INVESTOR EVENT

Rare Disease

06 SEPTEMBER 2022

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AstraZeneca Rare Disease

Forward-looking statements

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Rare Disease Investor Event | Agenda

I. Introduction & Alexion Strategy

II. Sustained Leadership in Complement

III. Expanding Beyond Complement

IV. Geographic Expansion

V. Building Scientific Bridges

VI. Closing Remarks

VII. Q&A Session

Marc Dunoyer
Chief Executive Officer, Alexion

Gianluca Pirozzi
SVP, Head of Development & Safety

Scott Weintraub
VP, Global Marketing & Commercial Strategy

Sharon Barr
SVP, Head of Research & Product Development

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INTRODUCTION AND Strategy

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Alexion & AstraZeneca

Unique opportunity to enhance long-term value, meeting AstraZeneca strategic criteria

Aligned with AstraZeneca strategy

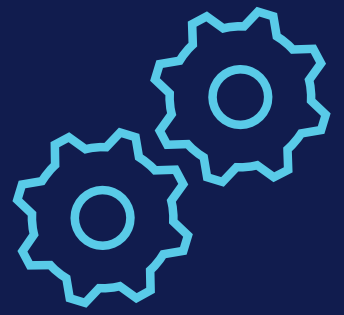
Accelerate innovative science

Supports AstraZeneca financial profile

Supports top-line growth, earnings accretive

AstraZeneca will be able to add value

Potential for geographic expansion



Feasible integration

Shared cultural values

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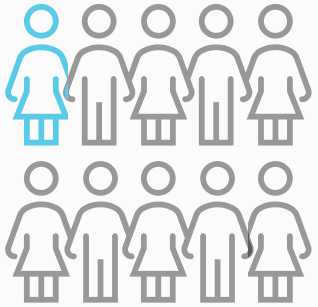
Transforming the treatment of rare diseases

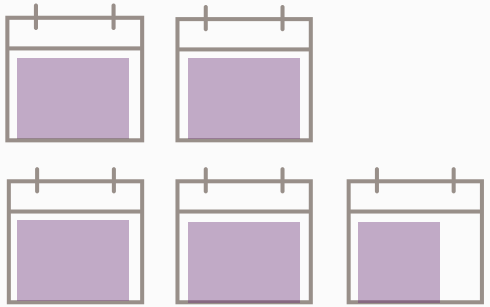
80%

of rare diseases are genetic[1]



1 in 10

people live with a rare disease[2]



4.8 years

average time to diagnosis;

40% receiving > 1 misdiagnosis[3]

50%

of rare disease patients are children[4]

OUR VISION is to transform the future of rare disease, increasing access to our medicines globally and innovating to treat more patients, earlier, with greater precision and efficacy

1. Global Genes, https://globalgenes.org/rare-disease-facts/ 2. 1 in 10 people live with a rare disease in the US; estimated 400 million people globally diagnosed with a rare disease 3. Wakap et al. 2019; Global Genes: RARE Facts 2020 4. Global Genes, https://globalgenes.org/ 2016 WRDD Fact Sheet.

Alexion, AstraZeneca Rare Disease: strategic priorities

Sustained Leadership in Complement

Expanding Beyond Complement

Organic Innovation & Collaboration with AstraZeneca

Alexion, AstraZeneca Rare Disease: approved medicines[1]

Five approved medicines indicated for seven rare diseases

Soliris
(eculizumab)

Ultomiris
(ravulizumab-cwvz)

Strensiq
(asfotase alfa)

Kanuma
(sebelipase alfa)

Koselugo
(selumetinib)

FOR

paroxysmal nocturnal haemoglobinuria (PNH)

atypical haemolytic uraemic syndrome (aHUS)

generalised myasthenia gravis (gMG)

neuromyelitis optica spectrum disorder (NMOSD)

paroxysmal nocturnal haemoglobinuria (PNH)

atypical haemolytic uraemic syndrome (aHUS)

generalised myasthenia gravis (gMG)

hypophosphatasia (HPP)

lysosomal acid lipase deficiency (LAL-D)

neurofibromatosis type 1 with plexiform neurofibromas (NF1-PN)

1. Alexion medicines may not be approved in every geography across the globe.

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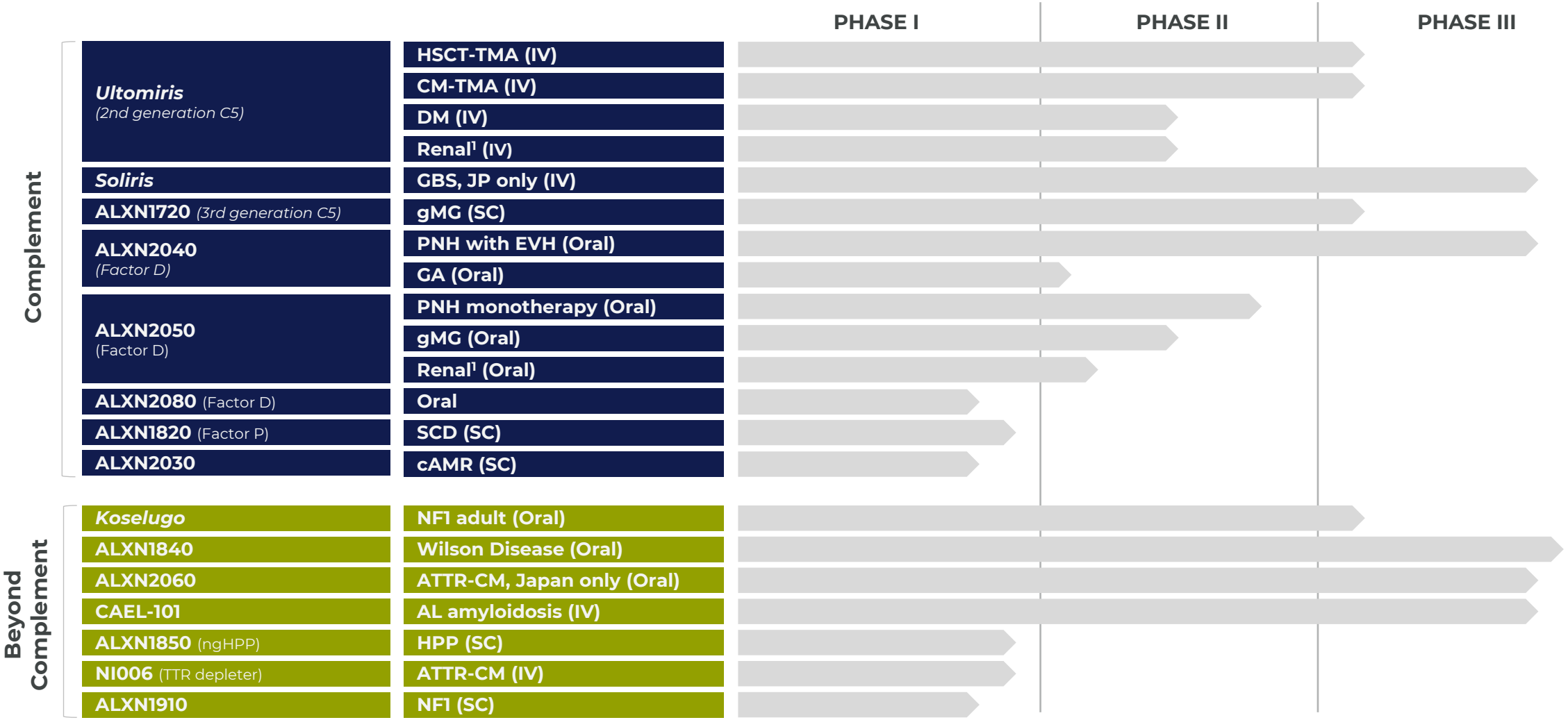
Broad pipeline across many high unmet need, high value indications



1. Renal basket trial including proliferative lupus nephritis or Immunoglobulin A Nephropathy; IV = intravenous; SC = subcutaneous; HSCT-TMA = haematopoietic stem cell transplant-associated thrombotic microangiopathy; CM-TMA = complement-mediated thrombotic microangiopathy; DM = dermatomyositis; GBS = Guillain-Barré syndrome; gMG = generalised myasthenia gravis; PNH = paroxysmal nocturnal haemoglobinuria; PNH-EVH = paroxysmal nocturnal haemoglobinuria with extravascular haemolysis; GA = geographic atrophy; SCD = sickle cell disease; cAMR = chronic antibody-mediated rejection; NF1 = neurofibromatosis type 1; ATTR-CM = transthyretin amyloid cardiomyopathy; AL amyloidosis = light chain amyloidosis; ng = next-generation; HPP = hypophosphatasia.

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SUSTAINED
LEADERSHIP IN

Complement

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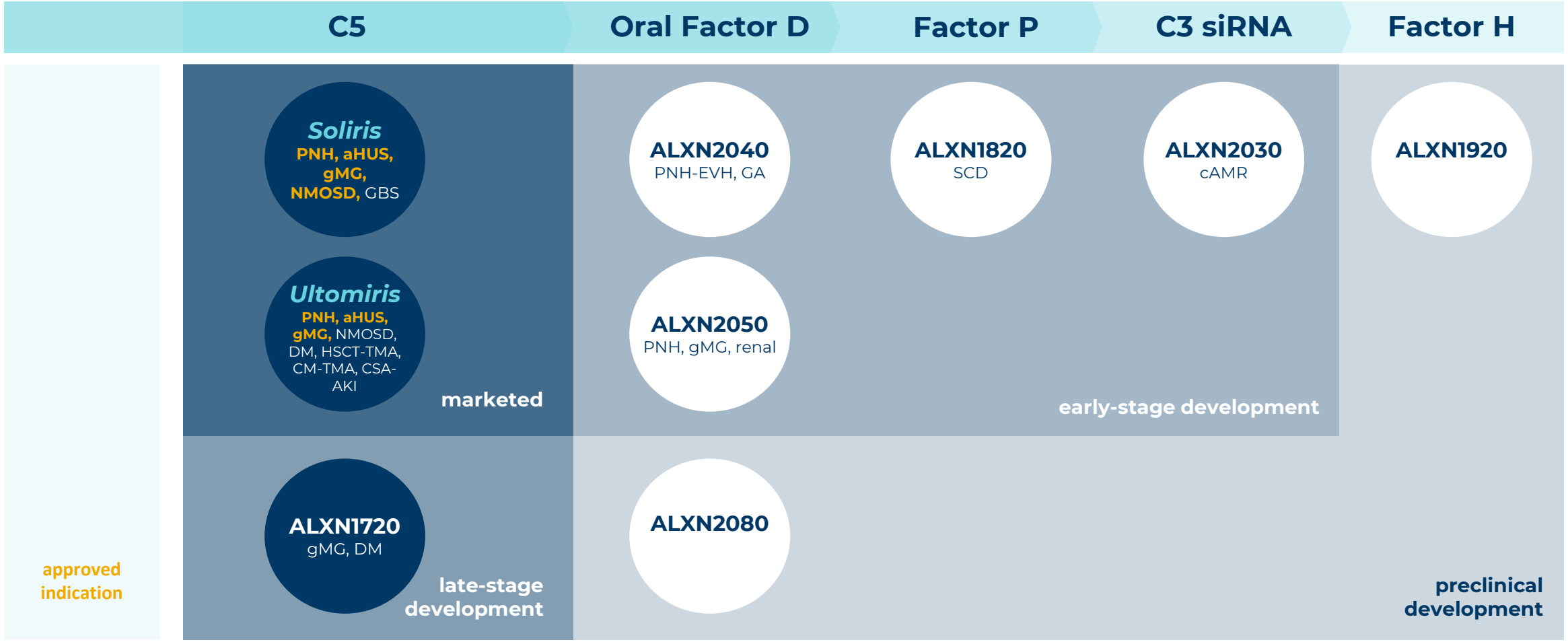
Broad expertise in complement biology

Multiple development-stage platforms, leveraging foundational complement expertise



PNH = paroxysmal nocturnal haemoglobinuria; aHUS = atypical haemolytic uraemic syndrome; gMG = generalised myasthenia gravis; NMOSD = neuromyelitis optica spectrum disorder; GBS = Guillain-Barré syndrome; DM = dermatomyositis; HSCT-TMA = haematopoietic stem cell transplant-associated thrombotic microangiopathy; CM-TMA = complement-mediated thrombotic microangiopathy; CSA-AKI = cardiac surgery-associated acute kidney injury; PNH-EVH = paroxysmal nocturnal haemoglobinuria with extravascular haemolysis; GA = geographic atrophy; SCD = sickle cell disease; siRNA = small interfering RNA; cAMR = chronic antibody-mediated rejection.

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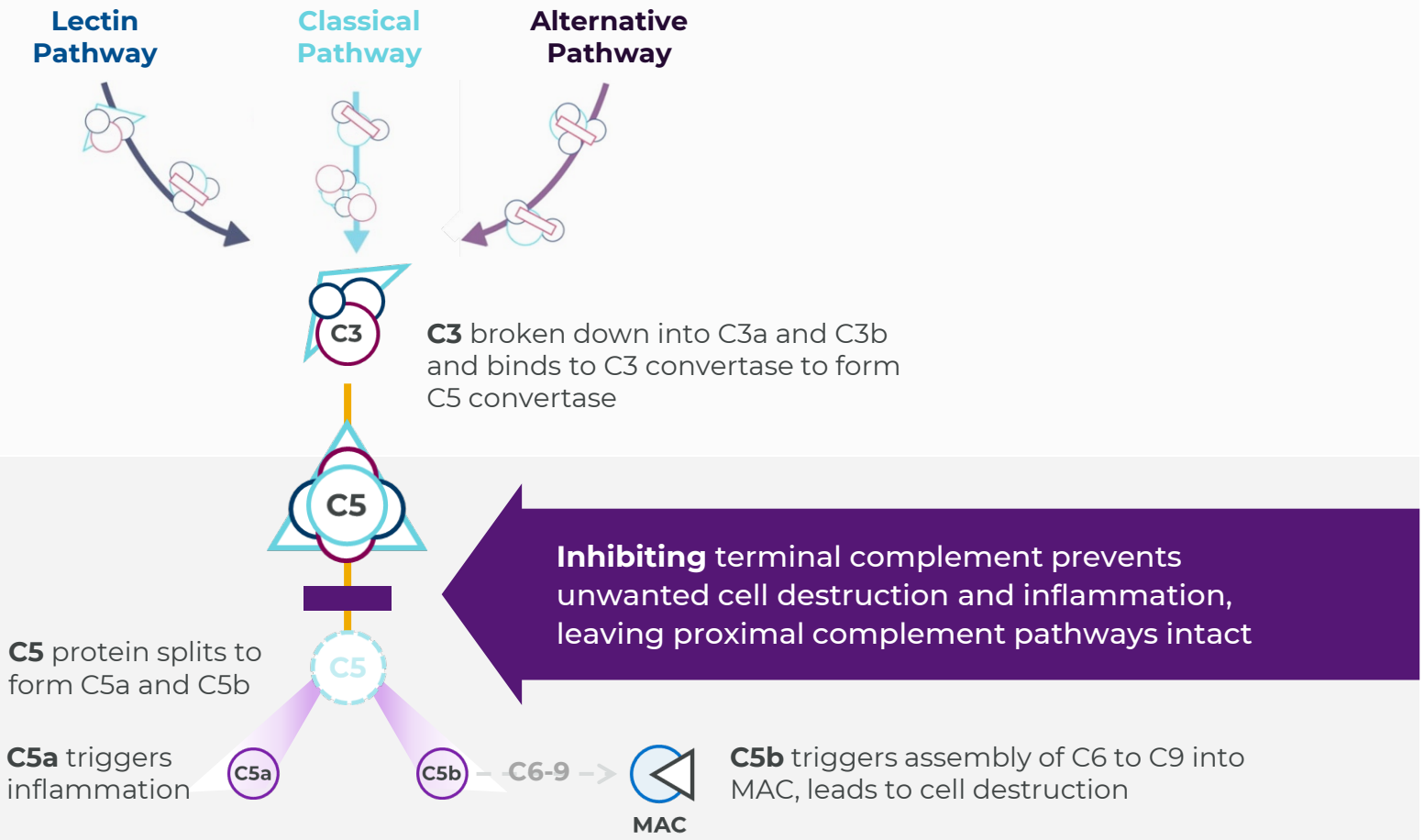
Foundation in terminal complement (C5) inhibition

Several areas of complement cascade are implicated in disease pathology

Complement system consists of >30 proteins activated in a cascade to maintain homeostasis in the body

Complement activation results in formation of MAC, which leads to destruction of target cells

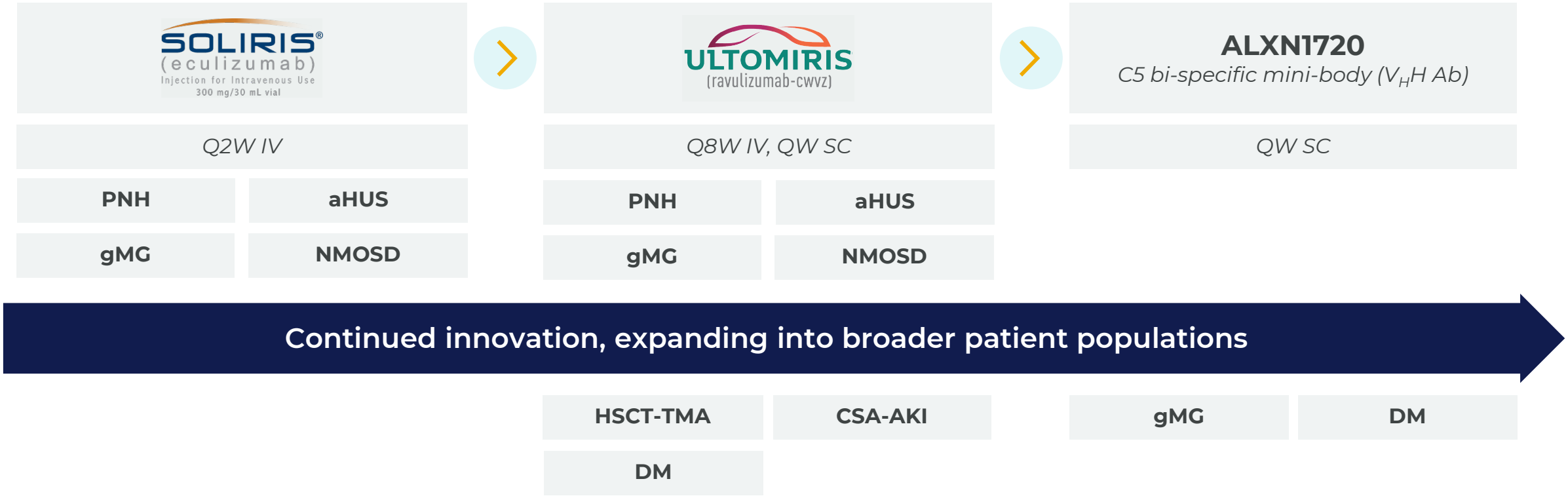
Overactivation of complement can trigger uncontrolled cascade of reactions that damage tissues



MAC = membrane attack complex.

Foundation in terminal complement (C5) inhibition

Diverse C5 inhibitor portfolio, optimised for differentiated indication selection

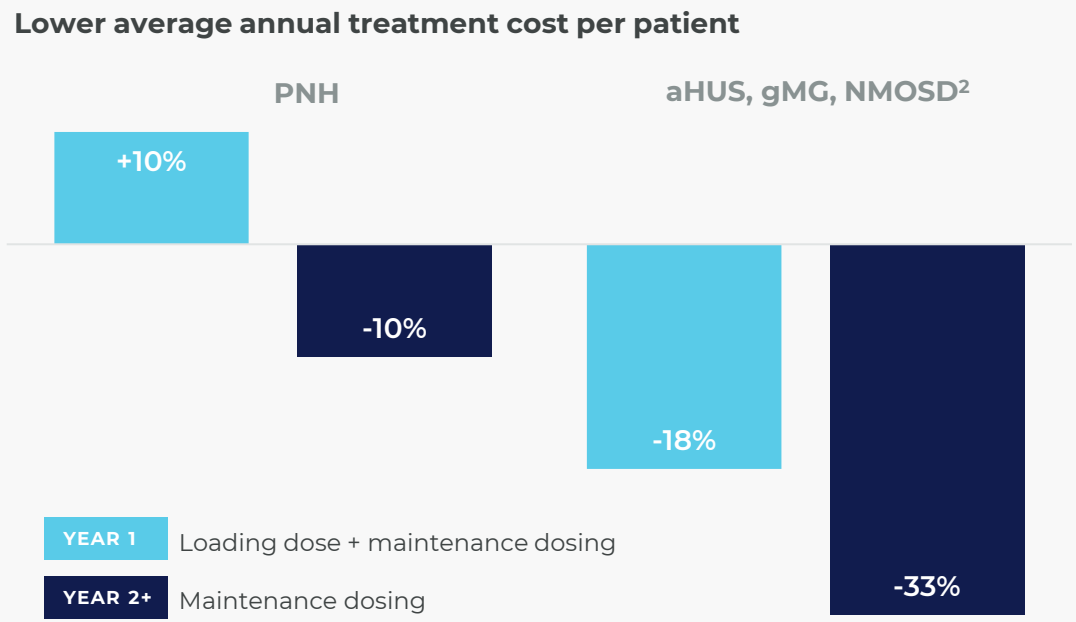


Q2W = every 2 weeks; IV = intravenous; Q8W = every 8 weeks; QW = once-weekly; SC = subcutaneous; V_HH Ab = single domain antibody; PNH = paroxysmal nocturnal haemoglobinuria; aHUS = atypical haemolytic uraemic syndrome; gMG = generalised myasthenia gravis; NMOSD = neuromyelitis optica spectrum disorder; HSCT-TMA = haematopoietic stem cell transplant-associated thrombotic microangiopathy; CSA-AKI = cardiac surgery-associated acute kidney injury; DM = dermatomyositis.

Establishing *Ultomiris* as the new standard of care

Value proposition supports rapid facilitated conversion and growth

Ultomiris vs. *Soliris* pricing dynamics[1]



Ultomiris potential to achieve best-in-class conversion across four *Soliris*-labelled indications by 2025[3]

PNH

best-in-class conversion, reaching saturation in **key markets**

aHUS

market share leader, variable duration of treatment

gMG

c.30k addressable population (3x *Soliris*)[4], including naïve and switch

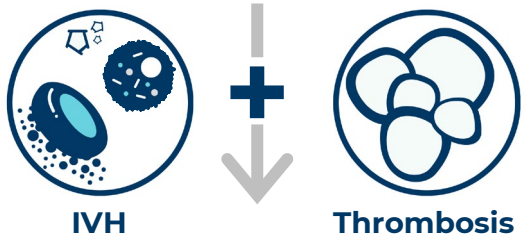
NMOSD

best-in-class efficacy, Q8W dosing expands addressable patient population; potential approval H1 2023

1. Depicted annual treatment cost differentials calculated based on US list prices. 2. *Ultomiris* NMOSD regulatory decision anticipated in H1 2023 in US and EU. 3. Defined as >70% conversion in the US. 4. US addressable population estimated to be 30k, representing a 3-fold increase compared to *Soliris* addressable population *(8-10k)*. PNH = paroxysmal nocturnal haemoglobinuria; aHUS = atypical haemolytic uraemic syndrome; gMG = generalised myasthenia gravis; NMOSD = neuromyelitis optica spectrum disorder; Q8W = every 8 weeks.

Compelling, durable C5 data in PNH

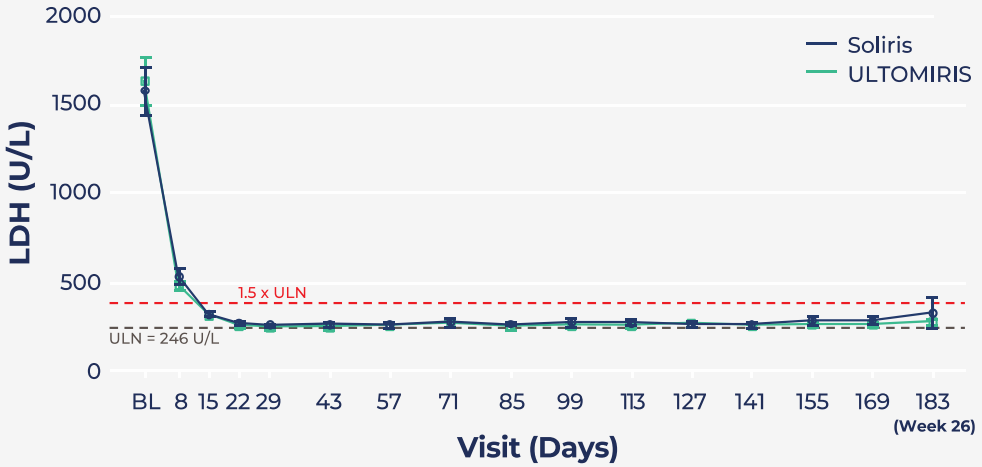
Pivotal 301 trial and longest registry data to date solidifies *Ultomiris* as standard of care



In PNH, uncontrolled terminal complement activity leads to IVH; **LDH is key biomarker of IVH**

- **Ultomiris demonstrated rapid and sustained reductions in LDH, with mean levels remaining stable and < 1.5 × ULN[2]**
- **LDH levels >1.5 × ULN is predictor for risk of thrombosis and mortality in PNH[3]**
- **LDH is one of the strongest predictors for improvement in patient-reported clinical outcomes[4]**

MEAN LDH LEVELS OVER TIME IN STUDY 301



SURVIVAL RATES REPORTED IN PNH REGISTRY TRIAL

97.5%

6-year survival analysis of >450 patients with PNH *Ultomiris*[1]

~65%

Historical 5-year survival rates in PNH patients with evidence of haemolysis not on anti-C5 treatment[2]

1. Kulasekararaj, Brodskey, Griffin et al., "Long-term complement inhibition and survival outcomes in patients with paroxysmal nocturnal haemoglobinuria: an interim analysis of the ravulizumab clinical trials." 2. Hillmen et al., 1995. 3. Lee et al., 2013; Jang et al., 2016 4. Schrezenmeier et al., "Predictors for Improvement in Patient-Reported Outcomes: Post-Hoc Analysis of a Phase III Randomised, Open-Label Study of Eculizumab and Ravulizumab in Complement Inhibitor-Naïve Patients with Paroxysmal Nocturnal Haemoglobinuria (PNH)." PNH = paroxysmal nocturnal haemoglobinuria; IVH = intravascular haemolysis; LDH = lactate dehydrogenase; ULN = upper limit of normal.

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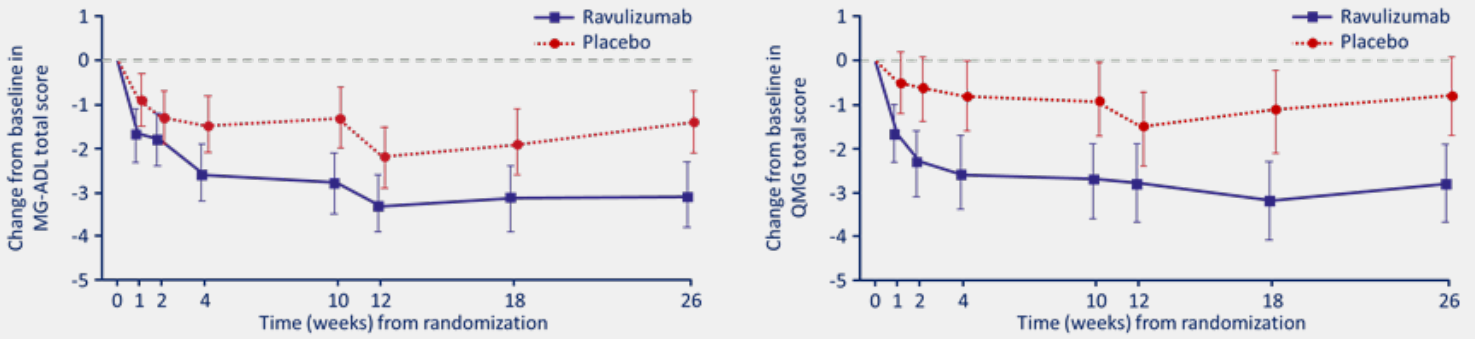
Ultomiris Phase III HLR confirms C5 leadership in gMG

Rapid and sustained improvement in key gMG measures of clinical benefit

Significant improvement in patient (MG-ADL)[1] and physician-reported (QMG)[2] assessments[3]



Improvement observed in one week on MG-ADL and QMG measures

Improvements sustained through the 60-week follow-up period

76% of patients in the *Ultomiris* arm experienced clinically meaningful improvement on MG-ADL (49% on QMG) by week 60

1. Myasthenia Gravis Activities of Daily Living is an 8-item outcome measure that reflects ocular, bulbar, respiratory and limb symptoms and their impact on function. 2. Quantitative Myasthenia Gravis scale is a 13-item evaluation of ocular, facial, bulbar, gross motor, axial and respiratory weakness. 3. Vu, Meisel, Mantegazza, et al. presented at Muscular Dystrophy Association Conference 2020; 2020, virtual. HLR = high-level results; gMG = generalised myasthenia gravis; MG-ADL = myasthenia gravis activities of daily living; QMG = quantitative myasthenia gravis.

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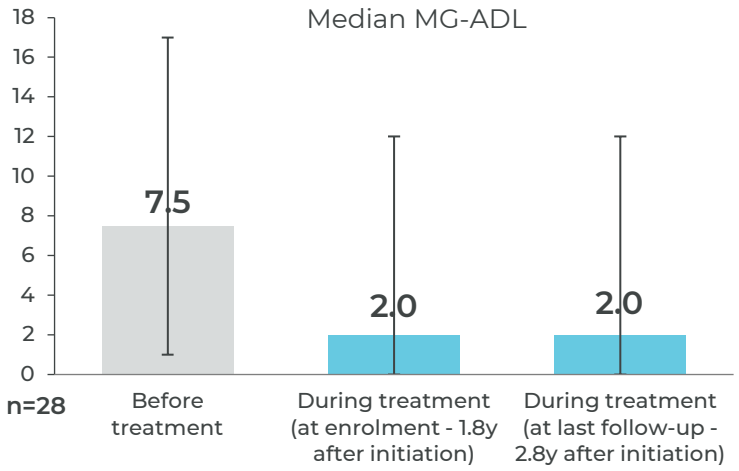
Durable C5 efficacy in gMG

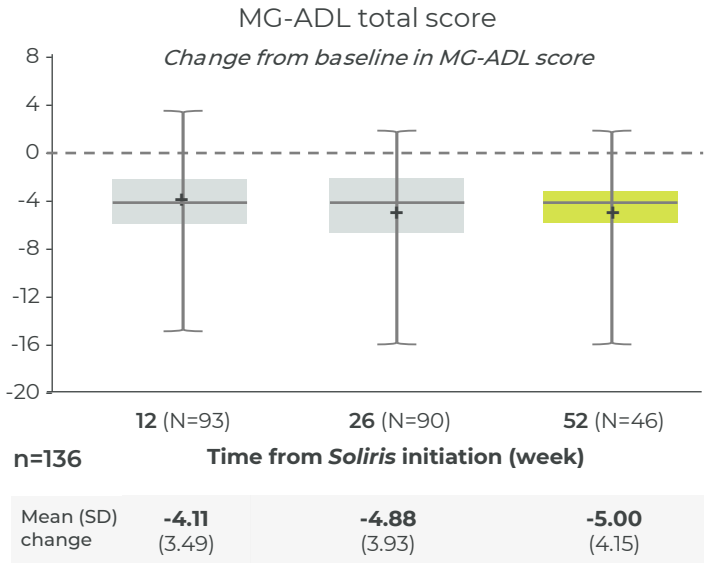
Soliris global registry trials reinforce benefit of long-term, continuous treatment

NEW DATA

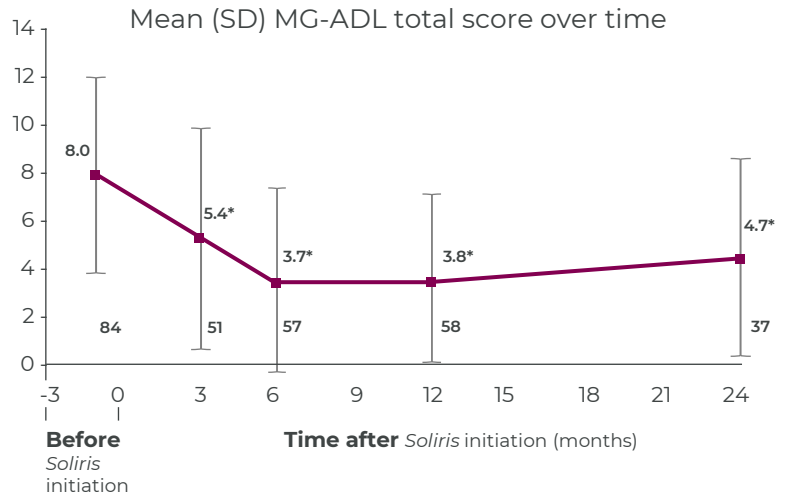
gMG registry shows 5.5-point MG-ADL reduction with treatment



Japan PMS trial shows 5-point MG-ADL reduction at 52 weeks



Project ELEVATE trial resulted in >3-point MG-ADL reduction at 24 months



46.4% of patients reached MSE status during treatment

Only 26.4% of patients on corticosteroids (≤5 mg/day) at 52 wks

72% of patients reduced or discontinued steroids

1. Muppidi et al. presented at International Congress on Neuromuscular Diseases 2022; July 2022, Brussels. 2. Murai et al, "Clin Exp Neuroimm;" May 2022. 3. Habib et al. presented at American Academy of Neurology 2022; April 2022, Seattle. gMG = generalised myasthenia gravis; MG-ADL = myasthenia gravis activities of daily living; MSE = minimal symptom expression; y = year; PMS = post-marketing surveillance; SD = standard deviation; wks = weeks.

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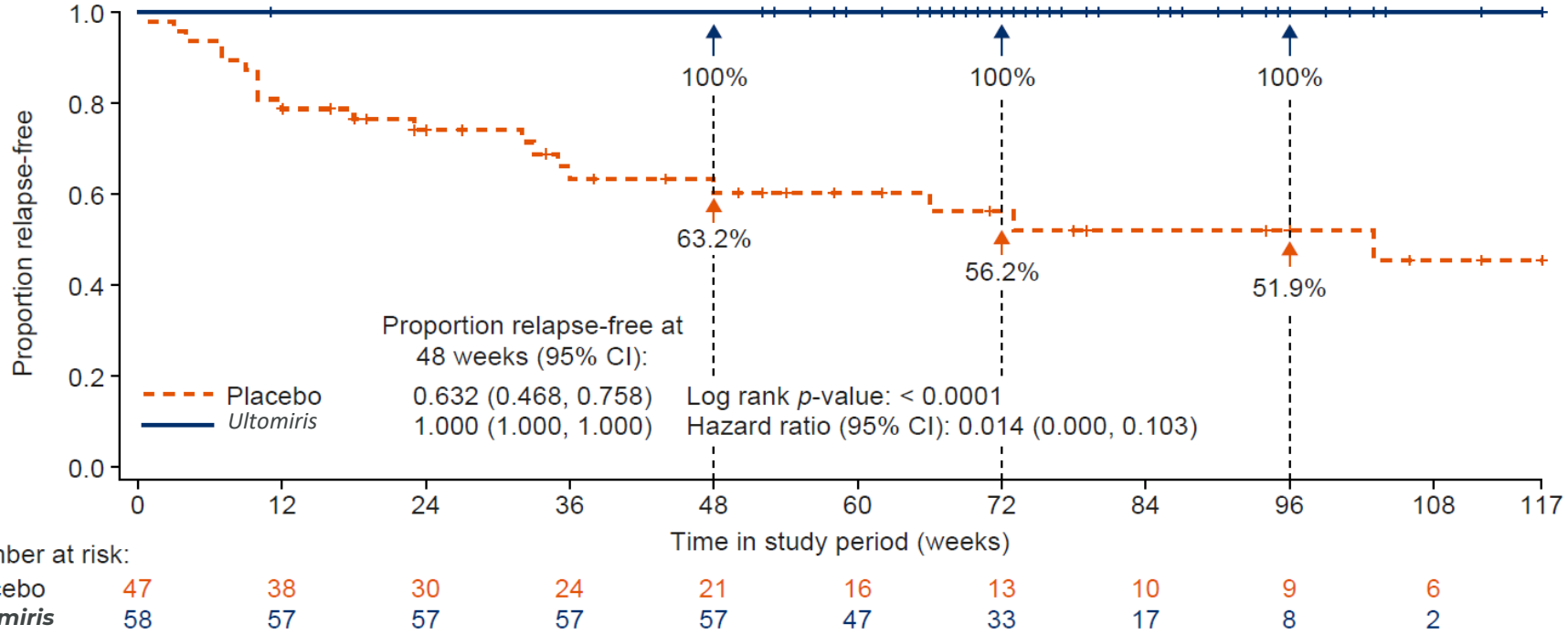
Ultomiris Phase III HLR confirms C5 leadership in NMOSD

Anticipated regulatory decision in H1 2023 (US, EU)

Ultomiris reduced the risk of relapse by 98.6% compared with placebo in CHAMPION-NMOSD trial[1]



Zero adjudicated relapses in *Ultomiris* arm over 73.5-week median treatment period

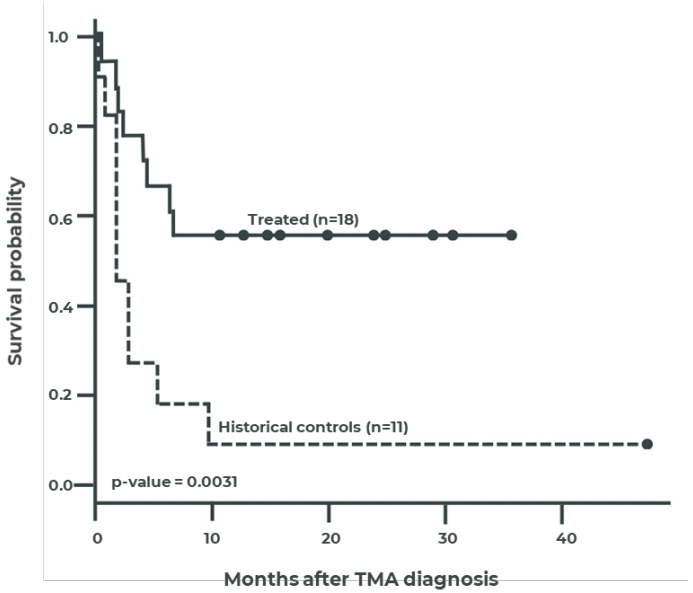
1. Friedemann, Pittock, Barnett, Bennett, Berthele, et al. presented at European Academy of Neurology 2022; June 2022, Vienna. 98.6% reflects model adjusted risk of relapse. HRL = high-level results; NMOSD = neuromyelitis optica spectrum disorder; EU = European Union; CI = confidence interval.

Ultomiris indication expansion will continue

Direct-to-Phase III trials and potential blockbuster opportunities in HSCT-TMA, CSA-AKI

HSCT-TMA

c.80% rate of mortality with no approved medicines



Proof-of-concept established with *Soliris* in HSCT-TMA[1]

Significantly improved survival outcomes vs. historical controls

c.9k diagnosed patients in US, EU5, JP[2]

CSA-AKI

Single-dose *Ultomiris*, pre-surgery has potential to prevent CSA-AKI

1/4
patients
develop AKI post-surgery[2]

60-80%
of mod-to-severe
CKD patients experience AKI post-CPB[2]

AKI post-CPB
can result in increased hospital mortality[2]

Patients with CKD at risk of AKI following CPB[2]

30k	**17k**	**7k**
US	EU5	Japan

Ultomiris potential to be first-and-only medicine for HSCT-TMA, and first-and-only preventative therapy for CSA-AKI

1. Jodele, Dandoy, Lane, et al., "Complement blockade for TA-TMA: lessons learned from a large pediatric cohort treated with eculizumab." "Blood." HSCT-TMA = haematopoietic stem cell transplant-associated thrombotic microangiopathy; 2. Pickering JW, James MT, Palmer SC, "Acute kidney injury and prognosis after cardiopulmonary bypass: a meta-analysis of cohort studies, Am J Kidney Dis. 2015 Feb; 2. Epidemiology data on file; CSA-AKI = cardiac surgery associated-acute kidney injury; TMA = thrombotic microangiopathy; EU5 = France, Germany, Italy, Spain, United Kingdom; Top 8 = US, EU5, JP, CN; AKI = acute kidney injury; CKD = chronic kidney disease; CPB = cardiopulmonary bypass.

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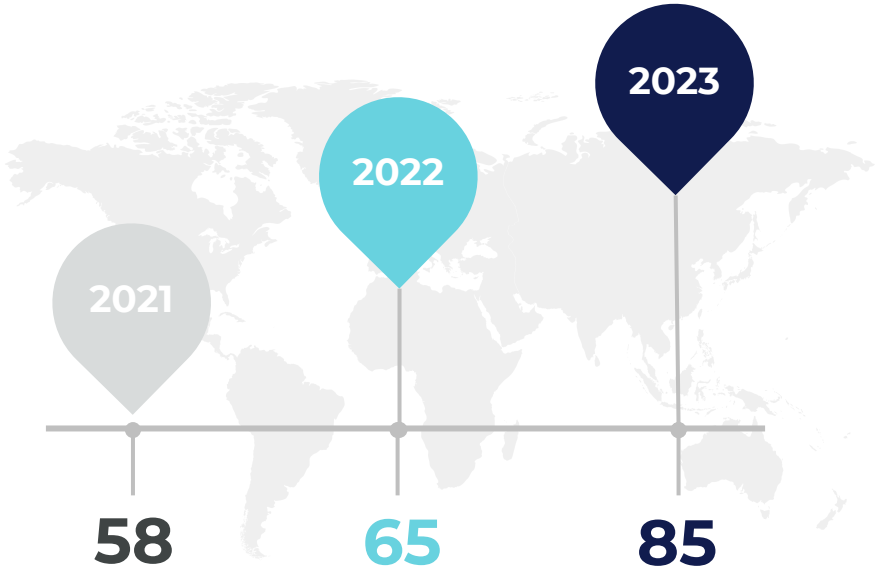
Ultomiris geographic expansion

Significant market expansion underway, demonstrated rapid conversion upon launch

Accelerating pace of *Ultomiris* launches[1] globally

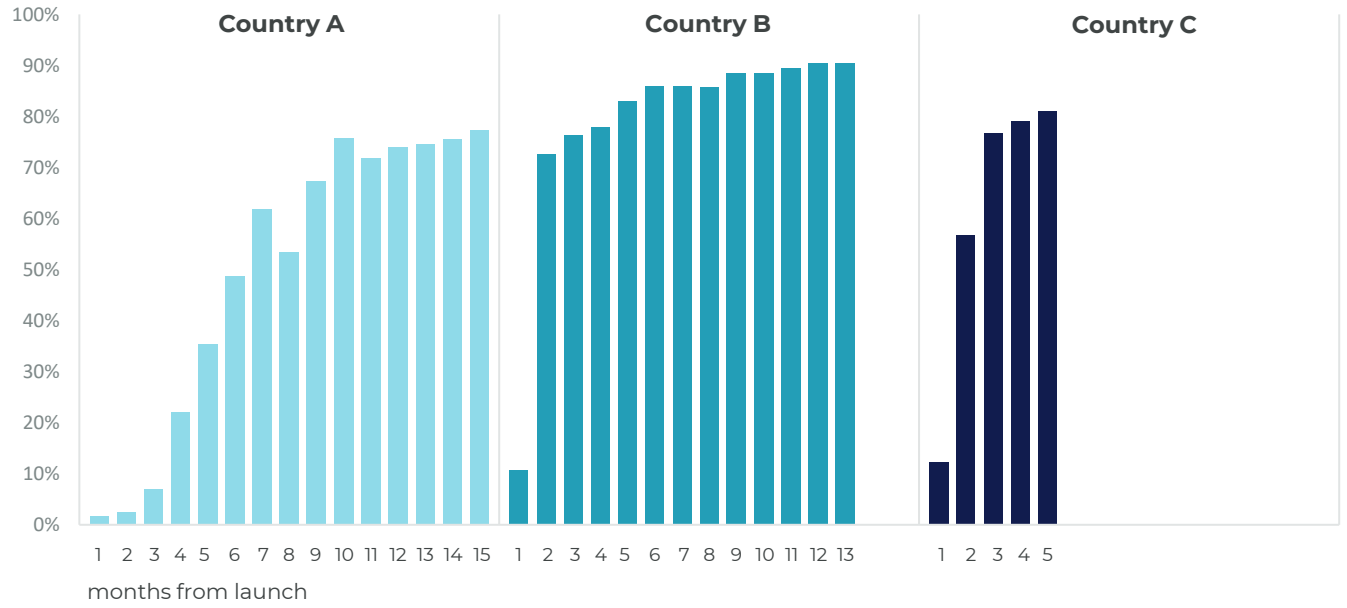


***Ultomiris* in 85 countries by 2023**

Rapid PNH conversion to *Ultomiris* in new country launches

c.80% of PNH patients convert to *Ultomiris* within 12 months of launch[2]

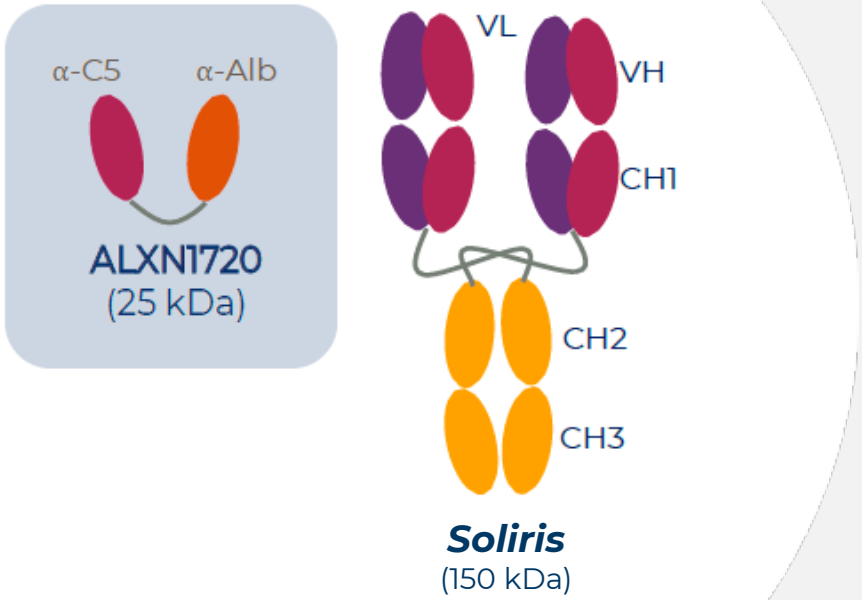
Conversion case study: PNH conversion in three recent country launches



1. Represents total FDA, MAA submissions, total count does not include additional indication submissions; cumulative filing count 2. *Ultomiris* patient share average calculated based on data from Germany, UK, Italy, France and Australia. PNH = paroxysmal nocturnal haemoglobinuria; FDA = Food and Drug Administration; MAA = Marketing Authorisation Application; UK = United Kingdom.

ALXN1720 supports further indication expansion

Third-generation C5 mini-body (V_HH Ab), potential best-in-class SC administration



- Low molecular weight, QW self-admin auto-injector
- Differentiated pricing expands indication opportunities
- Potential best-in-class SC in gMG with potential to capture majority of self-admin market share

ALXN1720 demonstrated strong safety and tolerability profile in Phase I, initiating Phase III in gMG by YE2022

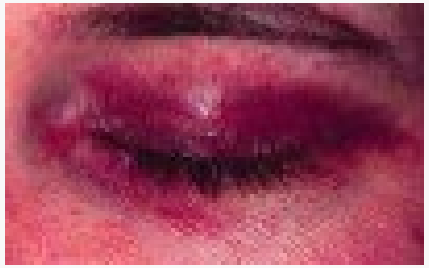
ALXN1720, QW low-volume SC, supporting neurology expansion in gMG[1] and DM

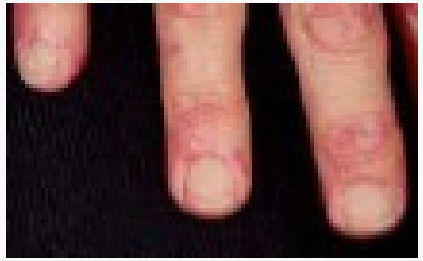
1. Direct to Phase III strategy. V_HH Ab = single domain antibody; SC = subcutaneous; ; QW = once-weekly; self-admin = self-administered; gMG = generalised myasthenia gravis; YE = year-end; DM = dermatomyositis.

C5 inhibition in Dermatomyositis

Potentially first novel mechanism, PoC complement inhibition data underway

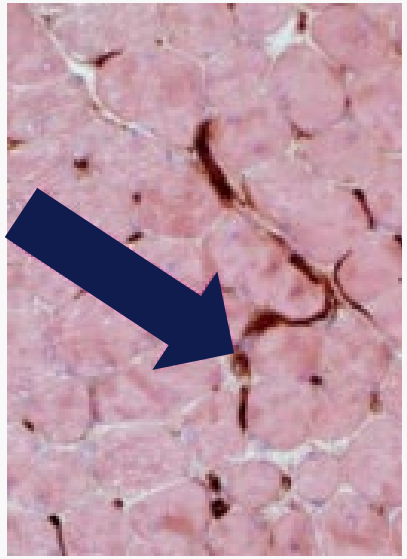
Autoimmune inflammatory myopathy





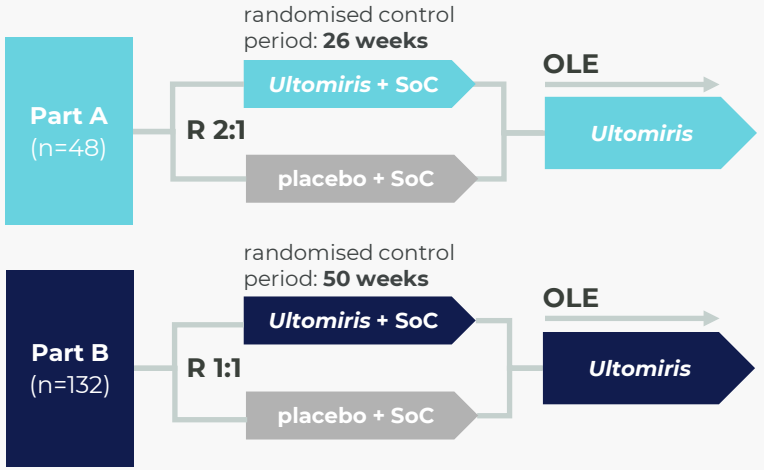
- **Inflammation** causing painful, itchy skin rashes across body
- **Progressive muscular weakness** may lead to respiratory failure and death

Established role of complement



Evidence of MAC deposition in transverse vessel, leading to destruction of muscle fiber

Establishing PoC with *Ultomiris*



***Ultomiris* Phase II/III PoC underway,** with potential to pursue *Ultomiris* and ALXN1720 for commercialisation

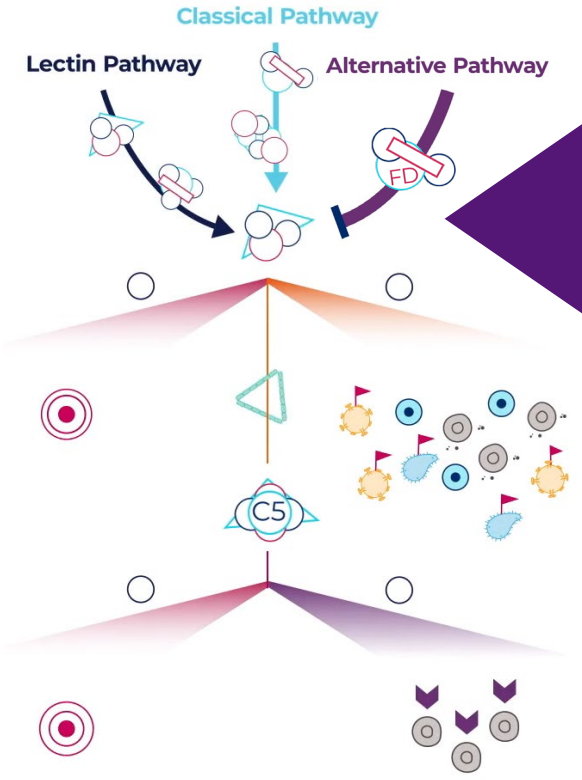
Significant unmet need, limited competition with c.189k diagnosed patients in Top 8 countries

PoC = proof-of-concept; MAC = membrane attack complex; SoC = standard of care; OLE = open-label extension; Top 8 = US, EU5, JP, CN; EU5 = France, Germany, Italy, Spain, United Kingdom.

Expanding into proximal complement (AP) inhibition

Novel small molecule, oral Factor D portfolio with ALXN2040, ALXN2050, ALXN2080

Alternative Pathway (AP) dysregulation triggers uncontrolled cascade of reactions, which may lead to cell destruction and harmful inflammation



Factor D inhibition blocks AP, leaving classical and lectin intact

In vitro analysis of small molecules, ALXN2040 and ALXN2050, demonstrate high affinity for Factor D and significantly reduced complement-mediated haemolysis at low concentrations

Factor D more likely to maintain consistent control than Factor B inhibitors

2.15 µM	0.08 µM
Factor B[1]	**Factor D**[1]
AP only	AP only

- Factor D more tractable target given lower circulating concentration in plasma
- Factor B is an acute phase reactant, circulating levels increase during inflammation

1. Based on human protein concentrations in the plasma; AP = alternative pathway.

Oral Factor D portfolio

Four PoC read-outs over next 18 months, un-gating several Phase III starts

ALXN2040
danicopan

Phase III PNH-EVH add-on underway
Ongoing Phase II trial GA monotherapy

Potential first oral medicine in Geographic Atrophy

ALXN2050
vemircopan

Phase II PNH monotherapy, gMG and renal (LN, IgAN) underway

Positive PoC Phase II PNH monotherapy

ALXN2080

Entering clinic in 2022

Potential application in non-rare indications

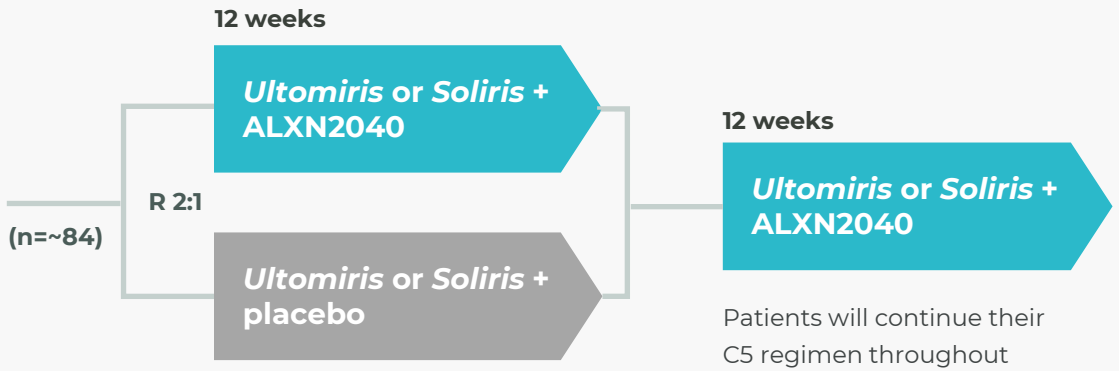
PoC = proof-of-concept; PNH-EVH = paroxysmal nocturnal haemoglobinuria with extravascular haemolysis; GA = geographic atrophy; PNH = paroxysmal nocturnal haemoglobinuria; gMG = generalised myasthenia gravis; LN = lupus nephritis; IgAN = immunoglobulin A nephropathy.

Demonstrated PoC for Factor D inhibitors in PNH

Phase II ALXN2050 PoC in PNH, Phase III ALXN2040 add-on enrollment complete

NEW DATA

Phase III ALXN2040 trial in subset of PNH patients with clinically significant EVH as add-on



Patients will continue their C5 regimen throughout study duration to ensure continued IVH control

Potential to address remaining 10-15% of PNH patients that continue to experience clinically significant EVH

FDA Breakthrough Designation

Phase III fully enrolled, HLR H1 2023

ALXN2050 positive PoC in PNH monotherapy

1. Patients on a C5 inhibitor with anemia and reticulocytes > ULN
2. PNH treatment naïve patients
3. Patients receiving ALXN2040 monotherapy

(n=~26)

12 weeks: ALXN2050

LT extension: ALXN2050

- Robust control of IVH and addresses EVH
- ALXN2050 resulted in 3.9 g/dL increase in Hgb
- Clinically meaningful improvements across haemolysis markers and QoL measures at 12 weeks

Phase II data to be presented at upcoming congress

PoC = proof-of-concept; PNH = paroxysmal nocturnal haemoglobinuria; EVH = extravascular haemolysis; HLR = high-level results; ULN = upper limit of normal; FDA = Food and Drug Administration; LT = long-term; IVH = intravascular haemolysis; Hgb = haemoglobin; QOL = quality of life.

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SELECT INDICATIONS

Portfolio Approach

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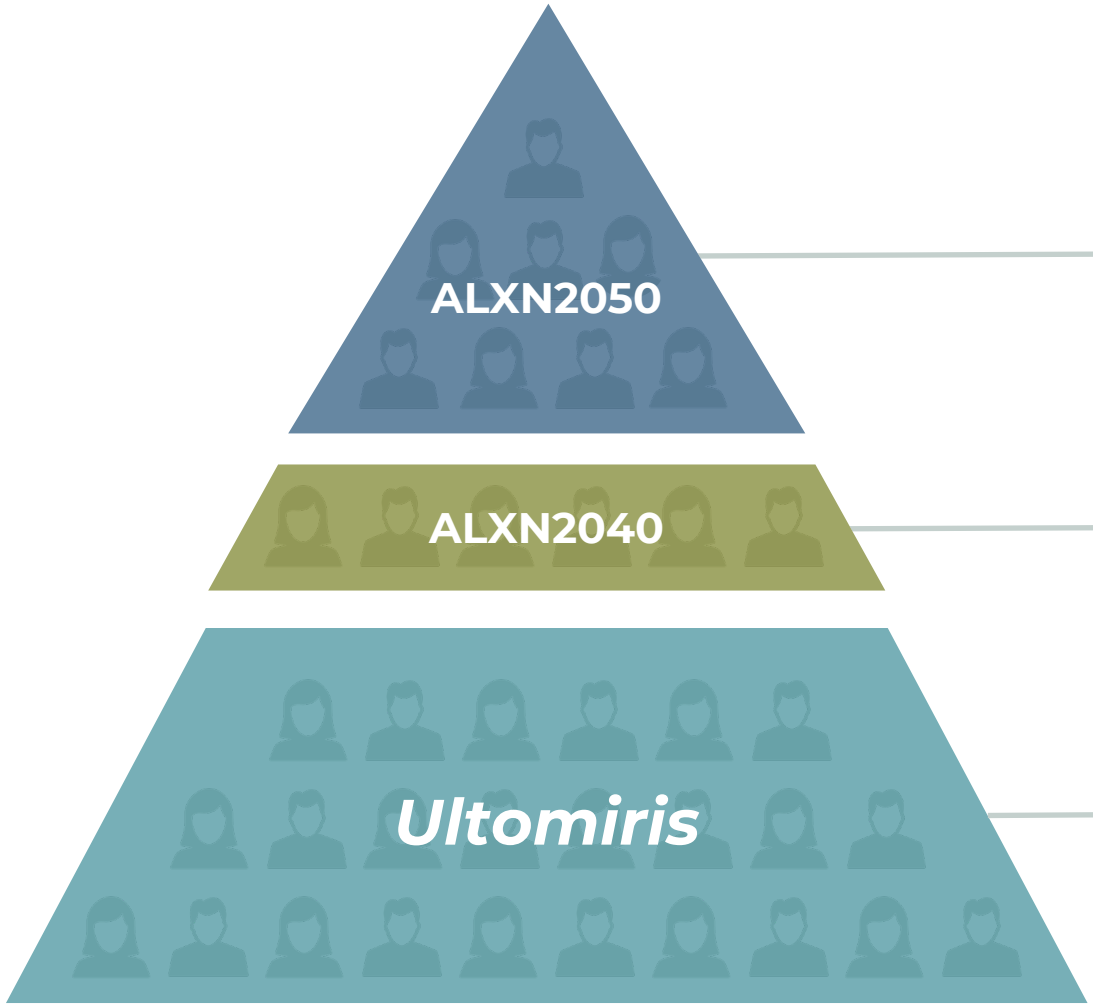
AstraZeneca Rare Disease

Alexion portfolio approach in PNH

PNH market evolution requires multiple modalities to address spectrum of patient needs



ALXN2050 monotherapy addresses subset of PNH patients who prefer and will be compliant on oral

ALXN2040 add-on to C5 inhibitors with potential to address c.10% of patients with clinically significant EVH

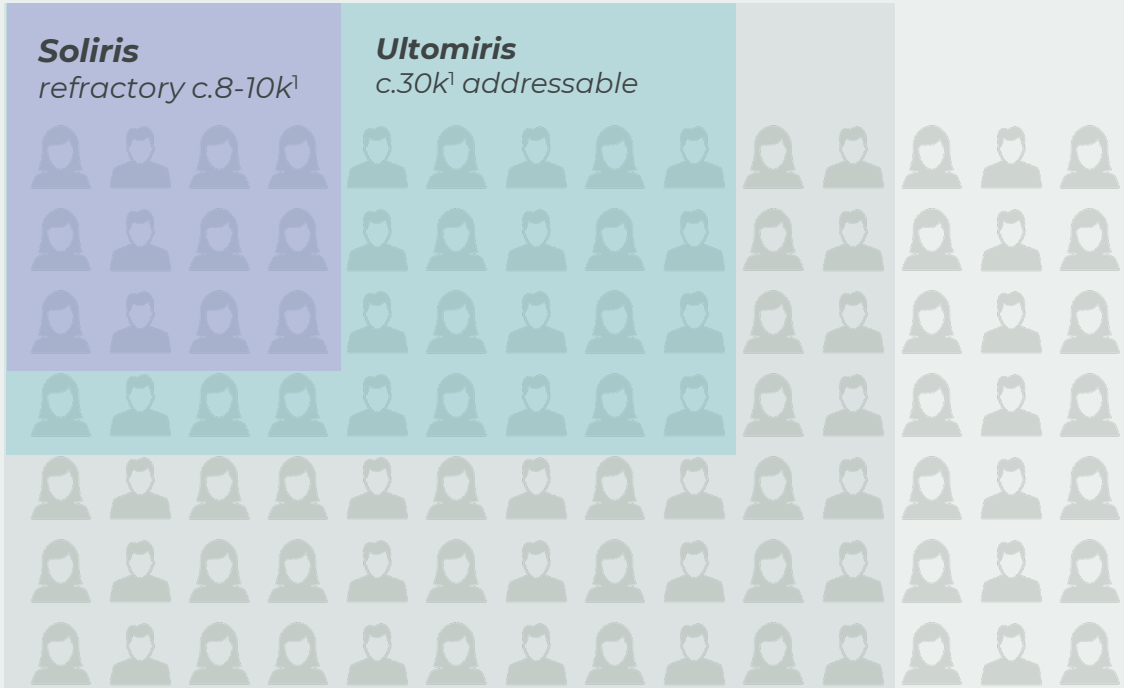
Ultomiris expected to remain standard of care for existing and newly diagnosed PNH patients

PNH = paroxysmal nocturnal haemoglobinuria; EVH = extravascular haemolysis.

Alexion portfolio approach in gMG

Complement inhibitors offer sustained symptom control and disease improvement

gMG portfolio breadth expands addressable patient population[1]



ALXN1720 (QW SC) and ALXN2050 (oral Factor D)
potential to expand further given consistent efficacy, patient-friendly RoA, differentiated pricing

Q2W

Soliris

- SoC for refractory patients
- Proven foundational efficacy of C5 inhibition in gMG

Q8W

Ultomiris

- First branded choice with durable, sustained efficacy
- Improved dosing profile

QW

ALXN1720

Additional, convenient dosing option for improved patient experience

oral

ALXN2050

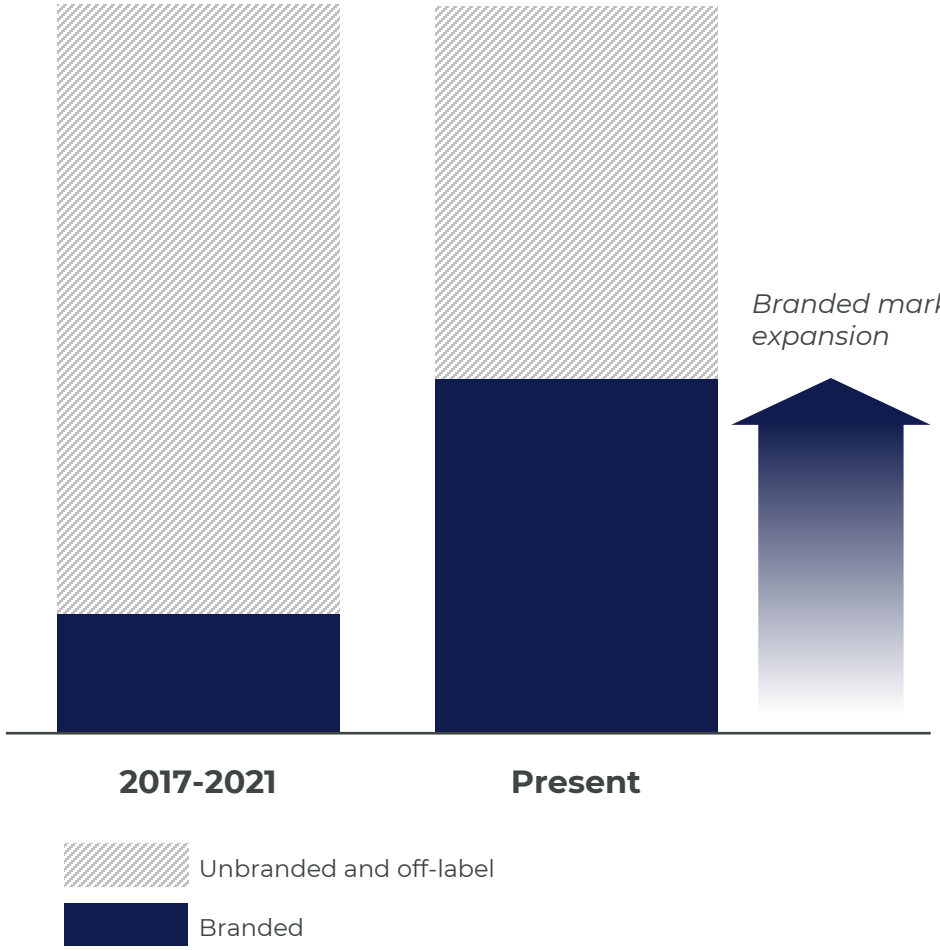
Innovative oral to break IST cycling for less severe patients

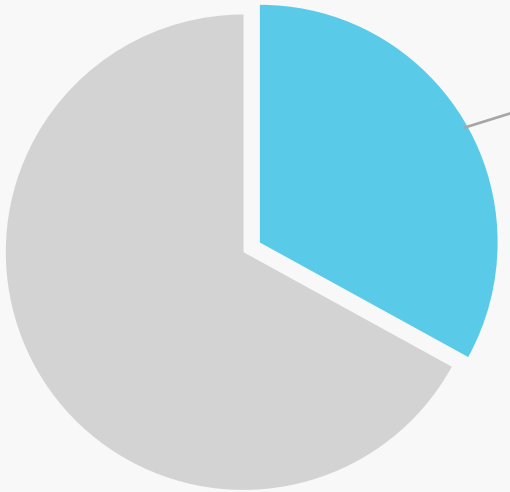
Ultomiris gMG launch underway, ALXN2050 Phase II FPCD

1. US gMG population. gMG = generalised myasthenia gravis; QW = once-weekly; SC = subcutaneous; RoA = route of administration; FPCD = first patient commenced dosed; Q2W = every 2 weeks; Q8W = every 8 weeks; BID = twice-daily; SoC = standard of care; IST = immunosuppressive therapy.

Ultomiris first step to expand reach in gMG

3x addressable patient population[1], new market entrants expand branded market





1/3 of *Ultomiris* utilization since launch from complement naïve patients

***Ultomiris* offers continuous disease control with minimal doses per year, compared to other branded medicines**

1. *Ultomiris* addressable population c.30k patients in the US compared to 8-10k for *Soliris*, due to requirement to fail two prior IST regimens in *Soliris* Phase III REGAIN trial. gMG = generalised myasthenia gravis

Alexion portfolio approach in IgAN and LN

Complement inhibition in renal represents potential multi-blockbuster opportunity

Evidence for the role of alternative and terminal pathways in IgAN

- **Increased levels** of C3 proteolytic fragments associated with IgAN disease progression
- **Urinary C5b-9 elevated** in patients with IgAN
- **In-human PoC** recently presented with terminal pathway inhibition

PoC trials with *Ultomiris* and ALXN2050 in renal indications

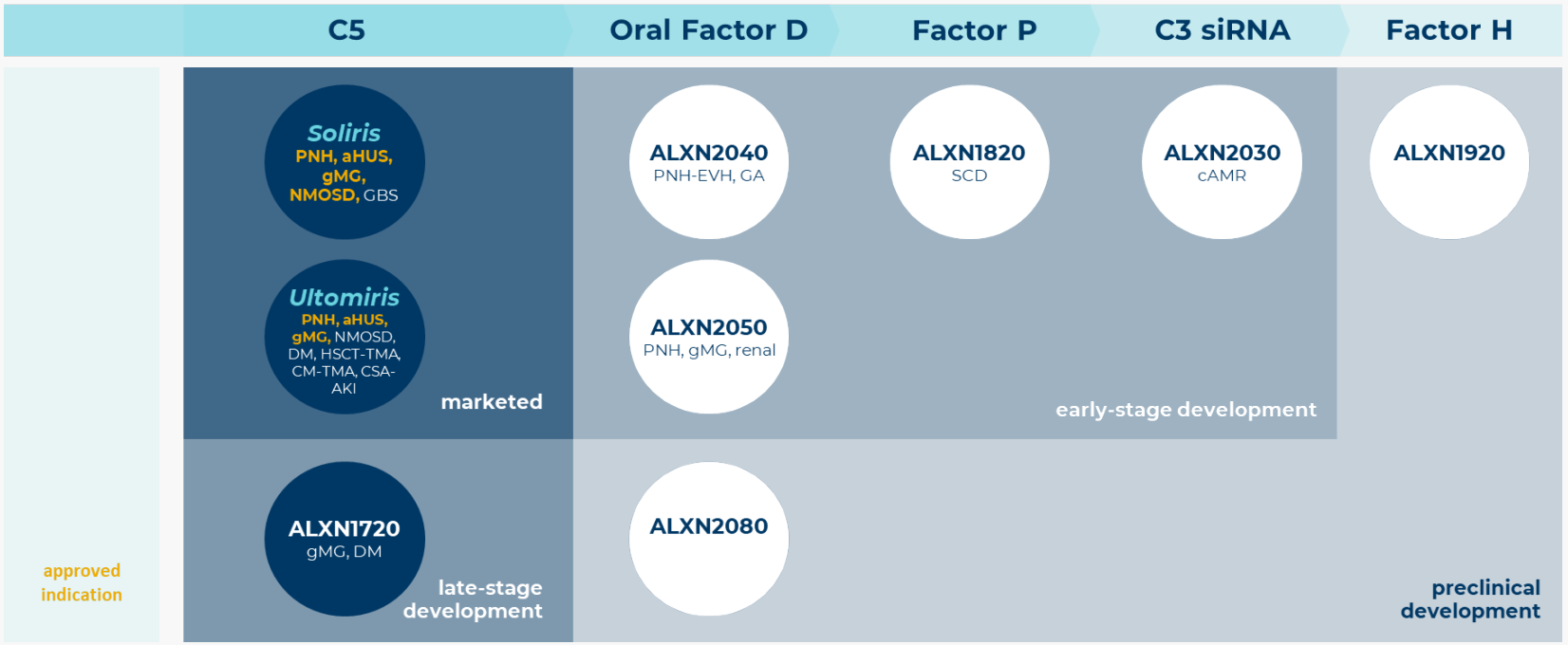
	IgAN	LN[1]
Diagnosed patients (US, EU5, JP)	**>250k**	**>130k**
Treatment landscape	**Lack of approved treatments, significant unmet need**	
Trial status	***Ultomiris* trial achieved 80% enrollment in IgAN and >1/3 enrollment in LN** **ALXN2050 Phase II FPCD in IgAN**	

PoC data will inform Phase III investment decision for either *Ultomiris*, ALXN1720 or ALXN2050

1. Renal class III-IV, with or without class V. IgAN = IgA nephropathy; LN = lupus nephritis; PoC = proof-of-concept; EU5 = France, Germany, Italy, Spain, United Kingdom; FPCD = first patient commenced dosing.

Innovating in new complement frontiers

Multiple novel complement platforms, both established and emerging



Five platforms serving multiple complement-mediated diseases

Range of offerings including orals, biologics and siRNA

LCM portfolio allows for differentiated pricing strategy

Multiple assets across development stages reinforce long-term complement leadership

PNH = paroxysmal nocturnal haemoglobinuria; aHUS = atypical haemolytic uraemic syndrome; gMG = generalised myasthenia gravis; NMOSD = neuromyelitis optica spectrum disorder; GBS = Guillain-Barré syndrome; DM = dermatomyositis; HSCT-TMA = haematopoietic stem cell transplant-associated thrombotic microangiopathy; CM-TMA = complement-mediated thrombotic microangiopathy; CSA-AKI = cardiac surgery-associated acute kidney injury; PNH-EVH = paroxysmal nocturnal haemoglobinuria with extravascular haemolysis; GA = geographic atrophy; SCD = sickle cell disease; siRNA = small interfering RNA; cAMR = chronic antibody-mediated rejection; LCM = lifecycle management.

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BONE
DISEASE &
CARDIOMYOPATHY

Beyond Complement

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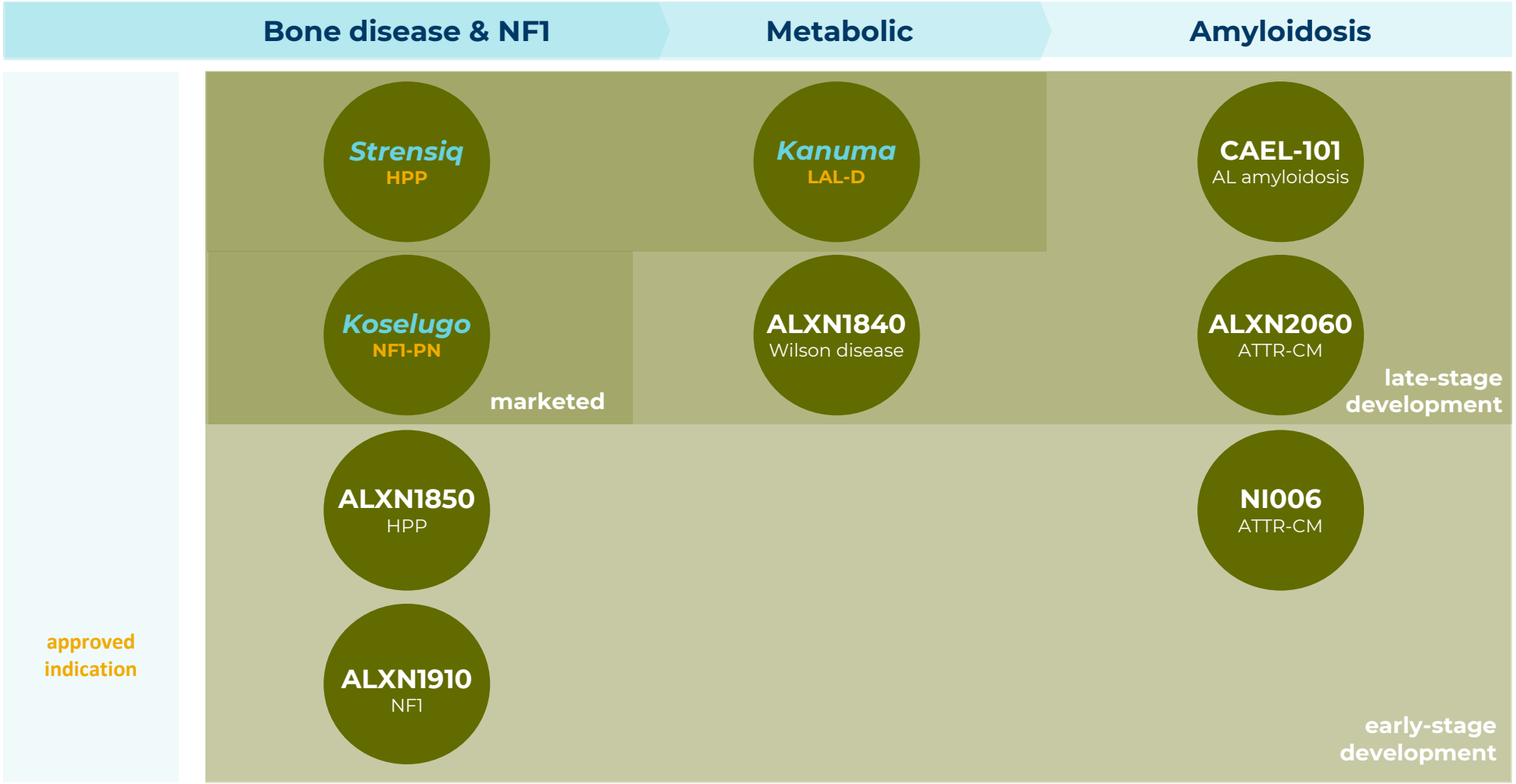
Expanding beyond Complement

Initial expansion in skeletal manifestations and NF1, metabolic and amyloidosis

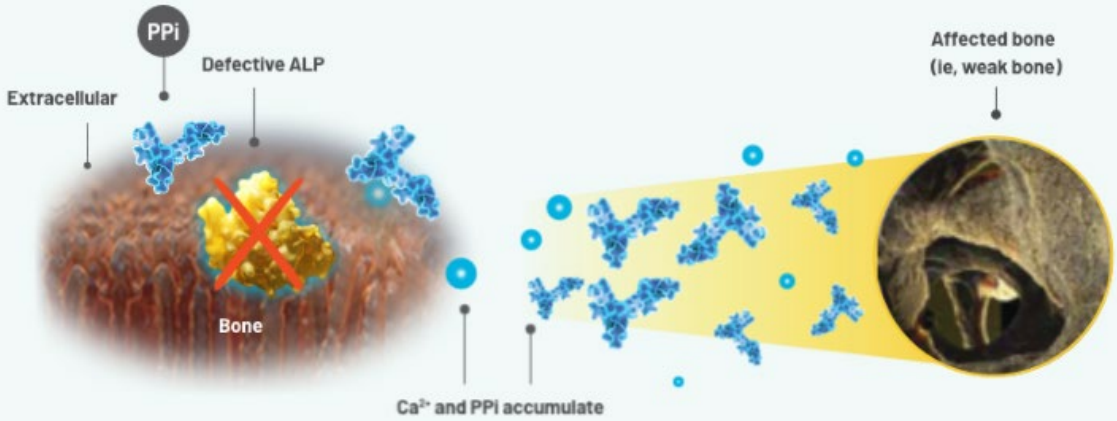


HPP = hypophosphatasia; NF1 = neurofibromatosis type-1 with plexiform neurofibromas; LAL-D = lysosomal acid lipase deficiency; AL amyloidosis = light-chain amyloidosis; ATTR-CM = transthyretin amyloid cardiomyopathy.

Hypophosphatasia

Strensiq is standard of care, foundational ERT for HPP patients

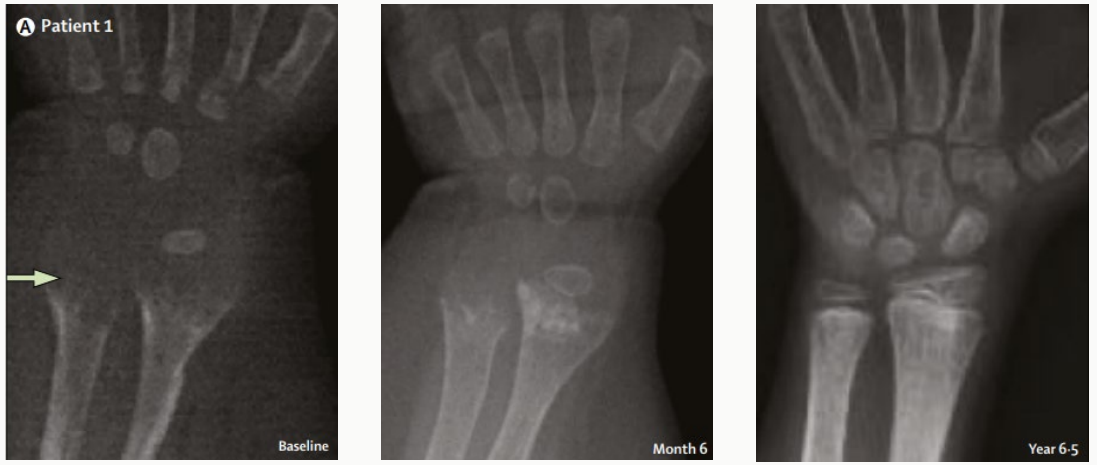
Inherited metabolic disorder characterised by ALP deficiency



- **Mutations** in ALPL gene cause low ALP activity
- **PPi** accumulates and prevents bone mineralization, resulting in skeletal defects and multi-systemic complications
- **HPP is an ultra-rare disease**, defined as <6,000 in US

Clinical manifestations of HPP

Radiographic changes from baseline to year 6.5 in patients treated with ***Strensiq***

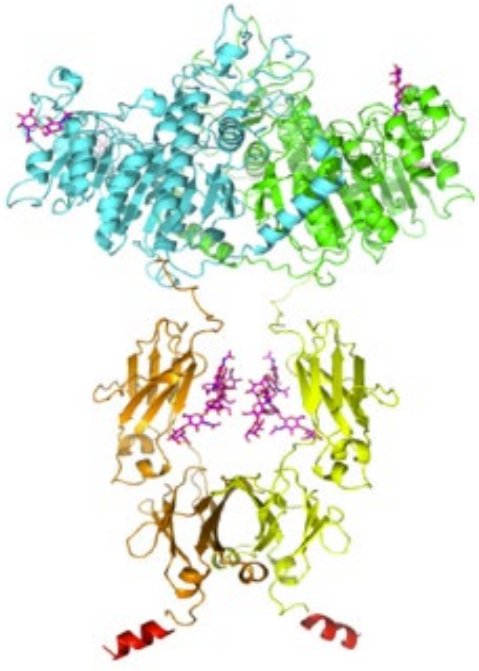


Strensiq replaces deficient tissue-nonspecific ALP (TNSALP) enzyme to enable bone mineralisation

ERT = enzyme replacement therapy; HPP = hypophosphatasia; ALP = alkaline phosphatase; PPi = inorganic pyrophosphate; ALPL = TNSALP production gene; TNSALP = tissue-nonspecific ALP.

ALXN1850: next-generation HPP

Patient-centered innovation, optimised molecule to extend half-life, less frequent dosing



ALXN1850

- Longer half-life, less frequent QW SC dosing
- Improved PK
- Increased enzymatic activity
- Higher bioavailability
- Higher in-vivo exposure
- Improved manufacturing process

Planning to initiate Phase III trial in 2023

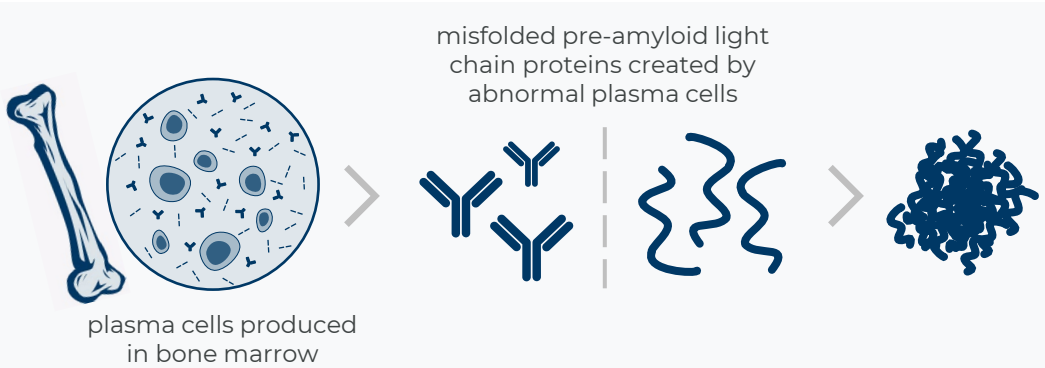
1. Increase in addressable population driven by expanded indication of ALXN1850 to include patients with adult-onset HPP (vs perinatal/infantile and juvenile onset only with *Strensiq* (ex-JP)) HPP = hypophosphatasia; QW = once-weekly; SC = subcutaneous; PK = pharmacokinetics.

Amyloidosis

Progressive accumulation of toxic amyloid fibrils in tissues and organs

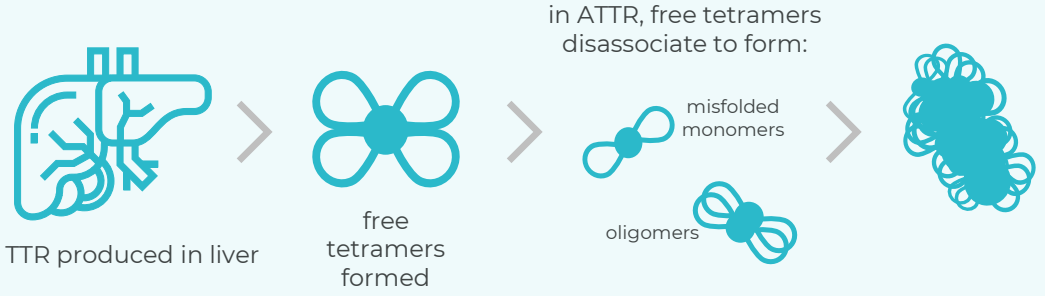
AL amyloidosis: fatal disease caused by the deposition of light chain amyloid fibrils, leading to multiorgan dysfunction and failure

- Primarily impacts kidney and heart in **>60% of patients**
- Median OS in most severe stage (IIIb) is **4 months**



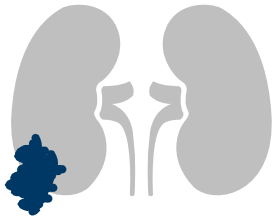
ATTR amyloidosis: fatal disease caused by the deposition of TTR amyloid fibrils, leading to cardiomyopathy and polyneuropathy

- With a cardiopathy, life expectancy **1-5 years** with only **1-2 years NYHA class III-IV patients**

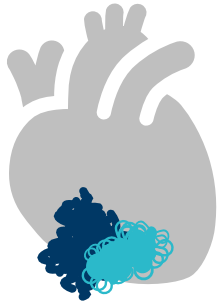


amyloid deposition

primarily impacting:



kidneys and/or heart



Amyloid deposition leads to progressive organ damage or failure that can ultimately be fatal

AL amyloidosis = light-chain amyloidosis; OS = overall survival; ATTR amyloidosis = transthyretin amyloidosis; TTR = transthyretin; NYHA = New York Heart Association.

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Amyloidosis portfolio strategy

CAEL-101, NI006 novel mAb depleters designed to bind and clear amyloid fibrils

AL amyloidosis

45k Top 8

c.20k US, EU5

CAEL-101
AL-CM

Phase III programme enrollment ongoing

ATTR-CM

274k Top 8

44k US, 39k EU5

NI006
ATTR-CM

Planning to initiate Phase III 2023

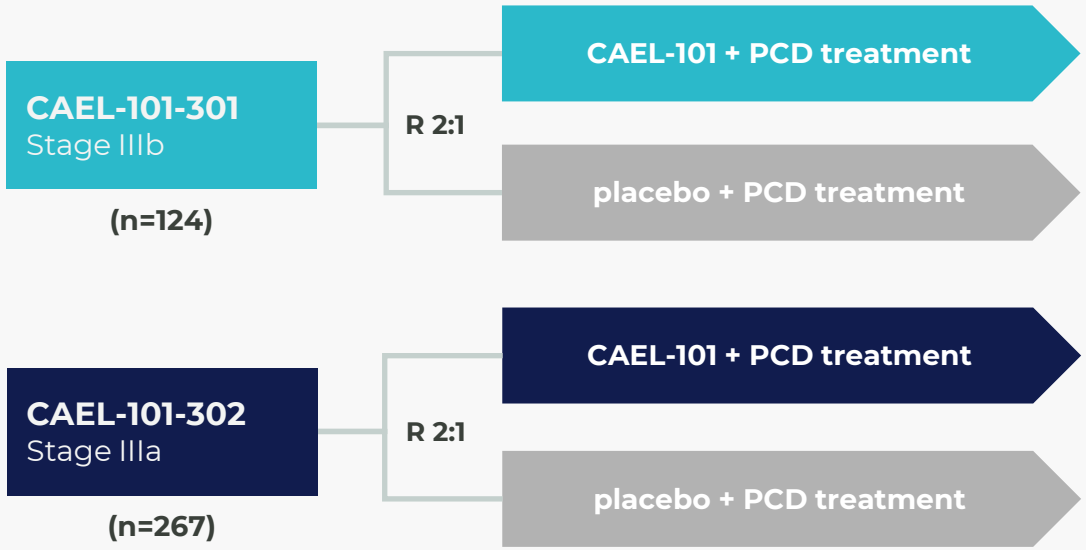
Ability to clear toxic fibril deposition in tissues may reverse course of disease

mAB = monoclonal antibody; AL Amyloidosis = light chain amyloidosis, Top 8 = US, EU5, JP, CN; EU5 = France, Germany, Italy, Spain, United Kingdom; AL-CM = light-chain amyloid cardiomyopathy; ATTR-CM = transthyretin amyloid cardiomyopathy.

CAEL-101 in AL amyloidosis

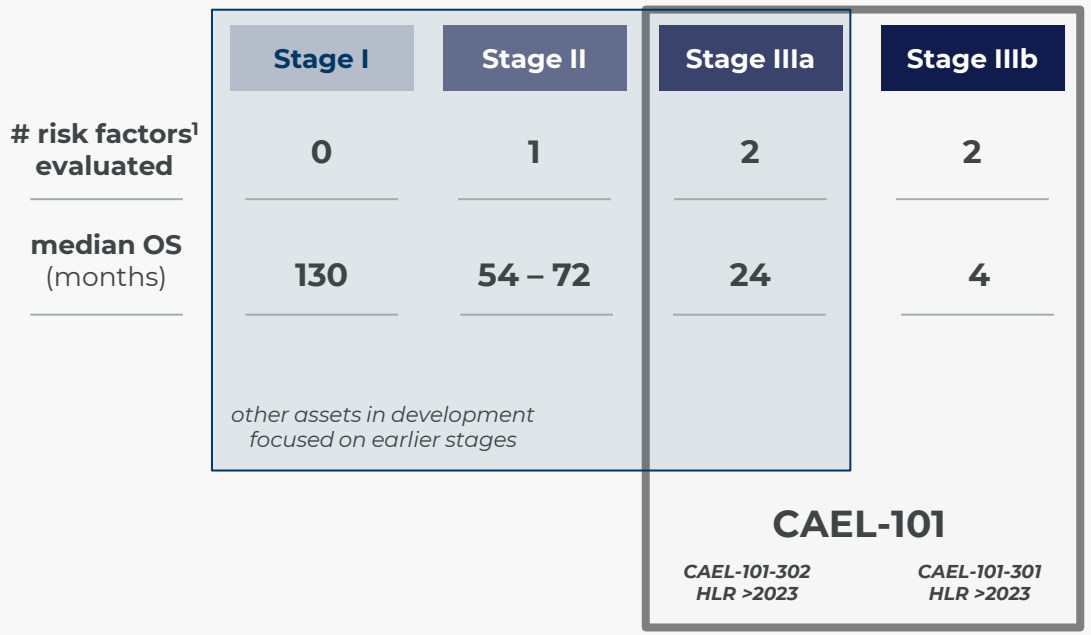
Tailored to address mortality cause by removing amyloid fibrils, improving overall survival

Phase III CAEL-101 twin study



Minimum 12-month active treatment QW IV infusions for 4 weeks, then Q2W

Designed to show overall survival benefit given CAEL-101 targeted MoA to bind and clear amyloid fibrils

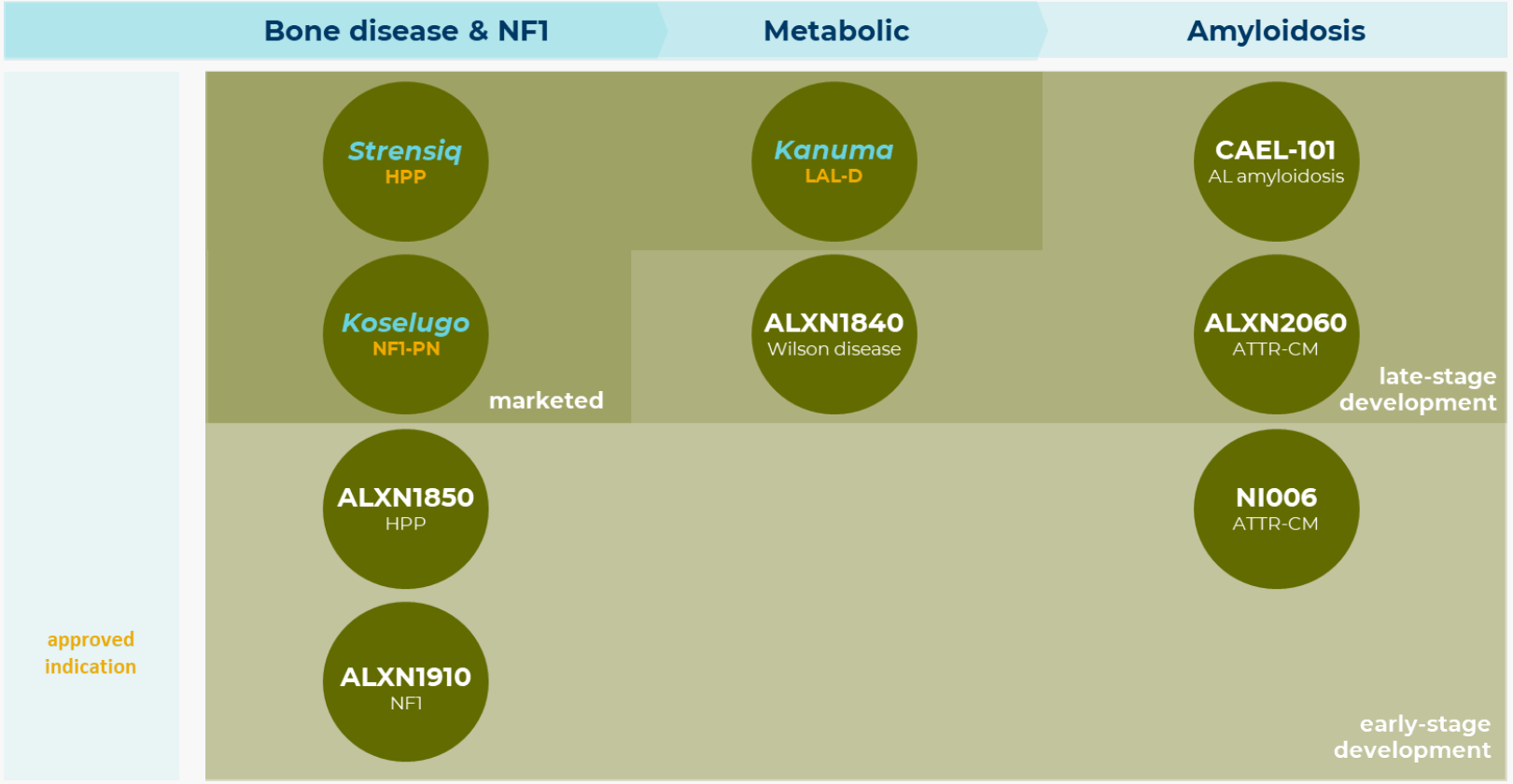


First-and-only medicine for both Stage IIIa and IIIb AL amyloidosis patients

1. Risk factors include cTnT and NT-proBNP. AL amyloidosis = light-chain amyloidosis; PCD = plasma cell dyscrasia; QW = once-weekly; IV = intravenous; Q2W = every 2 weeks; MoA = mechanism of action; OS = overall survival; HLR = high-level results.

Expanding beyond Complement

Initial expansion opportunities in skeletal manifestations, metabolic and amyloidosis



Strensiq in HPP is $1bn+ franchise and growing

Opportunity to expand geographic reach in HPP with ALXN1850

Novel amyloid fibril depleters with CAEL-101, NI006

Opportunity to treat range of NF1 patients with Koselugo and NF1 patients with skeletal manifestations with ALXN1910

HPP = hypophosphatasia; NF1 = neurofibromatosis type-1 with plexiform neurofibromas; LAL-D = lysosomal acid lipase deficiency; AL amyloidosis = light-chain amyloidosis; ATTR-CM = transthyretin amyloid cardiomyopathy.

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GEOGRAPHIC

Expansion

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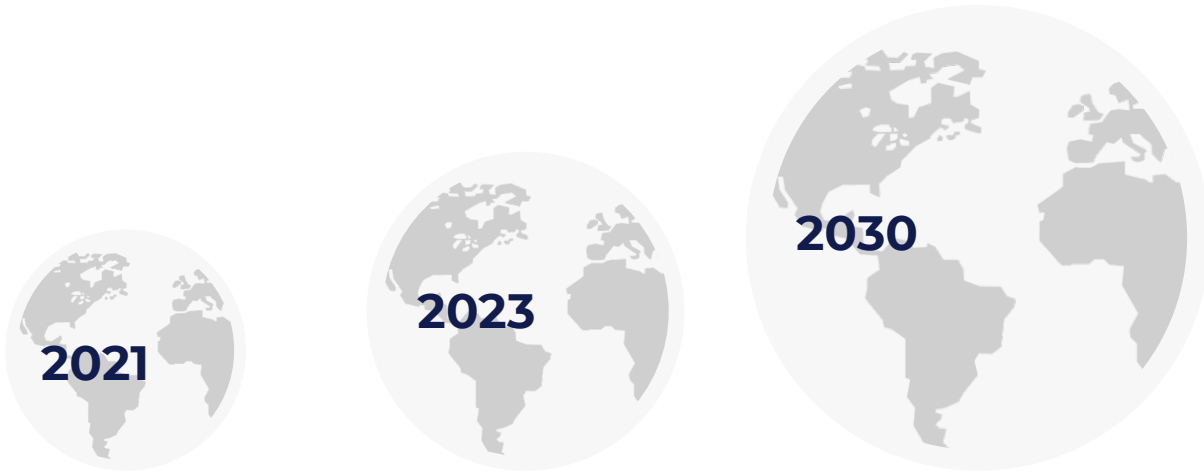
Geographic expansion

Ambition to expand direct presence into nearly 100 countries by 2030

Leveraging AstraZeneca's geographic footprint to enable rapid expansion, predominantly in EM[1]



20 countries

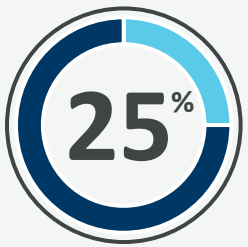
>40 countries

c.100 countries

Emerging Markets represent significant growth opportunity to 2030

High-teens % CAGR

for EM revenues to **2030**



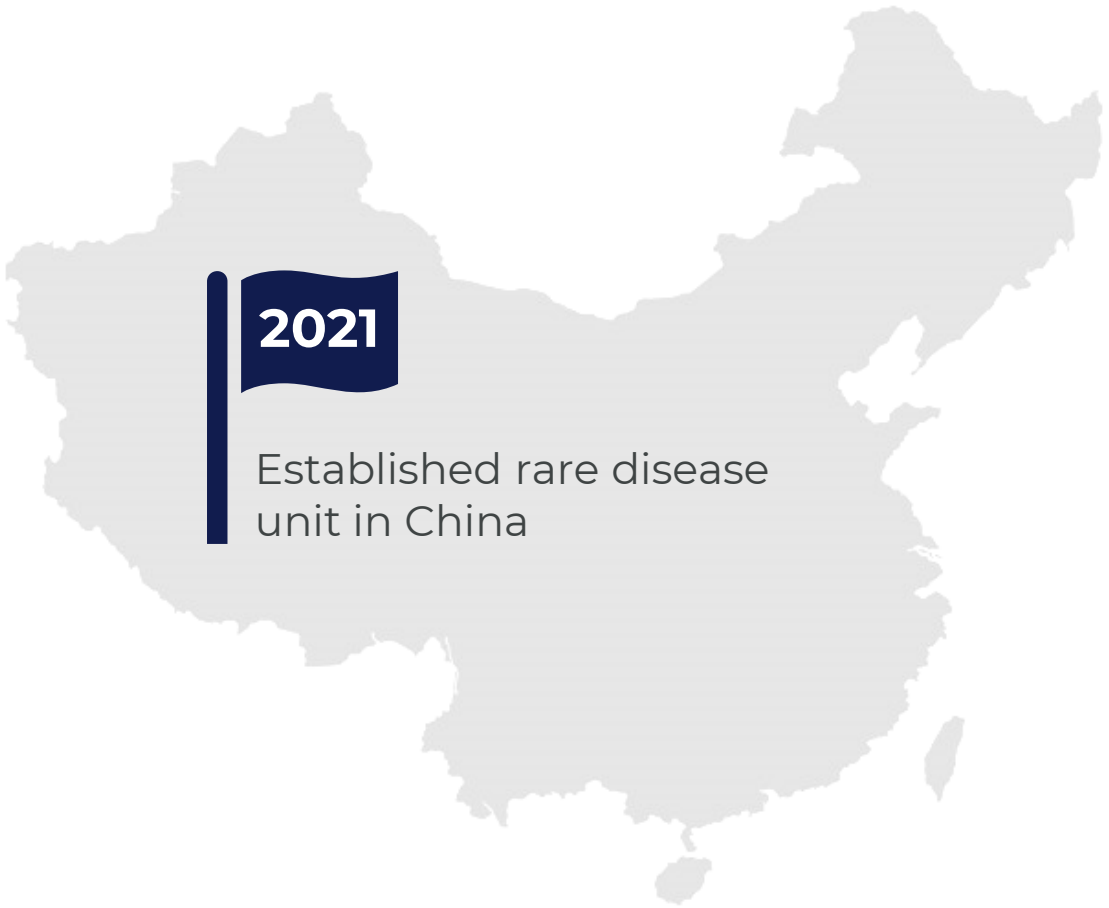
c.25% of international[2] revenue

comes from EM by **2030**

1. Reflects direct market presence. 2. International excludes US and Japan. EM = Emerging Markets; CAGR = compound annual growth rate.

China represents significant opportunity for rare disease

Ambition to launch 10 trials with 10 potential approvals by 2028



2021

Established rare disease unit in China

Complement

PNH	Soliris	2023 Approval[1]
	ALXN2050	
aHUS	Soliris	2023 Approval[1]
gMG	Soliris	2023 Approval
	ALXN2050	
	ALXN1720	
NMOSD	Soliris	2023 Approval

Beyond Complement

Amyloidosis	CAEL-101
HPP	Strensiq
	ALXN1850

1. In final stages of approval. PNH = paroxysmal nocturnal haemoglobinuria; aHUS = atypical haemolytic uraemic syndrome; gMG = generalised myasthenia gravis; NMOSD = neuromyelitis optica spectrum disorder; HPP = hypophosphatasia.

ORGANIC INNOVATION

Scientific Bridges

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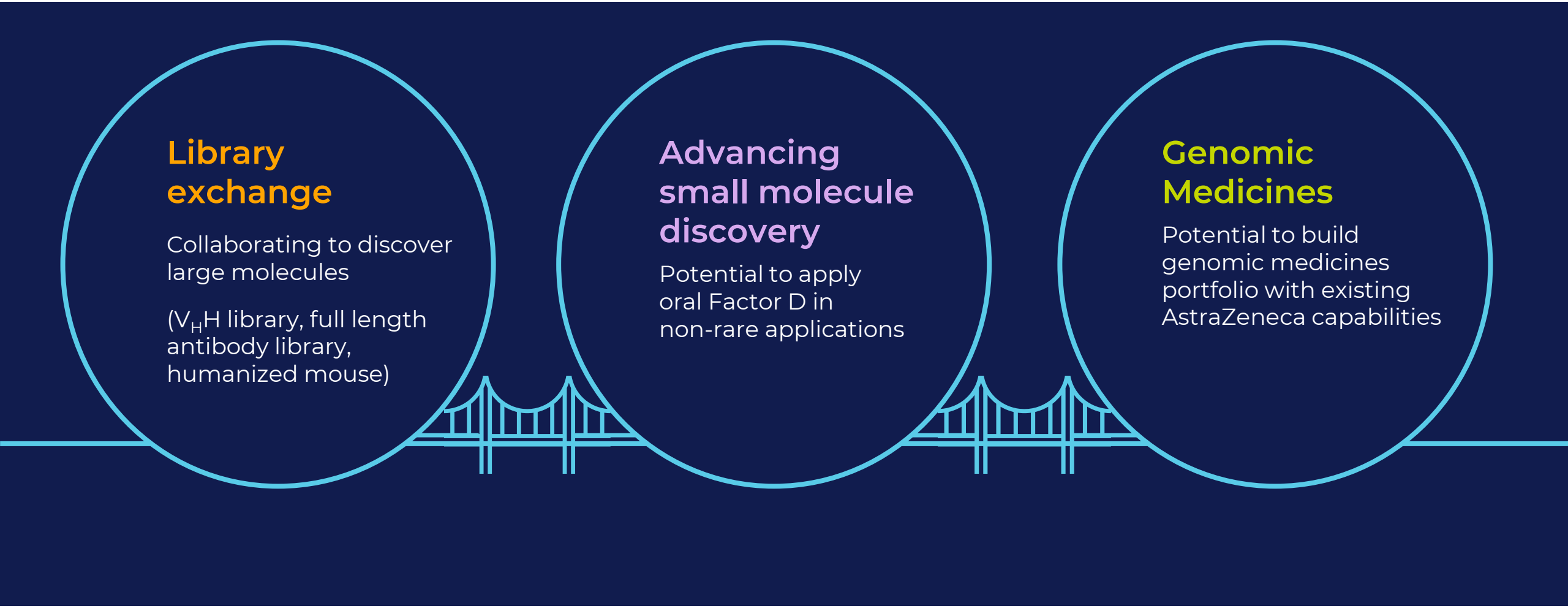
Accelerating discovery and research

Scientific bridges enable collaboration across Alexion and AstraZeneca

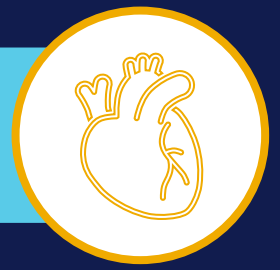


V_HH = single domain antibody.

Three genomic medicine projects underway

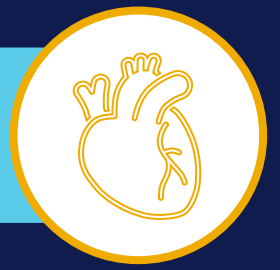
Leveraging existing AstraZeneca capabilities and applying to rare disease

Gene therapy



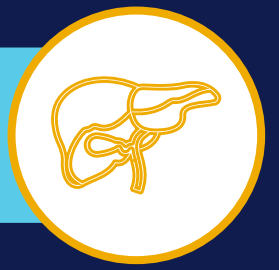
- Novel AZN AAV capsids
- In-house promoters

Antisense oligonucleotides



- Innovative ASO-mediated exon skipping

Gene editing



- AstraZeneca proprietary CRISPR platform
- Superior safety profile

AZN = AstraZeneca; AAV = adeno-associated virus; ASO = antisense oligonucleotides; CRISPR = clustered regularly interspaced short palindromic repeats.

CLOSING

Summary

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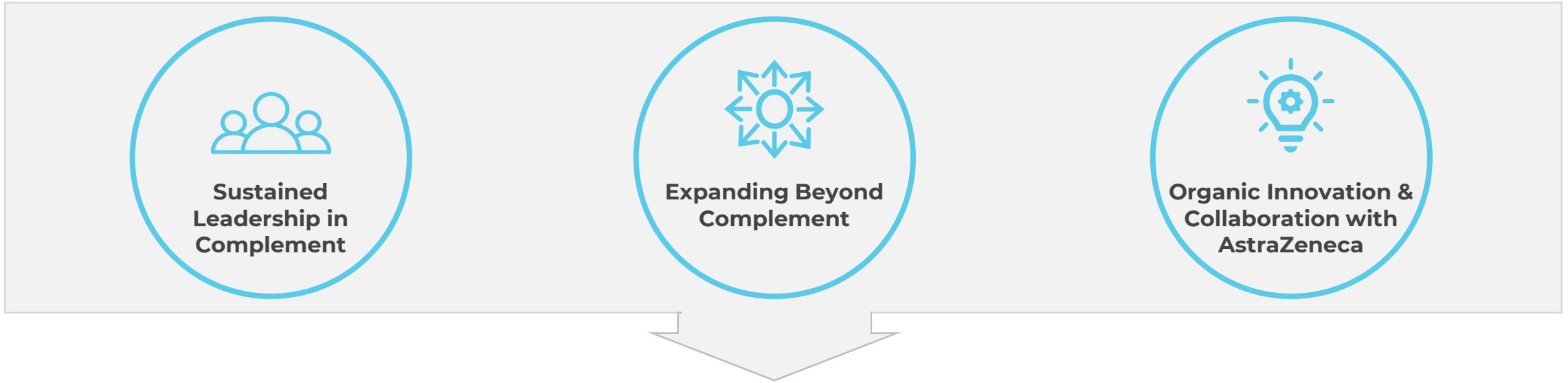
Alexion, AstraZeneca Rare Disease

Supporting AstraZeneca's industry-leading growth profile, delivering pioneering science



Alexion by 2030

- **>5 NME launches**
- **5-6x patient growth across portfolio**
- **Expand into c.100 countries, Emerging Market high-teens % revenue CAGR**
- **Leading rare disease company by 2027[1]**

1. Based on EvaluatePharma revenue projections for all companies (orphan non-oncology sales); NME = new molecular entity; CAGR = compound annual growth rate.

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RARE DISEASE
INVESTOR EVENT

Q&A Session

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Marc Dunoyer
Chief Executive Officer,
Alexion

Gianluca Pirozzi
SVP, Head of
Development & Safety

Scott Weintraub
VP, Global Marketing &
Commercial Strategy

Sharon Barr
SVP, Head of Research
& Product Development

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