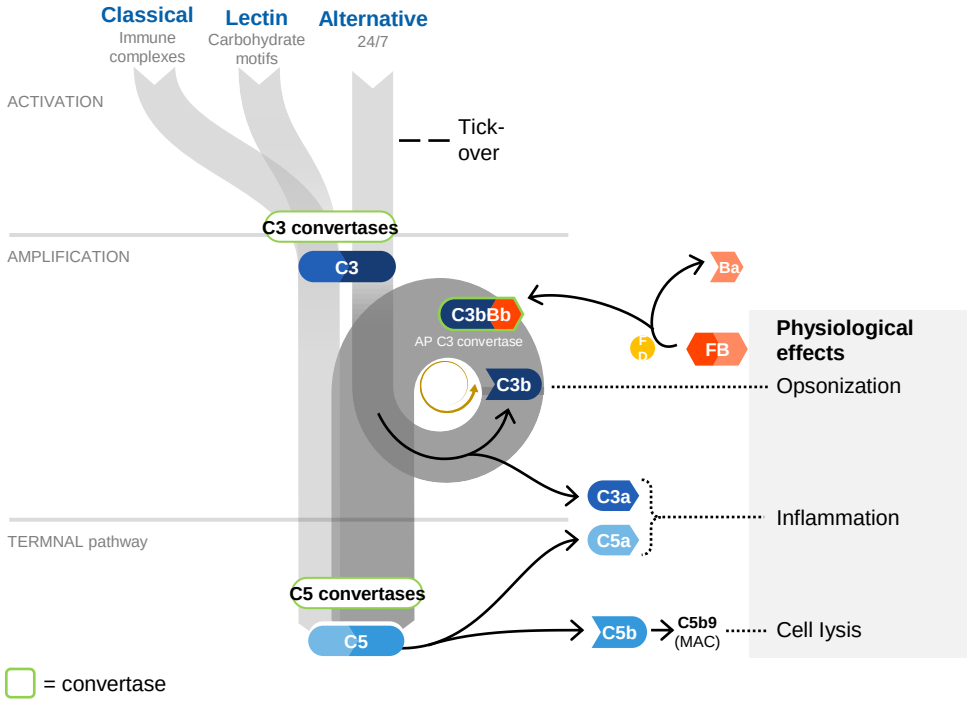
C3G

Disease background and unmet need

Prevalence

US	10k[1]
Global[2]	22k[1]
Clinical manifestations	Wide spectrum including fatigue, edema, HTN, proteinuria, hematuria, reduced GFR, low serum C3 levels, and elevated creatinine levels[3,4]
Diagnosis	Requires kidney biopsy and Immuno-fluorescence microscopy[3]
Current management	No approved treatments targeting disease pathogenesis[5]
Disease progression	~50% of patients develop kidney failure requiring dialysis or transplant within 10 years of diagnosis[3,5]

Disease pathophysiology[4]

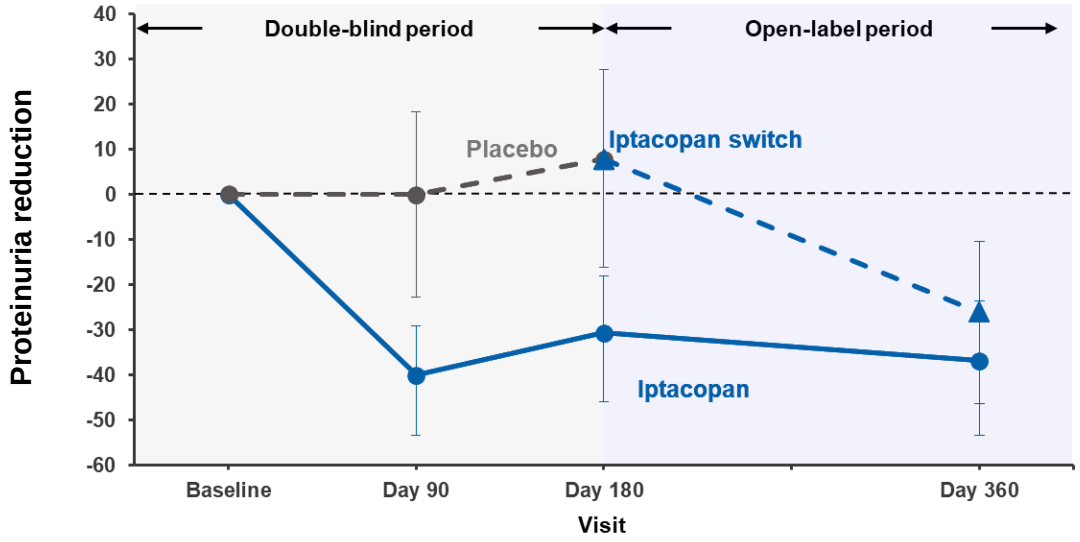


For references 3-5 see page 45 in Appendix. 1. Biopsy diagnosed prevalent patients based on Novartis internal estimates, 2024. 2. Includes prevalence estimates of 7 largest mature pharmaceutical markets (United States, France, Germany, Italy, Spain, United Kingdom, and Japan).

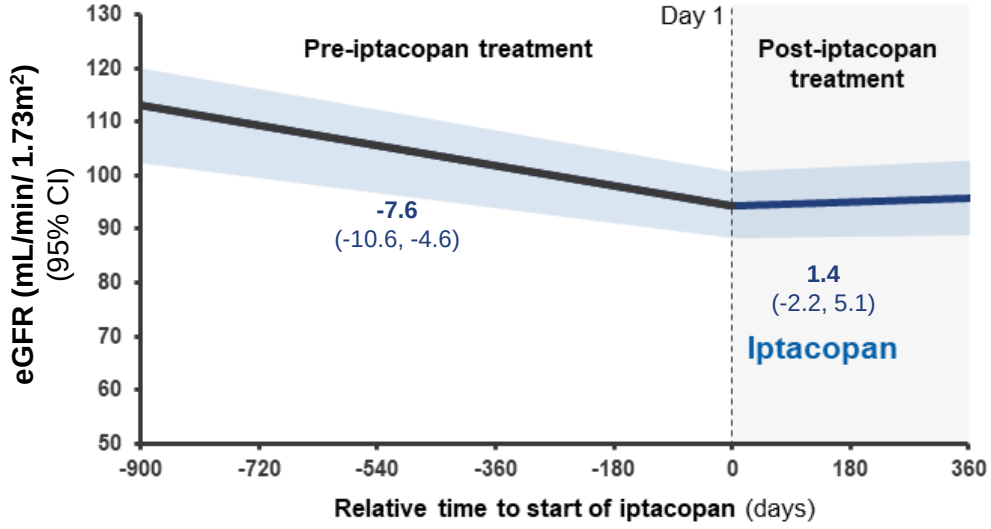
Iptacopan: 12-month APPEAR-C3G data presented at ASN[1] support global regulatory filings by year-end 2024

ASN American Society of Nephrology | C3G

Change in UPCR[2] - reduction sustained over 12 months and replicated in placebo arm after switch to iptacopan



Stabilization of eGFR[3,4] - change in eGFR slope vs. historic slope decline maintained over 12 months

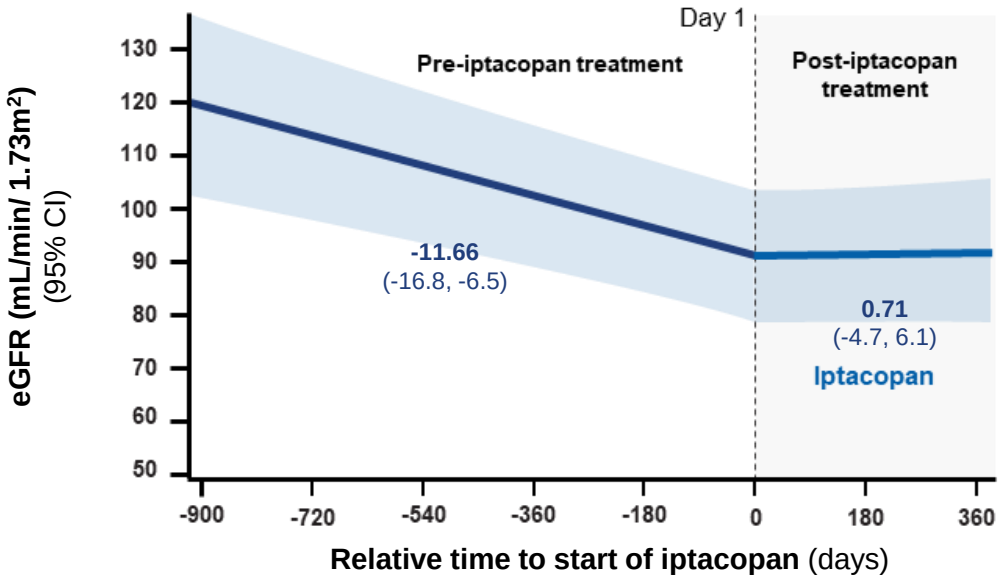


Next steps 〉 Ongoing health authority reviews in EU and other countries. Submission expected in US by year-end.

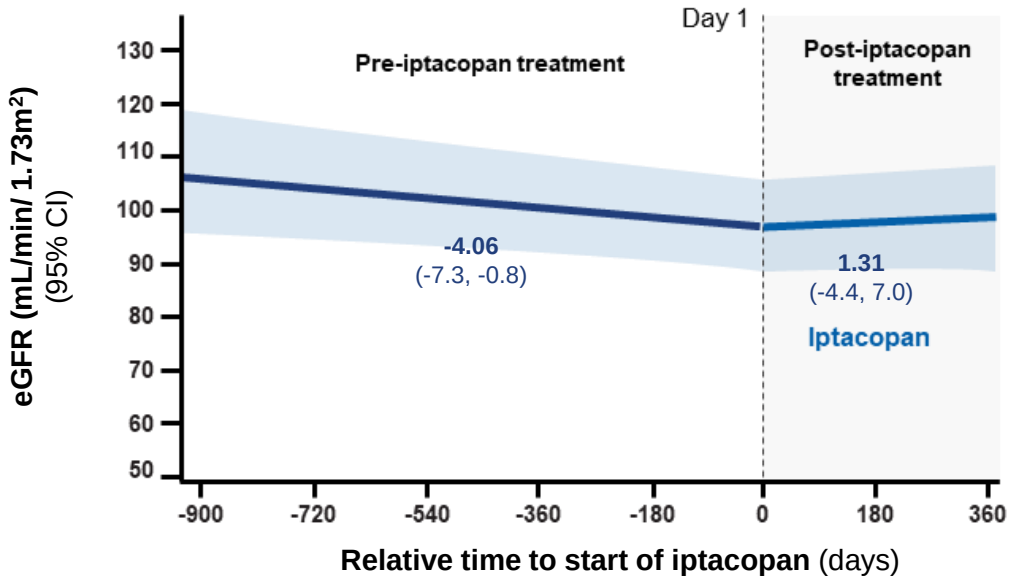
For references see page 45 in Appendix. Iptacopan is the INN (international non-proprietary name) of Fabhalta for unapproved indications.

Iptacopan: Observed change in eGFR slope vs. historic slope decline across UPCR categories[1] underscores iptacopan potential

Stabilization of eGFR[2,4] - Baseline 24h UPCR ≥3 g/g



Stabilization of eGFR[3,4] - Baseline 24h UPCR <3 g/g



For references see page 45 in Appendix. Iptacopan is the INN (international non-proprietary name) of Fabhalta for unapproved indications.

Lupus Nephritis is a glomerulonephritis that constitutes one of the most severe organ manifestations of the autoimmune disease SLE

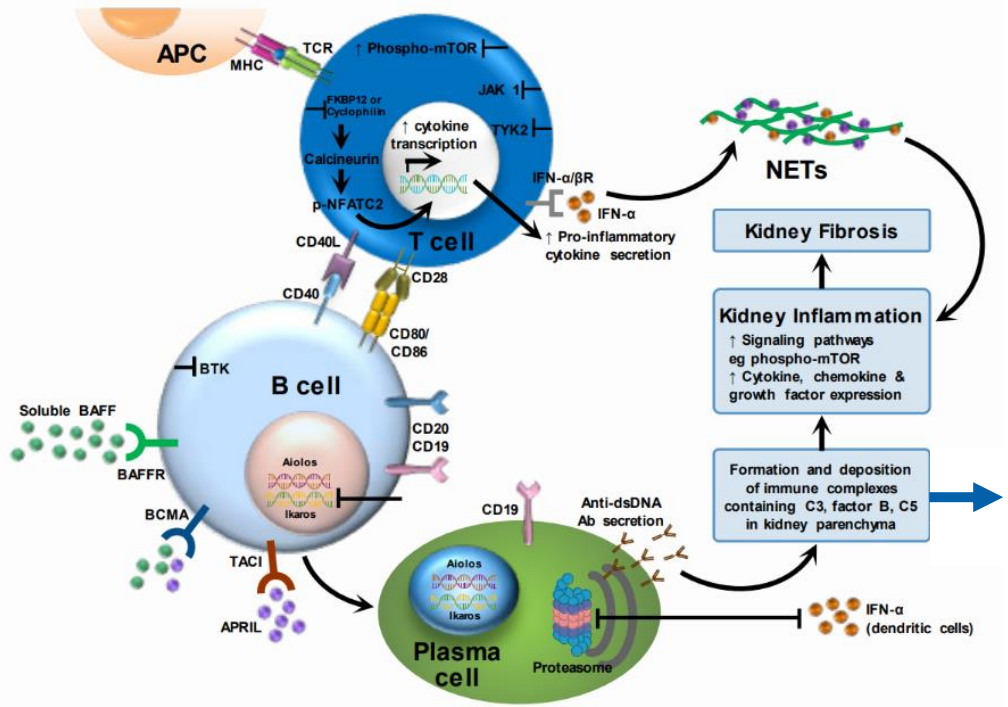
LN

Disease background and unmet need

Prevalence

US	111k[1]
Global[2]	455k[1]
Clinical manifestations	Varies from being asymptomatic to progressing nephrotic syndrome (sudden elevated proteinuria) or nephritic syndrome (hematuria, proteinuria, and abnormal kidney function)[3-5]
Diagnosis	Confirmed by kidney biopsies[6]
Current management	Corticosteroids and broad-spectrum immunosuppressants
Disease progression	~10-20% patients develop kidney failure requiring dialysis/transplant within 10 years of diagnosis[7,8]

Disease pathophysiology[9]



Complement activation through AP

For references 3-9 see page 45 in Appendix. 1. DRG Epidemiology Report 2021. 2. Includes prevalence estimates of 7 largest mature pharmaceutical markets (United States, France, Germany, Italy, Spain, United Kingdom, and Japan).

Advancing a range of assets with diverse MoA in Lupus Nephritis

LN

	Iptacopan	Ianalumab	YTB323
Mechanism	Complement Factor B inhibitor	BAFF-R inhibitor, ADCC-mediated B-cell depleter	CD19 CAR-T
Modality	Small molecule	Monoclonal antibody	Cell therapy
Administration	Oral	Subcutaneous injection	Intravenous infusion
Development stage	Phase 2 (NCT05268289)	Phase 3 (NCT05126277)	Phase 2 (NCT06581198)
Trial size	240	420	144
Next readout	2026	2027	2029
Primary endpoint	% patients achieving CRR at week 24 in the absence of renal flares	Frequency and % participants achieving stable CRR at 72 weeks	% patients achieving CR[1] at week 52

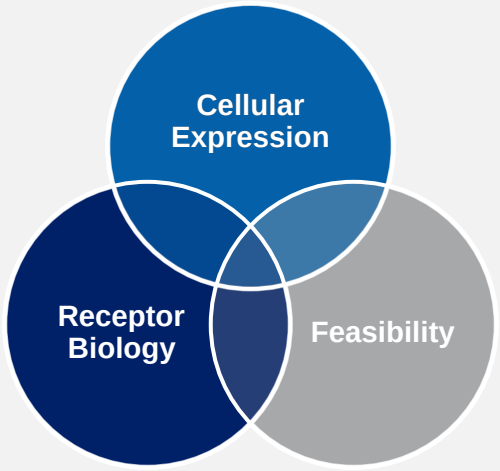
1. Complete response defined as meeting the DORIS and maintaining low dose GCs from week 24 onward.

Borealis: Convergence of Novartis priorities in renal diseases and cutting-edge RNA technology

NOVARTIS + CHINOOK THERAPEUTICS + VERSANT ventures

BOREALIS

Targeted delivery platform + Prioritized target pool



Optimization of cellular targeting + RNA modality

Development programs

Novartis optionality to acquire two future development-ready programs

We are committed to have a transformative impact on renal diseases

- ✓ **We are advancing a comprehensive pipeline** to tackle glomerular diseases with high unmet need
- ✓ **We have a broad portfolio in IgAN**, with unique MoAs to potentially achieve multiple treatment goals
- ✓ **Starting with the Fabhalta launch in IgAN**, we are building commercial capabilities that will scale across our renal portfolio
- ✓ **Atrasentan** has the potential to be a foundational therapy in IgAN; Ph3 data submitted to FDA H1 2024
- ✓ **Zigakibart** addresses the underlying root cause of IgAN; Ph3 readout expected 2026
- ✓ **Fabhalta in C3G:** 12-month APPEAR-C3G data support worldwide regulatory filings by YE 2024
- ✓ **Lupus Nephritis:** Advancing 3 clinical programs with diverse mechanisms and modalities
- ✓ **We have emerging efforts in siRNA for renal disease**, which could be the next frontier of targeted interventions

Agenda

1 Novartis aspiration in renal diseases

2 Building launch capabilities to scale across the renal portfolio

3 Advancing a comprehensive renal pipeline

4 Q&A

Q&A

NOVARTIS | Reimagining Medicine

Appendix

NOVARTIS | Reimagining Medicine

Abbreviations

Abbreviation	Full Form
AP	Alternative Pathway
APRIL	A Proliferation-Inducing Ligand
ASN	American Society of Nephrology
AAV	Anti-Neutrophil Cytoplasmic Antibody-Associated Vasculitis
ADPKD	Autosomal Dominant Polycystic Kidney Disease
AKI	Acute Kidney Injury
AI/ML	Artificial Intelligence/Machine Learning
BAFF	B-cell activating factor
CKD	Chronic Kidney Disease
CRR	Complete Renal Response
C3G	Complement 3 Glomerulopathy
eGFR	Estimated Glomerular Filtration Rate
ERA	Endothelin Receptor Antagonist
FSGS	Focal Segmental Glomerulosclerosis
FTE	Full-Time Equivalent
Gd-IgA1	Galactose-Deficient Immunoglobulin A1
HCP	Healthcare Professional

Abbreviation	Full Form
HTN	Hypertension
ICD	International Classification of Diseases
IC-MPGN	Immune Complex-Mediated Membranoproliferative Glomerulonephritis
IgAN	Immunoglobulin A Nephropathy
KDIGO	Kidney Disease Improving Global Outcomes
LN	Lupus Nephritis
MALT	Mucosa-Associated Lymphoid Tissue
MAS825	A specific drug candidate (context-specific)
MRA	Mineralocorticoid Receptor Antagonist
MoA	Mechanism of Action
PNH	Paroxysmal Nocturnal Hemoglobinuria
RASi	Renin-Angiotensin System Inhibitor
REMS	Risk Evaluation and Mitigation Strategy
SGLT2i	Sodium-Glucose Cotransporter-2 Inhibitor
srLN	Severe Renal Lupus Nephritis
TIN816	A specific drug candidate (context-specific)
UPCR	Urine Protein-to-Creatinine Ratio

References (1/4)

Slide 8

3 Figure adapted from Boyd et al. 2012.
4 Zhang H, Barratt J. *Semin Immunopathol.* 2021;43:707–15.
5 https://www.niddk.nih.gov/health-information/kidney-disease/iganephropathysymptoms.
6 https://rarediseases.org/rare-diseases/iga-nephropathy/.
7 Xie J, *et al. PLoS One.* 2012;7;e38904.
8 Rodrigues J, *et al. Clin J Am Soc Nephrol.* 2017;12(4):677-686.
9 Pitcher D, *et al. Clin J Am Soc Nephrol.* 2023;18(6):727-738.
10 Hastings MC, *et al. Kidney Int Rep.* 2018;3(1):99-104.
11 Sim JJ, *et al.* Poster TH-PO615 presented at: ASN Kidney Week 2023.
12 Bobart SA, *et al. Nephrol Dial Transplant.* 2021;36(5):840-847.
13 Saha MK, *et al.* Poster TH-PO1016 presented at: ASN Kidney Week 2019.

Slide 10

1 Boyd JK, *et al. Kidney Int.* 2012;81(9):833-843.
2 Gesualdo L, *et al. Semin Immunopathol.* 2021;43(5):657-668.
3 Tecklenborg J, *et al. Clin Exp Immunol.* 2018;192(2):142-150.
4 Gesualdo L, Suzuki H, *et al. Semin Immunopathol.* 2021;43(5):657-668
5 Kohan DE, *et al. Kidney Int.* 2014;85:962-971
6 Raina R, *et al. Kidney Dis (Basel).* 2020 Jan;6(1):22-34.
Figure adapted from Boyd et al. 2012.

Slide 11

1 Exploratory analyses of biomarkers.
2 Exploratory sub-cohort not included in the key efficacy analyses with the main study population.
3 Perkovic V, *et al. N Engl J Med.* 2024. DOI: 10.1056/NEJMoa2410316

References (2/4)

Slide 13

1 Xie J, *et al. PLoS One.* 2012;7:e38904.
2 Rodrigues J, *et al. Clin J Am Soc Nephrol.* 2017;12(4):677-686.
3 Pitcher D, *et al. Clin J Am Soc Nephrol*. 2023;18(6):727-738.
4 Hastings MC, *et al. Kidney Int Rep*. 2018;3(1):99-104.
5 Sim JJ, *et al.* Poster TH-PO615 presented at: ASN Kidney Week 2023; November 2-5, 2023; Philadelphia, PA.
6 Bobart SA, *et al. Nephrol Dial Transplant*. 2021;36(5):840-847.
7 Saha MK, *et al.* Poster TH-PO1016 presented at: ASN Kidney Week 2019; November 5-10, 2019; Washington, DC.

Slide 24

1 Boyd JK, *et al. Kidney Int.* 2012;81(9):833-843.
2 Gesualdo L, *et al. Semin Immunopathol.* 2021;43(5):657-668.
3 Tecklenborg J, *et al. Clin Exp Immunol.* 2018;192(2):142-150.
4 Gesualdo L, Suzuki H, *et al. Semin Immunopathol.* 2021;43(5):657-668
5 Kohan DE, *et al. Kidney Int.* 2014;85:962-971
6 Raina R, *et al. Kidney Dis (Basel).* 2020 Jan;6(1):22-34.

Figure adapted from Boyd et al. 2012[1].

Slide 25

1 Lehrke I, *et al. J Am Soc Nephrol.* 2001;12(11):2321-29.
2 Zanatta CM, *et al. Ren. Fail.* 2012(34):308-15.
3 Kohan DE, *et al. Kidney Int. Rep.* 2023;8:2198-2210.
4 Tycová I, *et al. Physiol Res.* 2018;67(1):93-105.
5 Benigni, A, *et al. Pediatric Nephrology,* 2021;36, 763–775.
6 de Zeeuw, *et al,* 2014, JASN.
7 Heerspink, *et al.* 2019, WCN.

Figure adapted from Kohan DE, 2023[3].

References (3/4)

Slide 26

1 Heerspink HJL, *et al.* Efficacy and safety of atrasentan in IgA nephropathy: A pre-specified interim analysis of a Phase 3 randomized controlled clinical trial. ERA. May 25, 2024.

2 Heerspink HJL, *et al.* ALIGN Subgroup Analyses: Clinically Meaningful Urinary Protein-to-Creatinine Ratio Reductions across Subgroups. ASN 2024 Oral Presentation FR-OR62.

3 Heerspink HJL, *et al. N Engl J Med.* 2024. DOI: 10.1056/NEJMoa2409415.

Slide 27

1 Mathur M, *et al*. *J Clin Med*. 2023;12(21):6927.

2 Boyd JK, *et al. Kidney Int* 2012;81:833–43.

3 Yeo SC, Barratt *J. Clin Kidney J* 2023;16(Suppl 2):ii9–18. Data from UK retrospective cohort of 2299 adults and 140 children with IgAN of the UK National registry of Rare Kidney Diseases (RaDaR). Patients enrolled has a biopsy-proven diagnosis of IgAN plus proteinuria >0.5 g/day or eGFR <60 ml/min per 1.73 m2 at any time in their history of their disease. Analyses of kidney survival were conducted using Kaplan-Meier and Cox regression. Recruitment into RaDaR was initiated in 2013. Availability of patient medication and blood pressure data was a limiting factor in this study.

4 Barratt J, *et al*. Abstract presented at ERA 2023; June 15-18, 2023; Milan, Italy. Abstract 4337.

5 Barratt J, *et al.* Oral presentation presented at ERA 2024; May 23-26, 2024; Stockholm, Sweden.

6 Yeo SC & Barratt J. *Clin Kidney J.* 2023; 16(Suppl 2):ii9–ii18.

7 Knoppova B, *et al. J Clin Med*. 2021;10:4501.

Slide 7 and Slide 30

1 Diagnosed lifetime prevalent cases, DRG estimates, 2023.

2 Biopsy diagnosed prevalent C3G patients based on Novartis internal estimates, 2024.

3 DRG Epidemiology Report, 2021.

4 Novartis internal estimates, 2023.

5 IQVIA estimates, 2024.

6 Includes prevalence estimates of 7 largest mature pharmaceutical markets (USA, France, Germany, Italy, Spain, UK, and Japan).

7 Fabhalta received accelerated approval from the FDA based on UPCR data from the interim analysis at 9 months. It has not been established whether Fabhalta slows kidney function decline in patients with IgAN.

References (4/4)

Slide 31

3 Smith RJH, *et al. Nat Rev Nephrol.* 2019;15(3):129–43.

4 Caravaca-Fontán F, *et al. Nephron.* 2020;144(6):272–80.

5 Ahmad SB, Bomback AS, *Adv Chronic Kidney Dis.* 2020;27(2):104–10.

Figure adapted with permission from Caravaca-Fontán, *et al.* 2020[4].

Slide 32

1 ASN 2024 presentation Smith R., *et al.*

2 Primary endpoint. Model estimated geometric mean of ratio to baseline in % change (95% CI) in proteinuria measured via 24-hour UPCR. N=74.

3 Based on pre-specified exploratory endpoint. N=74; Change in eGFR slope vs. pre-iptacopan treatment: +9.0 mL/min/1.73m^2/year (p<0.0001).

4 eGFR slopes per year analyzed using a linear mixed effects model including time (analysis day before or after change point (day 1 of iptacopan treatment) as a continuous covariate, participant-level intercept and slope (time) as random effects. Intercurrent events handled with a treatment policy strategy.

Slide 33

1 ASN 2024 presentation Smith R., *et al.*

2 Based on prespecified exploratory endpoint. N=32; Change in eGFR slope vs. pre-iptacopan treatment: +12.37 mL/min/1.73m^2/year (p<0.0001).

3 Based on prespecified exploratory endpoint. N=42; Change in eGFR slope vs. pre-iptacopan treatment: +5.37 mL/min/1.73m^2/year (p=0.0856).

4 eGFR slopes per year analyzed using a linear mixed effects model including time (analysis day before or after change point (day 1 of iptacopan treatment) as a continuous covariate, participant-level intercept and slope (time) as random effects. Intercurrent events handled with a treatment policy strategy.

Slide 34

3 Anders HJ, *et al. Nat Rev Dis Primers.* 2020; 6(1):7.

4 Liu R, *et al. Mol Med Rep.* 2023;28:204.

5 Khanna R, *et al. Mo Med.* 2011;108(1):33-6.

6 Weening JJ, *et al. Kidney Int.* 2004;65(2):521–30.

7 Hanly JG, *et al. Rheumatology (Oxford).* 2016;55(2):252–62.

8 Anders HJ, *et al. Nat Rev Dis Primers.* 2020; 6(1):7.

9 Figure adapted from Yung S, *et al.* F1000Research. 2020; 9(Faculty Rev):905.