Iptacopan (LNP023) update

Investor presentation
June 22, 2021
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Iptacopan could become a potentially preferred treatment option for several diseases with high unmet need – a pipeline in a pill

- The complement system is a foundational component of the innate immune system; dysregulation and/or overactivation of the cascade leads to and characterizes several diseases

- Iptacopan development program covers several nephrology and hematology indications that currently have limited (PNH\textsuperscript{1}, aHUS\textsuperscript{2}, LN\textsuperscript{3}) or no approved treatments (IgAN\textsuperscript{4}, C3G\textsuperscript{5}, CAD\textsuperscript{6}, iMN\textsuperscript{7})

- Positive Ph2 data in IgA nephropathy (IgAN) and C3 glomerulopathy (C3G) presented at ERA-EDTA 2021

- Positive Ph2 results for paroxysmal nocturnal hemoglobinuria (PNH) presented at ICKSH 2021 and EHA 2021

- Regulatory designations granted: PRIME for C3G, Breakthrough for PNH, and five orphan drug designations

- Ph3s ongoing in PNH, IgAN and expected to start in C3G and aHUS in coming months; iMN Ph2 ongoing

- First filings expected 2023; multi-billion potential if efficacy and safety confirmed across multiple indications

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1. PNH = paroxysmal nocturnal hemoglobinuria  
2. aHUS = atypical hemolytic uremic syndrome  
3. LN = Lupus nephritis  
4. IgAN = IgA nephropathy  
5. C3G = C3 glomerulopathy  
6. CAD = cold agglutinin disease  
7. iMN = idiopathic membranous nephropathy
Iptacopan is an oral, potent, selective factor B inhibitor...

- Dysregulation of the complement pathway is associated with a range of rare kidney and hematological diseases
- **Iptacopan (LNP023)** is an oral, first-in-class, potent and selective small-molecule inhibitor of factor B (FB)
- Iptacopan binds to FB to suppress the activity of C3 convertase and thus signaling from the alternative complement pathway (AP) and activation of the amplification loop
- This prevents downstream generation of the C5 convertase complex, opsonization, and formation of C3a and C5a anaphylatoxins and membrane attack complex (MAC)
- Direct classical and lectin pathway signaling remains intact, resulting in a potentially lower meningococcal infection risk in vaccinated patients compared to terminal complement pathway inhibitors

... with a promising profile enabling its broad development...

Illustrative, selected examples of approved or currently developed therapeutics

Eculizumab, Ravulizumab (i.v. /s.c.)

Narsoplimab (i.v.)

Pegcetacoplan (s.c.)

Iptacopan (oral)

FD-inhibitors (oral)

Danicopan, ALXN2050, BCX 9930
... across both nephrology and hematology

<table>
<thead>
<tr>
<th>Indication</th>
<th>2021</th>
<th>2022</th>
<th>2023</th>
<th>2024</th>
<th>2025</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgAN</td>
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<td></td>
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<td>♦</td>
<td>Interim analysis (IA) with 250 patients at 9 months (♦) could support filings in 2023 for conditional/accelerated approvals</td>
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<tr>
<td>C3G</td>
<td>Phase 3</td>
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<td></td>
<td>Ph3 to start enrollment imminently</td>
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<td>aHUS</td>
<td>Phase 3</td>
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<td>Ph3 to start enrollment in H2 2021</td>
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<tr>
<td>iMN</td>
<td>Phase 2</td>
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<td></td>
<td>Ph2 ongoing</td>
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<tr>
<td>LN</td>
<td>New</td>
<td>Phase 2</td>
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<td></td>
<td>Ph2 to start end 2021/early 2022; first read-out from initial cohort expected 2023</td>
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<td>Ph3 initiated based on positive data from two Ph2 trials</td>
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<td>ITP</td>
<td>New</td>
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IgAN = IgA nephropathy  
C3G = C3 glomerulopathy  
aHUS = atypical hemolytic uremic syndrome  
iMN = idiopathic membranous nephropathy  
LN = Lupus nephritis  
PNH = paroxysmal nocturnal hemoglobinuria  
ITP = immune thrombocytopenic purpura  
CAD = cold agglutinin disease
In IgA nephropathy, iptacopan could potentially delay the need for dialysis and/or transplant.

- **Most common primary glomerulonephritis**, most common cause of kidney failure in young adult Caucasians
- **Prevalence**: US: ~185k; EU5: ~32-51k; China: ~1m; Japan: ~130k
- **Standard of care (SoC)**: currently no approved therapies, focus on supportive care
- **Proteinuria ≥1g/day** is the strongest risk factor for poor prognosis in IgAN: ~30% of patients with proteinuria 1-2 g/day progress to kidney failure within 10 years
- **Proteinuria reduction is an important clinical goal in IgAN** and a relevant endpoint for accelerated registration pathways by FDA and other authorities
- **Activation of the alternative pathway (AP)** is present in almost 90% of biopsies
- By targeting the AP, iptacopan has the potential to slow disease progression and **delay the need for dialysis and/or transplant**

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3. TA = time averaged proteinuria; the strongest clinical predictor for IgAN kidney function decline

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**TA³-proteinuria:**

- p < 0.001

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**IgAN Ph2 study robustly designed for rapid development...**

**Population**
Biopsy-confirmed IgAN patients at risk of progression with elevated proteinuria (UPCR ≥0.75g/g) despite being on stable background therapy.

**Study design**
Adaptive, seamless, double-blind, placebo-controlled, dose-ranging

**Primary objective**
Dose response on the reduction in proteinuria vs. placebo after 90 days

**Secondary objectives**
Safety and tolerability, eGFR, and biomarkers reflecting activity of AP

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1. IA = interim analysis: analysis includes patients pooled from parts 1 and 2 of the study (n=112)
2. BID = twice daily
3. estimated glomerular filtration rate
4. AP = alternative pathway
5. Supportive care including a maximally tolerated dose of ACEi or ARB therapy for the individual, antihypertensive therapy or diuretics for at least 90 days before dosing
... showed 200mg BID\textsuperscript{3} led to a clinically meaningful proteinuria reduction of 23% at Day 90...

- Statistically significant effect of dose-response in proteinuria reduction\textsuperscript{8} by iptacopan versus placebo at 90 days
- Iptacopan 200mg BID\textsuperscript{3} led to a 23% reduction (80% CI: 8%, 34%)
- Treatment with iptacopan showed encouraging trend to early stabilization of renal function (eGFR\textsuperscript{7})
- Well tolerated; no serious infections

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**Primary endpoint data presented at ERA-EDTA 2021**

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- MCP-mod\textsuperscript{4} estimates
- MMRM\textsuperscript{6} estimates
- Estimated dose-response curve
- Pointwise 80% CI

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1. UPCR = Urine protein to creatinine ratio
2. Multiplicity-adjusted P-value; analysis adjusted for baseline UPCR (24-hour) and ancestry
3. BID = twice daily
4. MCP-mod = Multiple Comparison Procedure – Modelling
5. CI = confidence interval
6. MMRM = mixed model repeated measurements
7. eGFR = estimated glomerular filtration rate
8. 24-hour UPCR

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8. 24-hour UPCR
... with the 200mg BID delivering rapid, sustained, near complete inhibition of the alternative complement pathway...

Iptacopan
- Dose-dependent reduction of AP activation measured by serum Wieslab assay
- Rapid - Day 8 onwards
- Also reduced other complement biomarkers, including plasma Bb and urinary sC5b-9

Data presented at ERA-EDTA 2021
... providing the basis to initiate the APPLAUSE-IgAN Ph3 study

Population
Biopsy-confirmed IgAN patients at risk of progression with elevated proteinuria (UPCR² ≥1g/g) despite being on stable background therapy¹

Primary objectives
IA: Assess superiority of iptacopan vs. placebo in reduction of proteinuria² at 9 months; to support regulatory submission for accelerated/conditional approval

EoS: Assess superiority of iptacopan vs. placebo in slowing progression of IgAN measured by annualized total slope of eGFR decline over 24 months

1. Including at least maximally tolerated dose of ACEi/ARB for at least 90 days
2. UPCR (urine protein-to-creatinine ratio) from 24-h urine collection
3. BID = twice daily
Robust Ph2 data demonstrate clinically meaningful effect. Ph3 initiated to support worldwide regulatory filings

- First study to report safety and efficacy of an alternative complement pathway inhibitor in IgAN

- Robust Ph2 design provides confidence iptacopan has the potential to deliver a clinically meaningful effect
  - Randomized, double-blind and placebo-controlled study throughout the 90 days study period
  - 112 patients randomized to three (part 1) or four (part 2) different doses of iptacopan or placebo

- Primary study objective met: dose-dependent reduction in 24h UPCR at 90 days when compared to placebo
  - 23% UPCR reduction considered clinically meaningful; already observed after 90 days of treatment
  - Early trend of renal function stabilization (measured by eGFR)
  - Strong and dose-dependent inhibition of biomarkers of alternative complement pathway activity
  - Iptacopan treatment well tolerated at all doses

- Ph3 APPLAUSE-IgAN is ongoing globally to support iptacopan filings worldwide

- Potential first oral targeted anti-complement therapy in IgAN to delay dialysis and/or transplant

UPCR = Urine protein to creatinine ratio   eGFR = estimated glomerular filtration rate
Iptacopan has potential to be disease modifying, delaying or preventing need for dialysis and/or transplant in C3G

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

- **Prevalence:** US: ~10k; EU5: ~1.5-2.5k; China: ~32k; Japan: ~3.2k
- There are currently **no approved therapies**
- ~50% patients develop kidney failure within 10 years of diagnosis
- **Post-transplantation recurrence** and allograft loss is common (50% in DDD\(^2\), 75% in C3GN\(^3\))
- Characterized by complement dysregulation and complement C3 deposition in the kidney
- In C3G, iptacopan has the potential to be disease modifying and to **delay, or even prevent, the need for dialysis and/or transplant**

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1. End-stage kidney disease (ESKD) free renal survival
2. Dense Deposit Disease
3. C3 glomerulonephritis
Iptacopan Ph2 provides data on patients with both native and transplanted kidneys...

Population

Cohort A: Biopsy-confirmed C3G patients, with native kidneys and reduced serum C3 levels
Interim data available

Cohort B: patients with C3G recurrence following kidney transplantation
Data expected in Q3 2021

Primary objective (Cohort A)
Reduction in proteinuria at Week 12 measured as ratio to baseline of UPCR

Secondary objectives
eGFR, and biomarkers reflecting activity of AP, safety and tolerability

1. Patients aged ≥18 years
2. Not required for Cohort A unless most recent biopsy >12 months old
3. Optional for Cohort A
4. Patient may roll over into a separate extension study at Week 12
5. EOS = end of study
6. IF = immunofluorescence
7. UPCR = Urine protein to creatinine ratio
8. eGFR = estimated glomerular filtration rate
9. AP = alternative complement pathway
10. BID = twice daily
11. OD = once daily
... showing clinically meaningful 49% reduction in proteinuria...

**UPCR³ (24h urine collection) vs. baseline over time**

- **Geo-Mean (Geo-CV) UPCR³**
  - At baseline: 397 (55.9) g/mol
  - At Week 12: 202 (77.3) g/mol

- **Significant and clinically meaningful reduction** in proteinuria of 49% from baseline

- **Already at 3 months** there are signs of stabilization of kidney function (eGFR⁴)

- **Well tolerated** with no unexpected or new safety findings

- **ERA-EDTA 2021**: new retrospective observational cohort study data: longitudinal change in proteinuria strongly associated with kidney failure risk in C3G²

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1. Note: all patients from cohort A (with native kidney)  
3. UPCR = Urine protein to creatinine ratio  
4. eGFR = estimated glomerular filtration rate
... with improvements in trajectory of renal function decline compared to historical patients’ trend

Iptacopan treatment leads to stabilization of renal function

Patients experienced deterioration in renal function historically

Iptacopan’s estimated effect corresponds to a mean predicted eGFR preservation of 6.4 mL/min/1.73m² over 12 weeks (p=0.0459)

Mean eGFR\(^1\) slope and 95% CI\(^2\) indicated by bold blue line and surrounding shadowed area

1. eGFR = estimated glomerular filtration rate  
2. CI = confidence interval
Ph2 C3G data formed basis to initiate Ph3 APPEAR-C3G to support regulatory submission

**Population**
Adult patients with biopsy-confirmed C3G and native kidney. Proteinuria ≥1g/g (24h UPCR\(^1\))

**Primary objective**
Proteinuria reduction at 6 months

**Secondary objectives**
eGFR\(^3\), proportion achieving a composite renal endpoint, reduction in glomerular inflammation, safety and tolerability

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1. UPCR = urinary protein to creatinine ratio  
2. BID = twice a day  
3. eGFR = estimated glomerular filtration rate
Strong Ph2 data demonstrate clinically meaningful effect. Ph3 to be initiated to support worldwide regulatory filings

- Clinically meaningful reduction in 24h UPCR of 49% after 12 weeks and stabilization of renal function
  - Beneficial effects on proteinuria reduction and eGFR were seen very fast and sustained
  - Rapid increases in serum C3 levels and reductions in markers of complement activity provide mechanistic support
  - Favorable safety and tolerability profile

- New data presented at ERA-EDTA 2021 show statistically significant and clinically important improvements by iptacopan in eGFR slope when compared to pre-treatment period, suggesting that iptacopan may slow progression to, or potentially even prevent development of, kidney failure in patients with C3G

- Final Ph2 results, including from cohort B in patients with recurrent C3G after kidney transplant expected in Q3 2021 and planned to be presented at an upcoming congress

- Double-blind, placebo-controlled Ph3 APPEAR-C3G study projected to start enrollment imminently

- Potential to become first targeted and evidence-based treatment in C3G

UPCR = Urine protein to creatinine ratio  eGFR = estimated glomerular filtration rate
Iptacopan has the potential to be the first oral anti-complement mono-therapy in patients with PNH

- Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, life-threatening blood disorder caused by an acquired mutation in hematopoietic stem cells that leads to absence of complement-regulatory proteins.
- Prevalence: WW 7-16 cases/million; US 5-6k
- Many patients remain anemic and transfusion dependent despite eculizumab treatment:
  - C3-mediated extravascular hemolysis not addressed by anti-C5
  - ~40% remain anemic (Hb <10g/dl) of which ~50% are transfusion dependent
- By specifically targeting the complement pathway proximally, iptacopan could address both intra- and extravascular hemolysis and thereby address the remaining unmet need in PNH.
- Interim Ph2 data already showed that iptacopan provides clinical benefits as add-on to eculizumab in patients with residual hemolysis.

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2. Petropoulou AD 2010
3. Hb = Hemoglobin
Iptacopan Ph2 study in patients with PNH who are anti-C5 treatment naive

**Primary objective:**
Reduction of PNH-associated hemolysis (LDH\(^1\) levels at week 12)

**Secondary objectives:**
Dose-response, markers of intravascular and extravascular hemolysis (incl. Hb), markers associated with risk of thrombosis, safety and tolerability, pharmacokinetics

**Key exclusion criteria:**
Complement inhibition within prior 3 months, history of splenectomy

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1. LDH = Lactate dehydrogenase  
2. BID = Twice a day (QD = Once a day)  
3. EoS = End of study  
4. One patient in Cohort 1 started study drug taper prior to cutoff and discontinued after cutoff by patient preference, due to worsening of pre-existing neutropenia, one patient in Cohort 2 discontinued after 2 days of dosing due to non-severe AE of headache

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Interim analysis performed when 11 patients\(^4\) completed 12 weeks of iptacopan treatment
Ph2 PNH study met primary endpoint of reduction in LDH\(^1\) at week 12...

**New data (anti-C5 naive) presented at EHA 2021**

- Patients in both cohorts met the primary endpoint of reducing LDH\(^1\) levels by $\geq 60\%$ at Week 12
- After week 4, iptacopan achieved mean LDH reductions of 80-90%
- LDH reduction was **rapid and durable**, less variability observed in the higher dose cohort
- Markers of intra- and extravascular hemolysis normalized in the majority of patients

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1. LDH = Lactate dehydrogenase  
2. BID = Twice a day  
3. CI = Confidence interval  
4. ULN = Upper limit of normal
... with clinically meaningful increases in hemoglobin observed in all patients

All patients experienced rapid, durable increase in hemoglobin

All patients except one remained transfusion-free until Week 12

- One patient in cohort 2 (blue line) got one red blood cell (RBC) transfusion on study Day 3
- This patient (blue line) had pre-existing MDS², requiring 13 RBC transfusions during the year prior to study entry

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1. One patient in Cohort 2 was excluded for Hb analyses due to an RBC transfusion that occurred between screening and baseline, raising Hb from 71 to 110 g/L
2. MDS = Myelodysplastic syndrome
3. BID = twice a day
4. CI = confidence interval
**Ph2 data provide basis for iptacopan Ph3 APPLY-PNH**

**Population** (n ~91)
Adult PNH patients (Hb <10g/dL) on a stable regimen of anti-C5 therapy 6 months prior to randomization

**Primary endpoints**
- Proportion of patients achieving increase in Hb ≥2g/dL from baseline in the absence of RBC\(^1\) transfusion
- Proportion of patients achieving Hb ≥12g/dL in the absence of RBC\(^1\) transfusion

**Study period**
- **Screening period**
- **Randomized treatment period**
- **Treatment extension period**

**Time**
- Up to 8 weeks
- 24 weeks
- 24 weeks

**Duration**
- D-60
- D1
- D168
- D336

**Notes**
1. RBC = Red Blood Cell  
2. BID = twice a day  
3. EoS = end of study
Iptacopan has the potential to become the first oral anti-complement mono-therapy in patients with PNH

- Interim analysis (EBMT 2020) showed iptacopan provided clinical benefits as add-on to eculizumab in PNH patients with residual hemolysis
  - Marked reduction of hemolytic markers and transfusion-free improvement of hemoglobin in the majority of patients
  - Well tolerated with most common AE’s being headache, insomnia, rhinitis and rhinorrhea
  - Clinical benefits persisted upon discontinuation of eculizumab

- New data (EHA 2021) show clinically important benefits of monotherapy iptacopan in anti-C5 treatment naive PNH patients, including normalization of markers of intra- and extravascular hemolysis; resulting in a rapid and durable, transfusion-free improvement of hemoglobin levels in the majority of patients, with a favorable safety profile

- Ph3 APPLY-PNH study to assess superiority of iptacopan vs. anti-C5 therapy in patients with residual anemia despite standard of care treatment is ongoing to support filings as of 2023

- Iptacopan could become the first oral anti-complement mono-therapy in PNH offering significant convenience to patients along a potential superior benefit/risk

1. AE = adverse event
Iptacopan could improve nephrotic syndrome and remission rates in patients with idiopathic Membranous Nephropathy

Idiopathic Membranous Nephropathy (iMN) is a rare autoimmune glomerular disease and the most common cause of nephrotic syndrome in non-diabetic adults

**Prevalence:**
- US: ~80k
- EU5: ~82k
- China: ~422k
- Japan: ~32k

There are currently no approved therapies

30-40% of patients develop kidney failure within 5-15 years of diagnosis

Relapses after remission are common (15-30% of patients)

Complement pathway activation has been shown in kidney biopsies

In iMN, iptacopan has the potential to rapidly improve nephrotic syndrome and remission rates

Iptacopan has the potential to become first oral anti-complement therapy in patients with atypical Hemolytic Uremic Syndrome

**Glomerular changes in aHUS**

- aHUS arises from an initial EC injury. Defective complement control on endothelial surfaces results in cell lysis, (a) loss of EC, (b) followed by thrombus formation, (c) loss of mesangial cells and mesangiolysis. (d) In the chronic or repair phase, the newly formed EC produces new extracellular matrix, leading to double contours/GBM thickening.

**Kidney biopsy showing TMA**

- Fibrin thrombi and red blood cell fragments present in the capillary loops (white arrowheads).

- **Atypical Hemolytic Uremic Syndrome** (aHUS) is a life-threatening, progressive, rare form of thrombotic microangiopathy (TMA) often affecting children.
- **Prevalence:** US <10k
- **>50% of patients need dialysis** and/or develop more permanent renal damage within 12 months following the first episode of aHUS.
- **Unmet need** remains despite current SoC with C5 inhibitors such as patient burden.
- **Associated with dysregulation of the alternative pathway**
- **Iptacopan** has potential to become the first oral anti-complement therapy with a strong benefit/risk profile.

Iptacopan may have the potential to delay dialysis and/or transplant in patients with Lupus Nephritis (LN)

### Patient population
- Inflammation of the kidneys associated with proteinuria, hematuria, impaired kidney function and high blood pressure
- Affects up to 40% of adults (~90% women of childbearing age) and 80% of children with systemic lupus erythematosus (SLE); major cause of morbidity and mortality
- Remission achieved in only 30–50% of patients; 10-20% of patients develop kidney failure within 10 years of diagnosis
- Major ethnic disparities: Less frequent and severe for Caucasians; highly prevalent in African/Caribbean patients, Hispanic and Asian patients accounting for ~28-52% of the LN population

### Standard of care
- Induction with high dose corticosteroids + immunosuppressants (oral MMF or cyclophosphamide/CNIs), followed by lower doses as maintenance therapy; off-label rituximab used for refractory disease
- High unmet need for convenient and safe therapies with rapid nephron protection and durable CRR >20%, even after two novel entrants in 2020 (belimumab, voclosporin)

### Scientific rationale for iptacopan
- Strong complement activation in SLE
- In LN, deposition of nucleic acid-containing material in the glomeruli triggers the engagement of complement, activation of kidney stromal cells and recruitment of circulating pro-inflammatory cells
- Significantly decreased plasma C3 and increased Bb, C3a, C5a, and MAC found in active LN
- Reduced levels of C3 and C4 in plasma (overconsumption)

### Expected milestones
- Ph2 to start end 2021 / early 2022
- First read-out from initial cohort expected 2023
- Filing expected ≥2025

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2. MMF = mycophenolate mofetil
3. CNI = Calcineurin inhibitor
4. CRR = complete renal response
5. systemic lupus erythematosus

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Iptacopan (LNP023) update | June 22, 2021

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NOVARTIS | Reimagining Medicine
Initiating Ph2 iptacopan study in Q4 2021 in patients with Immune Thrombocytopenic Purpura (ITP)

**Patient population**
- Autoimmune thrombocytopenia (= platelets <100 k/µL) with increased risk of bleeding
- Annual incidence of ~3-10/ 100,000 and increasing with age
- Typical time of diagnosis during early adulthood (20-40y)
- Usually presents acutely with signs and symptoms of bleeding (petechiae, bruising, mucosal bleeding)

**Scientific rationale for iptacopan**
- Excessive platelet destruction in the spleen and liver and insufficient platelet production in the bone marrow, resulting in low platelet counts
- Evidence of complement involvement and/or reduced serum levels of complement factors in 30-50% of ITP patients
- Degree of platelet destruction / disease severity correlates with level of complement activation

**Standard of care**
- Steroids and/or IVIG\(^1\) in acute first-line therapy
- In persistent / chronic ITP: TPO-RAs\(^2\) and/or rituximab as 2\(^{nd}\) line and splenectomy and/or fostamatinib as 3\(^{rd}\) line
- Continued unmet medical needs exist particularly for durable remissions in relapsed / refractory patients (~30% of population)

**Expected milestones**
- Cohort in hematology basket study
- Ph2 start in Q4 2021 with first results expected 2023
- Filing projected ≥2025

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1. IVIG = Intravenous immunoglobulin  
2. TPO-RAs = thrombopoietin receptor agonists
Initiating Ph2 iptacopan study in Q4 2021 in patients with Cold Agglutinin Disease (CAD)

Scientific rationale for iptacopan
- IgM autoantibody-mediated disease
- Anemia primarily caused by extravascular hemolysis in spleen / liver and which is largely complement-dependent through C3 fragments deposition on RBCs¹

Expected milestones
- Cohort in hematology basket study
- Phase 2 start in Q4 2021, with first results expected 2023
- Filing projected ≥2025

Patient population
- Auto-immune hemolytic anemia, often triggered by cold temperatures or viral infections
- Prevalence of 1-9 / million
- More women than men affected; median age at diagnosis is 72 years and median age at the onset of symptoms 65 years
- Reduced quality of life due to anemia; symptoms include fatigue, dizziness, tachycardia, dyspnea, abdominal pain, acrocyanosis

Standard of care
- No approved therapy
- Plasma apheresis; steroids and rituximab used off-label
- Sutimlimab (anti-C1 mAb) Ph3 positive; approval pending
- Iptacopan has potential for first-in-class oral complement pathway inhibitor in CAD

¹ RBC = red blood cells
Iptacopan in parallel development across several nephrology and hematology diseases, with global multi-blockbuster potential

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<thead>
<tr>
<th>Market potential</th>
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<tbody>
<tr>
<td><strong>Indication</strong></td>
</tr>
<tr>
<td><strong>Nephrology</strong></td>
</tr>
<tr>
<td>IgAN</td>
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<td>C3G</td>
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<td><strong>Hematology</strong></td>
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<td>CAD</td>
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IgAN = IgA nephropathy  C3G = C3 glomerulopathy  aHUS = atypical hemolytic uremic syndrome  iMN = idiopathic membranous nephropathy  LN = lupus nephritis  PNH = paroxysmal nocturnal hemoglobinuria  ITP = Immune thrombocytopenic purpura  CAD = Cold agglutinin disease
Novartis is making significant efforts to prepare for a successful launch of iptacopan...

1. **Partnering with patient organizations**: Elevating the “voice of the patient” to raise awareness of high burden of illness and unmet need across the different diseases.

2. **Real world data generation**: Working with key registries across the world to demonstrate the potential value of iptacopan to the overall healthcare system.

3. **Patient journey mapping**: Identifying key clinical and non-clinical implementation barriers that need to be removed to ensure optimal patient outcomes.

4. **Medical education and evidence generation**: Establish a strong scientific “share of voice” at congresses to highlight the unmet need, build innovative partnerships with healthcare system stakeholders and ensure a robust evidence base for future implementation in clinical practice.
... which has the potential to become first-in-class for several rare complement driven diseases with high unmet need

Complement driven diseases are rare and often progressive diseases

Many of these diseases affect young patients, significantly impacting their QoL and even leading to premature death

Iptacopan could delay the progression or control the manifestations of these rare diseases, thus improving QoL for patients and easing the overall burden on healthcare systems

In renal diseases, our aspiration is to “extend dialysis-free life”

For many of these diseases\(^1\), there are no approved therapies and some current treatment options show limited efficacy/significant side effects

For others\(^2\), a need exists for options to better control the disease and ease the burden on patients and the overall healthcare system

Iptacopan is a first-in-class oral Factor B inhibitor that targets some of the key drivers of these complement driven diseases

QoL = quality of life  
1. IgAN, C3G, CAD, IMN  
2. PNH, aHUS, LN
Iptacopan is a pipeline in a single molecule, potentially addressing several diseases with high unmet need

- Pursued complement-driven diseases are rare and affect mostly young patients with no or limited evidence-based and approved treatment options

- Iptacopan is a first in class, oral, potent and selective Factor B inhibitor of the alternative complement pathway, which is postulated to play a key role in the underlying pathophysiology of the indications in scope

- **Positive efficacy results** along with a favorable safety profile from **four Ph2 studies in three indications**

- Due to its targeted MoA, iptacopan leaves the direct classical and lectin pathway signaling intact, resulting in a potentially lower meningococcal infections risk in vaccinated patients when compared to terminal complement pathway inhibitors such as anti-C5s

- **First filings expected 2023** to support outlook with multi-billion potential based on a differentiated profile addressing key unmet needs