



# Rare Disease: Amgen's Newest Therapeutic Area Pillar to Drive Long-Term Growth

February 22, 2024

**AMGEN**

# SAFE HARBOR STATEMENT

This presentation contains forward-looking statements that are based on the current expectations and beliefs of Amgen. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including any statements on the outcome, benefits and synergies of collaborations, or potential collaborations, with any other company (including BeiGene, Ltd. or Kyowa Kirin Co., Ltd.), the performance of Otezla® (apremilast) (including anticipated Otezla sales growth and the timing of non-GAAP EPS accretion), our acquisitions of Teneobio, Inc., ChemoCentryx, Inc., or Horizon Therapeutics plc (including the prospective performance and outlook of Horizon's business, performance and opportunities, any potential strategic benefits, synergies or opportunities expected as a result of such acquisition, and any projected impacts from the Horizon acquisition on our acquisition-related expenses going forward), as well as estimates of revenues, operating margins, capital expenditures, cash, other financial metrics, expected legal, arbitration, political, regulatory or clinical results or practices, customer and prescriber patterns or practices, reimbursement activities and outcomes, effects of pandemics or other widespread health problems on our business, outcomes, progress, and other such estimates and results. Forward-looking statements involve significant risks and uncertainties, including those discussed below and more fully described in the Securities and Exchange Commission reports filed by Amgen, including our most recent annual report on Form 10-K and any subsequent periodic reports on Form 10-Q and current reports on Form 8-K. Unless otherwise noted, Amgen is providing this information as of the date of this presentation and does not undertake any obligation to update any forward-looking statements contained in this document as a result of new information, future events or otherwise.

No forward-looking statement can be guaranteed and actual results may differ materially from those we project. Our results may be affected by our ability to successfully market both new and existing products domestically and internationally, clinical and regulatory developments involving current and future products, sales growth of recently launched products, competition from other products including biosimilars, difficulties or delays in manufacturing our products and global economic conditions. In addition, sales of our products are affected by pricing pressure, political and public scrutiny and reimbursement policies imposed by third-party payers, including governments, private insurance plans and managed care providers and may be affected by regulatory, clinical and guideline developments and domestic and international trends toward managed care and healthcare cost containment. Furthermore, our research, testing, pricing, marketing and other operations are subject to extensive regulation by domestic and foreign government regulatory authorities. We or others could identify safety, side effects or manufacturing problems with our products, including our devices, after they are on the market. Our business may be impacted by government investigations, litigation and product liability claims. In addition, our business may be impacted by the adoption of new tax legislation or exposure to additional tax liabilities. If we fail to meet the compliance obligations in the corporate integrity agreement between us and the U.S. government, we could become subject to significant sanctions. Further, while we routinely obtain patents for our products and technology, the protection offered by our patents and patent applications may be challenged, invalidated or circumvented by our competitors, or we may fail to prevail in present and future intellectual property litigation. We perform a substantial amount of our commercial manufacturing activities at a few key facilities, including in Puerto Rico, and also depend on third parties for a portion of our manufacturing activities, and limits on supply may constrain sales of certain of our current products and product candidate development. An outbreak of disease or similar public health threat, such as COVID-19, and the public and governmental effort to mitigate against the spread of such disease, could have a significant adverse effect on the supply of materials for our manufacturing activities, the distribution of our products, the commercialization of our product candidates, and our clinical trial operations, and any such events may have a material adverse effect on our product development, product sales, business and results of operations. We rely on collaborations with third parties for the development of some of our product candidates and for the commercialization and sales of some of our commercial products. In addition, we compete with other companies with respect to many of our marketed products as well as for the discovery and development of new products. Discovery or identification of new product candidates or development of new indications for existing products cannot be guaranteed and movement from concept to product is uncertain; consequently, there can be no guarantee that any particular product candidate or development of a new indication for an existing product will be successful and become a commercial product. Further, some raw materials, medical devices and component parts for our products are supplied by sole third-party suppliers. Certain of our distributors, customers and payers have substantial purchasing leverage in their dealings with us. The discovery of significant problems with a product similar to one of our products that implicate an entire class of products could have a material adverse effect on sales of the affected products and on our business and results of operations. Our efforts to collaborate with or acquire other companies, products or technology, and to integrate the operations of companies or to support the products or technology we have acquired, may not be successful. There can be no guarantee that we will be able to realize any of the strategic benefits, synergies or opportunities arising from the Horizon acquisition, and such benefits, synergies or opportunities may take longer to realize than expected. We may not be able to successfully integrate Horizon, and such integration may take longer, be more difficult or cost more than expected. A breakdown, cyberattack or information security breach of our information technology systems could compromise the confidentiality, integrity and availability of our systems and our data. Our stock price is volatile and may be affected by a number of events. Our business and operations may be negatively affected by the failure, or perceived failure, of achieving our environmental, social and governance objectives. The effects of global climate change and related natural disasters could negatively affect our business and operations. Global economic conditions may magnify certain risks that affect our business. Our business performance could affect or limit the ability of our Board of Directors to declare a dividend or our ability to pay a dividend or repurchase our common stock. We may not be able to access the capital and credit markets on terms that are favorable to us, or at all.

# Rare Disease Overview



# Advancing Our Mission to Serve Patients Across Four Pillars of Growth

GENERAL  
MEDICINE



ONCOLOGY



INFLAMMATION



RARE DISEASE



Marketed Products  
Innovative Pipeline  
Biosimilars





# Rare Disease Is a Strong Strategic Fit for Amgen

<b>Balanced Portfolio</b>	<ul style="list-style-type: none"><li>• Strengthens and balances Amgen's portfolio of first-in-class / best-in-class innovative medicines</li></ul>
<b>Commercial Capabilities</b>	<ul style="list-style-type: none"><li>• Leverages Amgen's global scale and decades of leadership in inflammation and nephrology</li></ul>
<b>Scientific Capabilities</b>	<ul style="list-style-type: none"><li>• Leverages Amgen's R&amp;D and manufacturing capabilities on a portfolio still early in its lifecycle</li></ul>
<b>Attractive Financial Profile</b>	<ul style="list-style-type: none"><li>• Robust combined cash flow enables sustained investment in innovation, on-schedule deleveraging, and growing dividend</li><li>• Additive to long-term revenue growth; accretive to non-GAAP earnings in 2024</li></ul>

# Rare Disease Business Anchored by Four Highly Innovative, Early-in-Lifecycle Medicines



**TEPEZZA**  
teprotumumab-trbw

**Only** thyroid eye disease (TED) treatment

**KRYSTEXXA**  
pegloticase

**First and only** uncontrolled gout treatment

**UPLIZNA**  
inebilizumab-cdon

**Fastest-growing biologic** in neuromyelitis optica spectrum disorder

**TAVNEOS**  
(avacopan)

**Only complement inhibitor** for ANCA-associated vasculitis

**INTERNATIONAL EXPANSION AND INNOVATIVE PIPELINE PROVIDE INCREMENTAL GROWTH OPPORTUNITIES**

ANCA = anti-neutrophil cytoplasmic antibody.

Provided February 22, 2024, as part of an oral presentation and is qualified by such, contains forward-looking statements, actual results may vary materially; Amgen disclaims any duty to update.



# Rare Diseases Require a Different Approach

- ~10,000 rare diseases, but only 5% have approved medicines<sup>1</sup>
- Low disease awareness and difficult to identify patients
- Challenges encountered with misdiagnosis, limited options, and insurance barriers
- Dedicated patient support needed through the duration of therapy, not just the onset
- Developing Rare Disease medicines requires unique insights

*“Rare Disease is in need of new champions and prioritization to help drive progress and to radically change patients' lives. Amgen, with its history in research and fearless drive for innovation, is perfectly positioned to create meaningful impact for rare patients and their families. The work being done is critical and much needed.”*

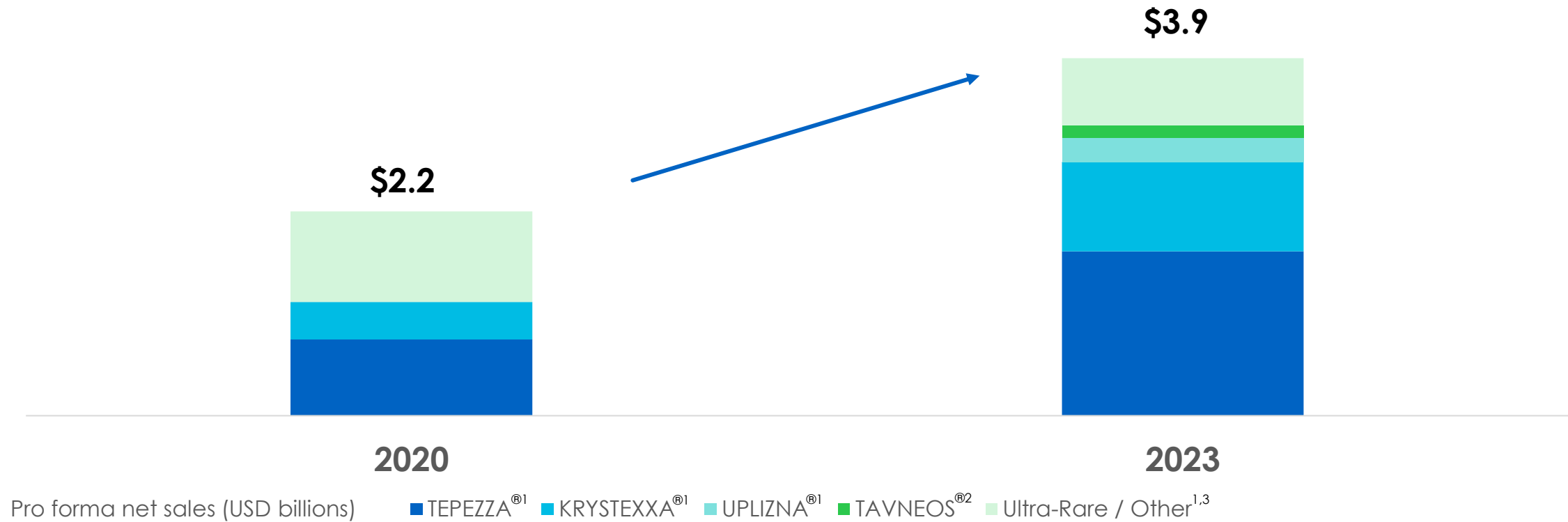
*–Nicole Boice, Founder and Chief Mission Officer, Global Genes*



1. National Organization for Rare Diseases (NORD) (<https://rarediseases.org/rare-diseases/>).

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# Rare Disease Products Generating Strong Growth, With Opportunities to Expand in the U.S. and Internationally



**INNOVATIVE PIPELINE WILL ALSO BE ADDITIVE TO LONG-TERM GROWTH**

1. FY'20 and H1'23 net sales based on Horizon Therapeutics, Plc, SEC filings; 2H'23 net sales information from Amgen earnings call webcasts on October 31, 2023 and February 6, 2024.

2. Based on disclosures in Amgen's 10-K for the year ended December 31, 2023.

3. Consists of ACTIMMUNE<sup>®</sup>, BUPHENYL<sup>®</sup>, DUEXIS<sup>®</sup>, PENNSAID 2%<sup>®</sup>, PROCYSBI<sup>®</sup>, QUINSAIR<sup>®</sup>, RAVICTI<sup>®</sup>, RAYOS<sup>®</sup>, and VIMOVO<sup>®</sup>.

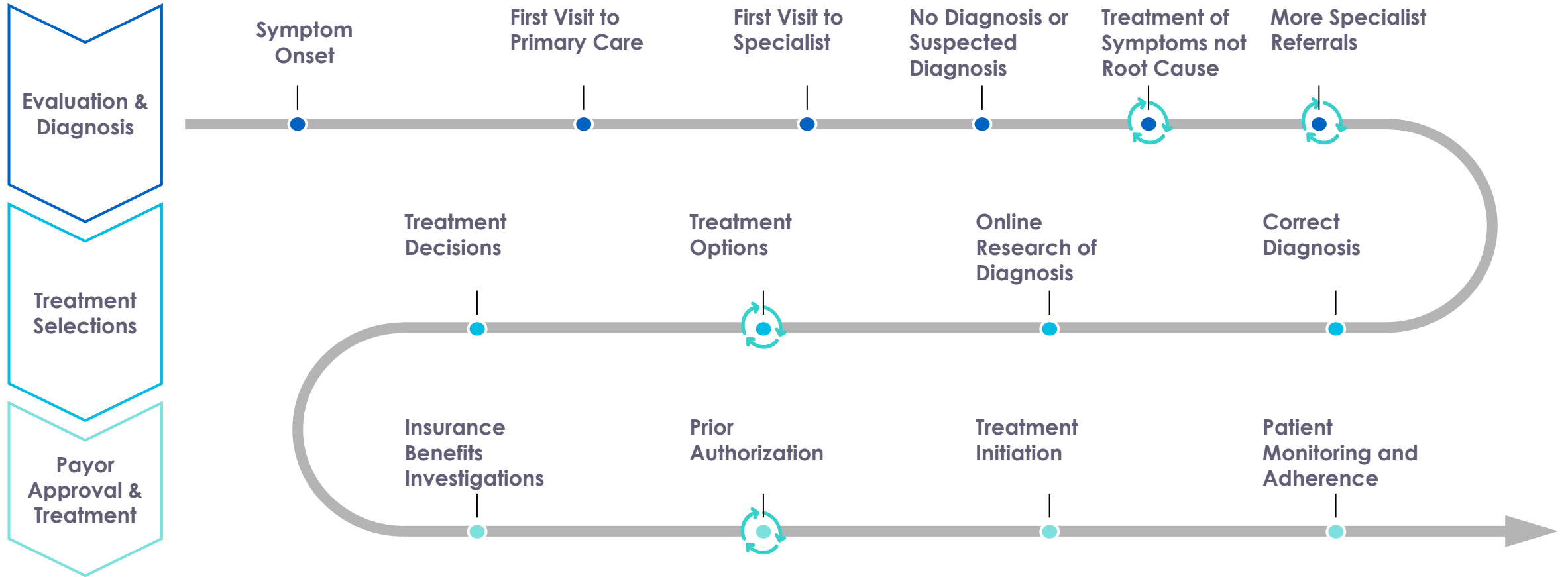
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# Rare Disease Patient Journey

The Amgen logo is displayed in white, bold, uppercase letters on a blue background. The letters are closely spaced and have a clean, sans-serif font. The background of the entire slide is a solid blue color with a pattern of faint, light blue rounded rectangles and circles scattered across the bottom half.

# Rare Disease Requires Specialized Skills to Help Patients Navigate the Long Journey to Diagnosis and Treatment



**ON AVERAGE, ~5 YEARS AND MORE THAN 7 SPECIALISTS FOR A PATIENT TO GET AN ACCURATE DIAGNOSIS**

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TEPEZZA® for  
Thyroid Eye Disease (TED)

**AMGEN**

# Thyroid Eye Disease (TED) Is an Autoimmune Disease That Significantly Impacts the Quality of a Patient's Life



- TED is a rare autoimmune disease in which the eye muscles and fatty tissue behind the eye become inflamed. TED is often associated with hyperthyroidism, but it is separate and distinct from Graves disease
- IGF-1R signaling is a key driver of TED-related symptomology



**Proptosis  
(Eye Bulging)**  
Inflammation and tissue expansion behind the eye causes proptosis, the most disfiguring sign of TED.

**Diplopia  
(Double Vision)**  
TED is associated with diplopia, which is a result of misalignment of the eyes.

**Pain, Redness,  
and Swelling**  
TED presents with highly variable signs, symptoms, and activity levels that differ from patient to patient.

IGF-1R = insulin-like growth factor-1 receptor.  
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# TEPEZZA® Is the First and Only FDA-Approved Treatment for Thyroid Eye Disease (TED)

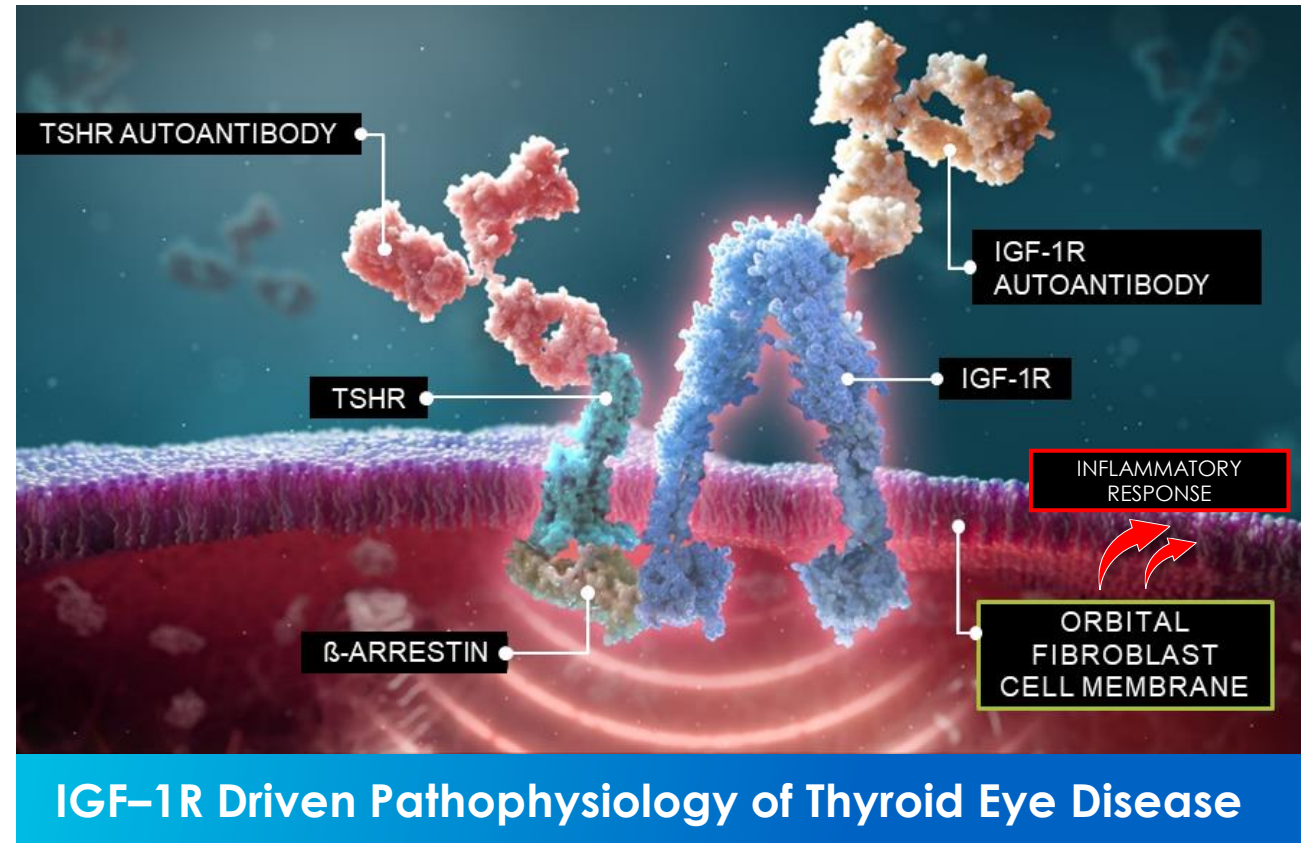


## Updated Indication

- TEPEZZA® is indicated for the treatment of TED **regardless of activity or duration**

## Mechanism of Action

- TEPEZZA® is designed to bind to IGF-1R, and block its activation and signaling
- By targeting IGF-1R, TEPEZZA® reduces inflammation and prevents muscle and fat tissue remodeling and expansion behind the eye
- Treatment administered via intravenous infusions over a total of 8 infusions

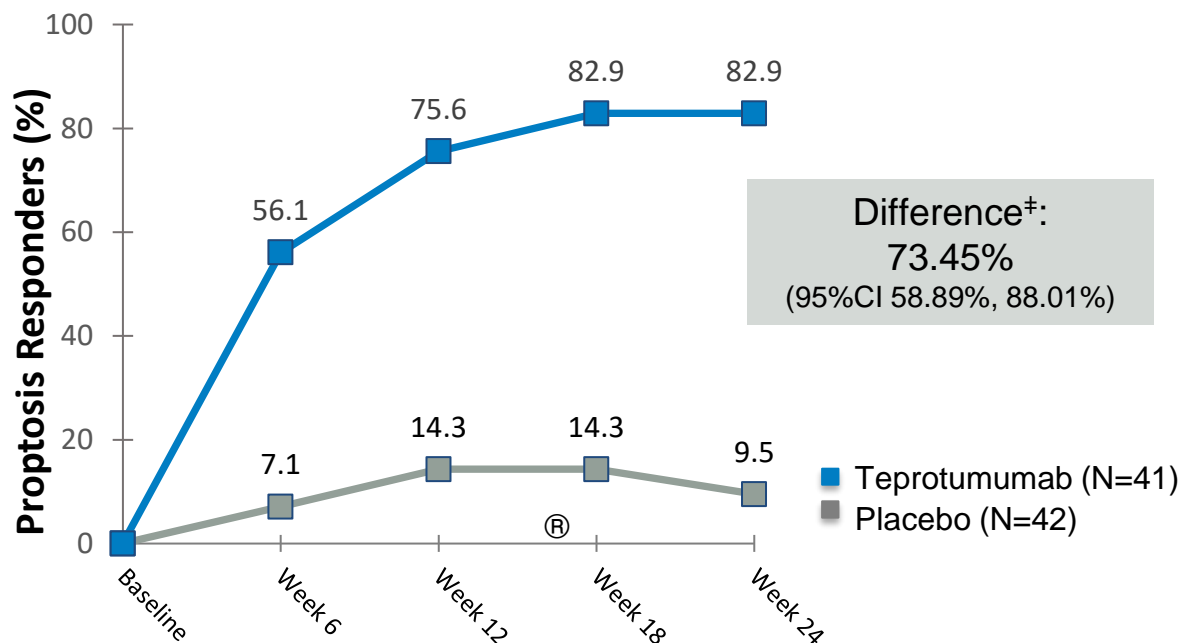


IGF-1R = insulin-like growth factor-1 receptor; TSHR = thyroid stimulating hormone receptor.  
Provided February 22, 2024, as part of an oral presentation and is qualified by such, contains forward-looking statements, actual results may vary materially; Amgen disclaims any duty to update.

# TEPEZZA® Provides Benefit in TED Patients Regardless of Disease Activity or Duration



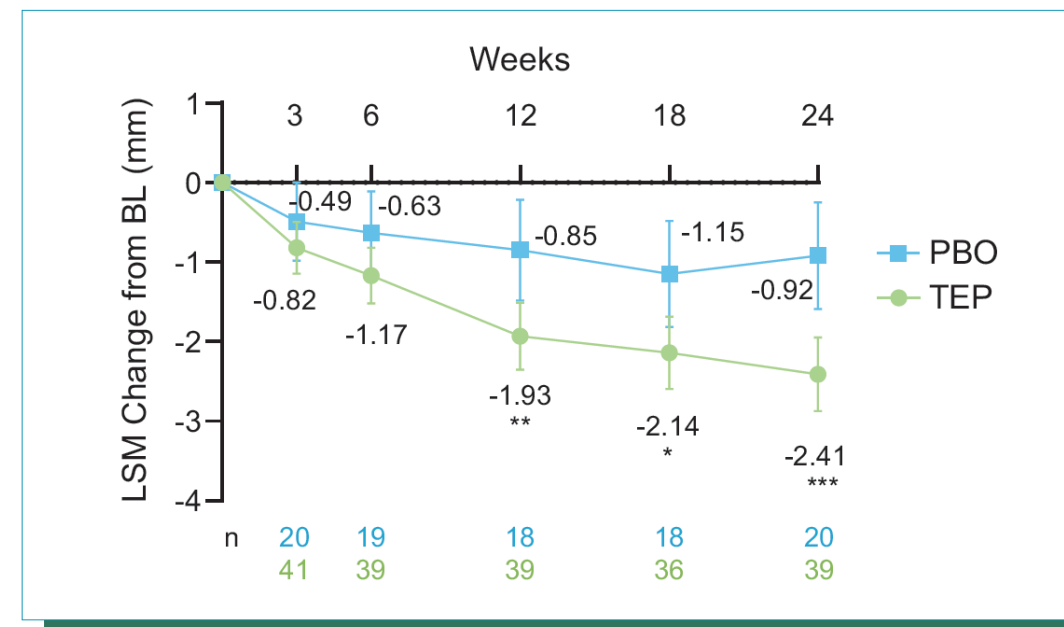
## Phase 3 Trial in High CAS TED Patients



- High CAS symptoms are illustrated by inflammation, pain, redness, and swelling
- Initial diagnosis < 9 months; CAS score ≥ 4
- Primarily seen by ocular specialists

TED = thyroid eye disease; CAS = clinical activity score; PBO = placebo; TEP = teprotumumab. Proptosis response is defined as a reduction of ≥ 2 mm at Week 24. Provided February 22, 2024, as part of an oral presentation and is qualified by such, contains forward-looking statements, actual results may vary materially; Amgen disclaims any duty to update.

## Phase 4 Trial in Low CAS TED Patients



\* p<0.02, \*\* p<0.01, \*\*\* p<0.001; Error bars represent 95% confidence intervals. MMRM analysis; LSM, least squares mean; ITT, intent-to-treat population; BL, baseline.

- Low CAS symptoms see reduced redness and swelling, but pain, proptosis, and diplopia remain
- Initial diagnosis between 2 and 10 years; CAS score < 2
- Primarily seen by ophthalmologists and endocrinologists

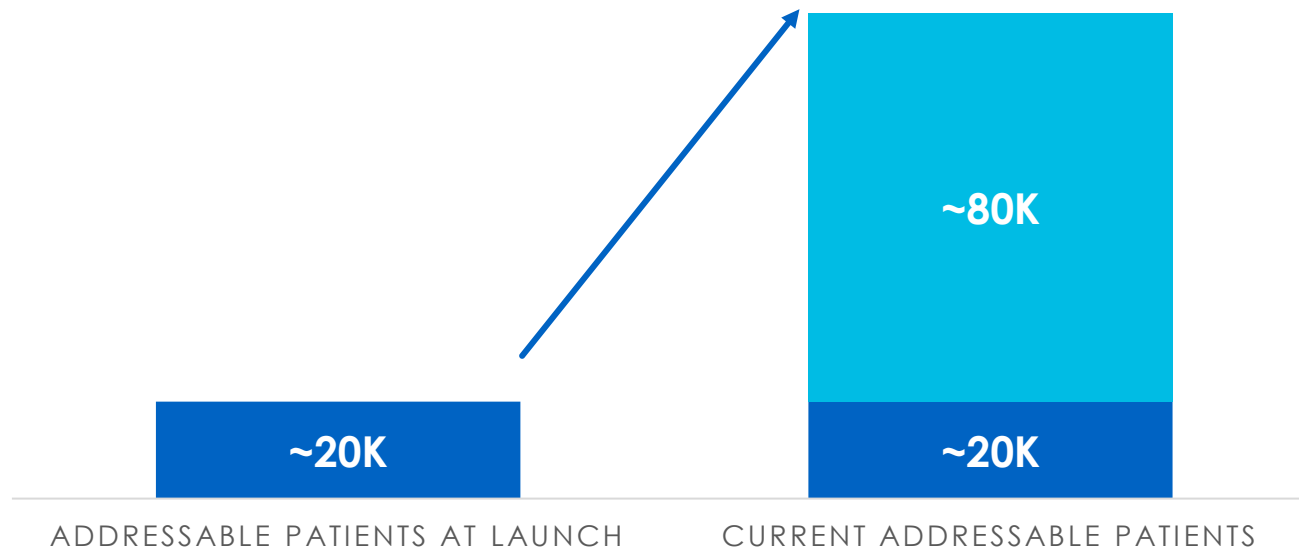


# Approval in Low-Activity Thyroid Eye Disease (TED) Setting has Significantly Increased TED Addressable Patient Population



## U.S. TED Patient Population

■ High Clinical Activity Score (CAS)   ■ Low Clinical Activity Score (CAS)



## U.S. TED Market Opportunity Is Attractive

- Current TEPEZZA<sup>®</sup> penetration in high single digits
- Opportunity in low CAS patients is increasing as we broaden the prescriber base and secure reimbursement
  - Despite significant burden of TED on patients, physicians generally underestimate the quality-of-life impact

# Executing on U.S. TEPEZZA® Growth Strategy Is Driving Positive Momentum



- Educating stakeholders on new clinical data and updated indication to drive uptake across full spectrum of Thyroid Eye Disease (TED) patients
- Expanding our reach and penetration to new prescribers, including ophthalmologists and endocrinologists, to reach broader patient populations
- Continuing to generate favorable medical policies leveraging our clinical data

**CONTINUING TO OPTIMIZE THE PATIENT EXPERIENCE THROUGH DEVELOPMENT OF A SUBCUTANEOUS ADMINISTRATION**



# Significant Opportunity to Leverage Existing Amgen Footprint to Drive Long-Term Growth



- **Japan: ~25K-35K addressable patients**
  - 50/50 split between High Clinical Activity Score (CAS) and Low CAS
  - Orphan Drug Designation granted in December 2023
  - Filing completed January; launch expected in 2025
  - Phase 3 trial in Low CAS Thyroid Eye Disease (TED) patients ongoing
- **Additional international markets**
  - Approved in Brazil and progressing in additional countries
  - Europe: ~90K-100K patients in France, Germany, Italy, Spain, and the U.K.
    - ~1/3 and ~2/3 of patients are High CAS and Low CAS, respectively
    - EMA and U.K. filings planned in H1 2024
    - No additional clinical trials required
  - Filings in Canada and Australia expected in 2024

**INTERNATIONAL LAUNCHES WILL CONTRIBUTE TO GROWTH IN 2025 AND BEYOND**

EMA = European Medicines Agency.

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# Subcutaneous Development Provides Opportunity for Increased Adoption and Improved Patient Experience



## Current state

**TEPEZZA<sup>®</sup> infusion duration currently  
60–90 minutes every 3 weeks**

## Opportunity

**Plan to initiate pivotal Phase 3  
global program in H1 2024**

# We Are Confident in the Growth Outlook for TEPEZZA®



- TEPEZZA® in the U.S. is early in its lifecycle and has significant growth potential given current penetration
- Strong experience partnering with providers and helping patients along the continuum of care
- Significant opportunity exists for expansion outside the U.S., which we are rapidly advancing through our existing footprint

**SUBCUTANEOUS DEVELOPMENT PROVIDES OPPORTUNITY FOR INCREASED ADOPTION AND IMPROVED PATIENT EXPERIENCE**

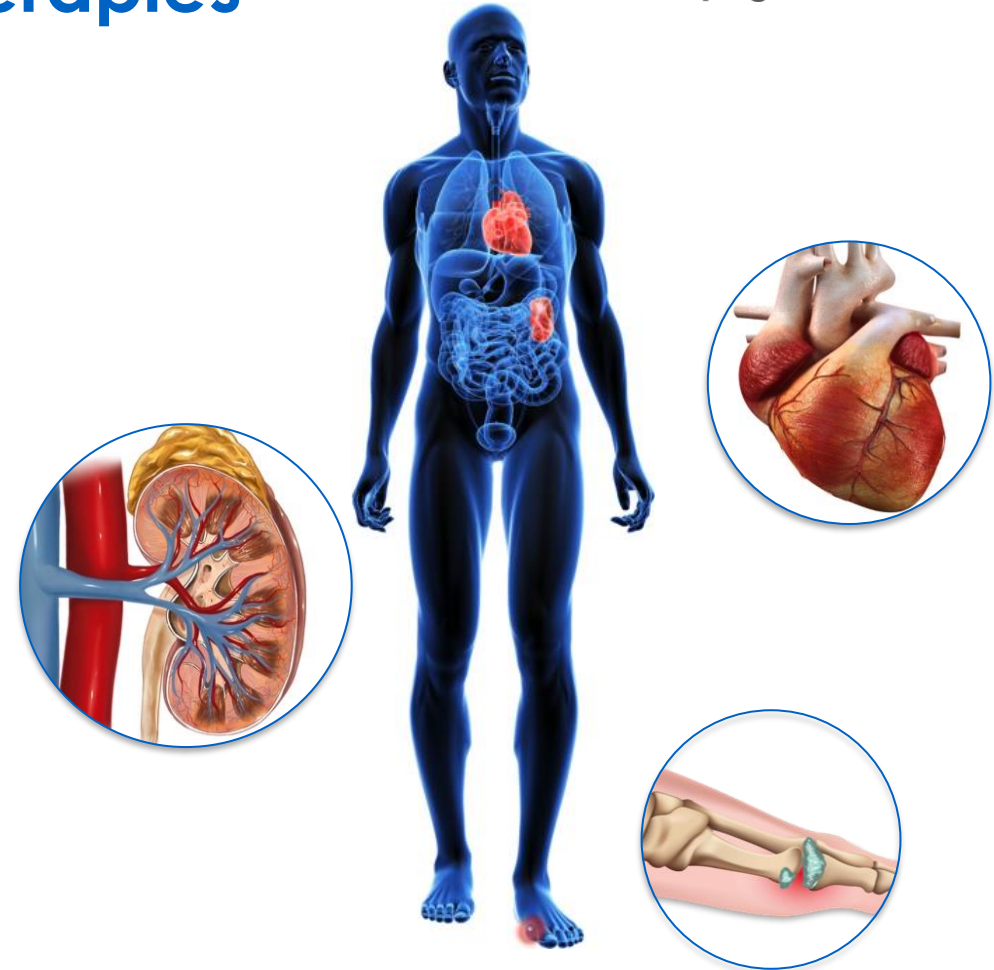
KRYSTEXXA<sup>®</sup>  
for Uncontrolled Gout

**AMGEN**

# Uncontrolled Gout Is a Systemic Disease That Is Unresponsive to Conventional Therapies

**KRYSTEXXA**  
pegloticase

- Gout is the most common inflammatory arthritis<sup>1</sup>
- Uncontrolled gout is a systemic disease that is unresponsive to conventional therapies and can affect bones, joints, and organs
- Characterized by multiple comorbidities, including chronic kidney disease and hypertension
- Buildup of uric acid crystals in many areas of the body
- Principle characteristics include elevated sUA levels, acute gout flares, and possible tophi



**UNCONTROLLED GOUT CAN IMPACT MORE THAN JOINTS**

sUA = Serum uric acid.

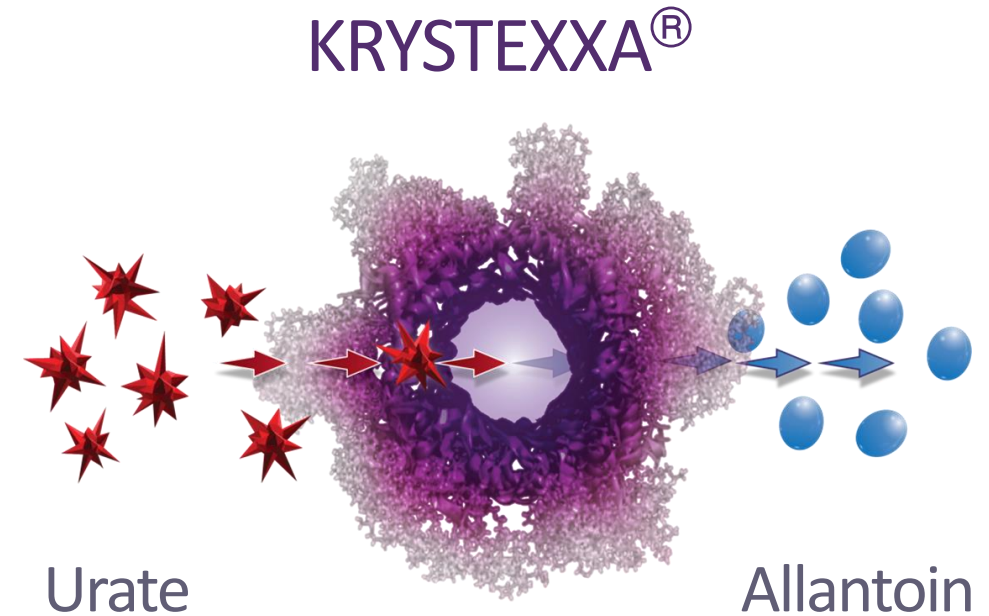
1. Zhu Y, Pandya BJ, Choi HK

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# KRYSTEXXA® Is a Pegylated Uricase Enzyme That Depletes Serum Uric Acid to Treat Uncontrolled Gout



- KRYSTEXXA® converts urate, the source of uric acid crystals, into a water-soluble substance, allantoin
  - Current oral urate-lowering therapies target patients' serum uric acid levels by addressing the overproduction or underexcretion of uric acid, whereas the body can rapidly and easily eliminate nearly all allantoin
- Renal excretion of allantoin is up to 10x more efficient than excretion of uric acid<sup>1</sup>



1. McDonagh EM, Thom CF, Callaghan JT, Altman RB, Klein TE. *Pharmacogenet Genomics*. 2014;24(9):464-476. Provided February 22, 2024, as part of an oral presentation and is qualified by such, contains forward-looking statements, actual results may vary materially; Amgen disclaims any duty to update.

# KRYSTEXXA® Significantly Lowers Uric Acid Levels, Dissolves Years of Gout Buildup, and Rapidly Reverses Progression<sup>1</sup>



**BASELINE**



**52 WEEKS**

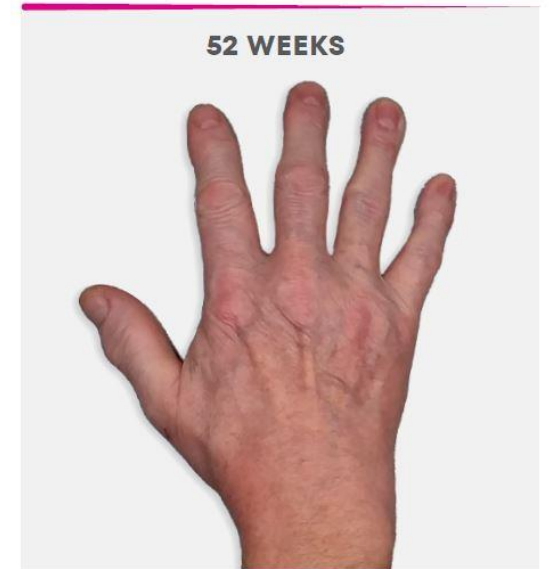
## **KRYSTEXXA® with methotrexate**

Photos and DECT images from a patient in MIRROR trial.

The optimal treatment duration has not been established. Individual results vary.



**BASELINE**



**52 WEEKS**

## **KRYSTEXXA® with methotrexate**

Photos and DECT images from a patient in MIRROR trial.

The optimal treatment duration has not been established. Individual results vary.

DECT = Dual-energy computed tomography.

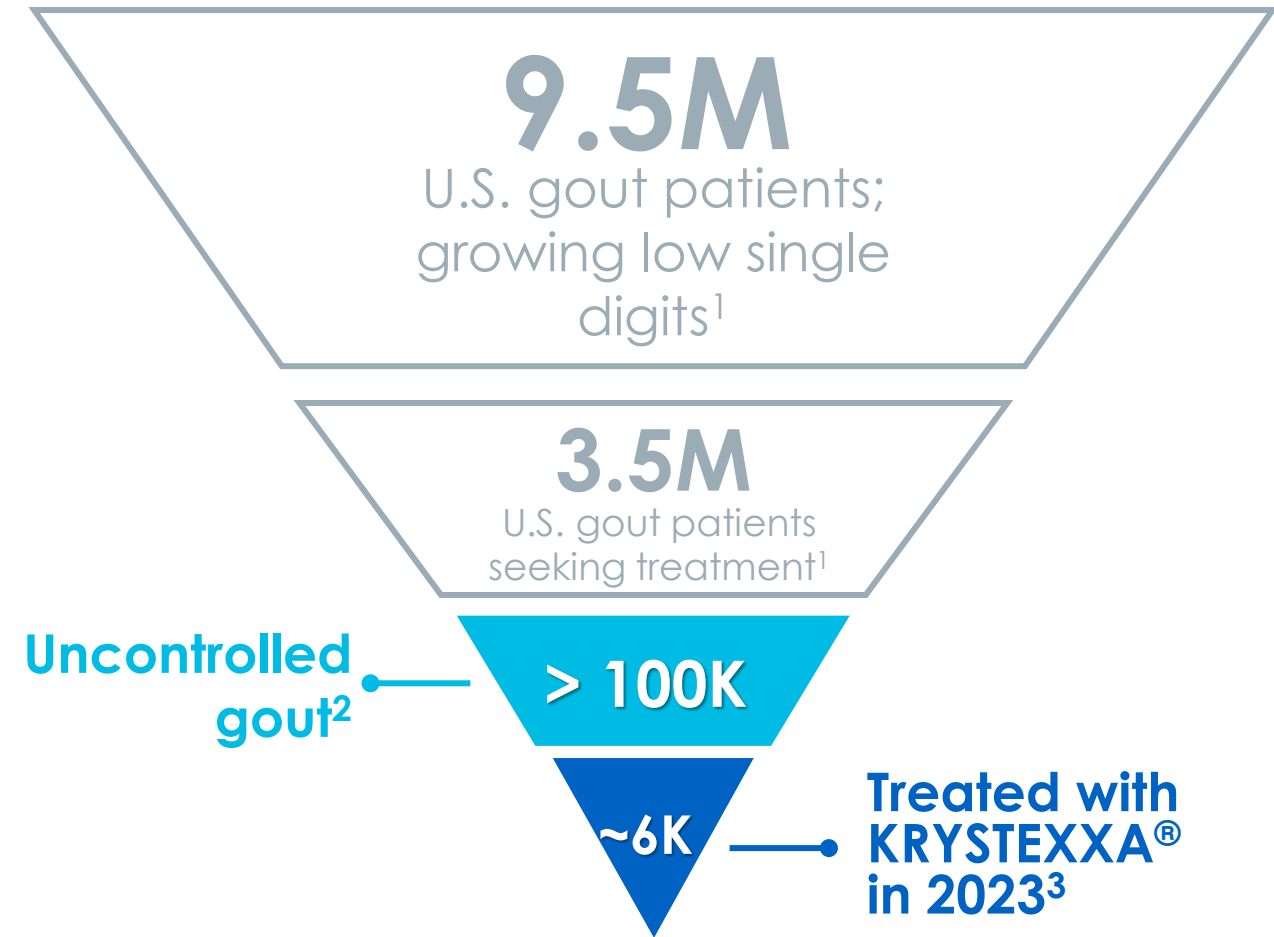
1. Sundy JS, Baraf HSB, Yood RA, et al. Efficacy and Tolerability of Pegloticase for the Treatment of Chronic Gout in Patients.

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# Significant Unmet Need in Uncontrolled Gout



- > 100K addressable uncontrolled gout patients in the U.S.
- Annual penetration of ~6%
- Primarily being seen by rheumatologists and nephrologists



1. Prevalence of gout and hyperuricemia in the U.S. general population: The National Health and Nutrition Examination Survey (NHANES) 2007–2016. *Arthritis Rheum.* 2019 Jun;71(6):991-999.

2. Approximate number of patients in our annual addressable target market in rheumatology and nephrology; Amgen estimate.

3. Source: Amgen-sponsored market research.

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# Executing on KRYSTEXXA® Growth Strategy



- Accelerate the urgency to treat uncontrolled gout
- Redefine KRYSTEXXA® with immunomodulation therapy as the standard of care
- Drive healthcare professional and patient conviction in KRYSTEXXA® as the treatment of choice
- Improve patient experience and perceived burden of treatment through current and future activities
  - Improve perceived burden of treatment with a focus on shorter and less-frequent infusions
  - Evaluate shorter infusion duration and monthly dosing through two Phase 4 clinical studies

# UPLIZNA<sup>®</sup> for Neuromyelitis Optica Spectrum Disorder (NMOSD)

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# Neuromyelitis Optica Spectrum Disorder (NMOSD) Can Lead to Permanent Disability From Blindness and Paralysis

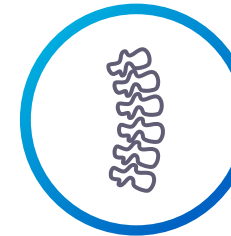
## WHAT IS NMOSD?

- NMOSD is an autoimmune, inflammatory disease of the central nervous system
- Attacks the optic nerve and the spinal cord and can also affect the brain and brainstem
- Can be severe, rare, and relapsing
- Attacks result in accumulation of neurological damage and can result in blindness, paralysis, and death

## NMOSD CAN LEAD TO INFLAMMATION OF THE



Optic Nerve (Optic Neuritis)



Spinal Cord (Myelitis)

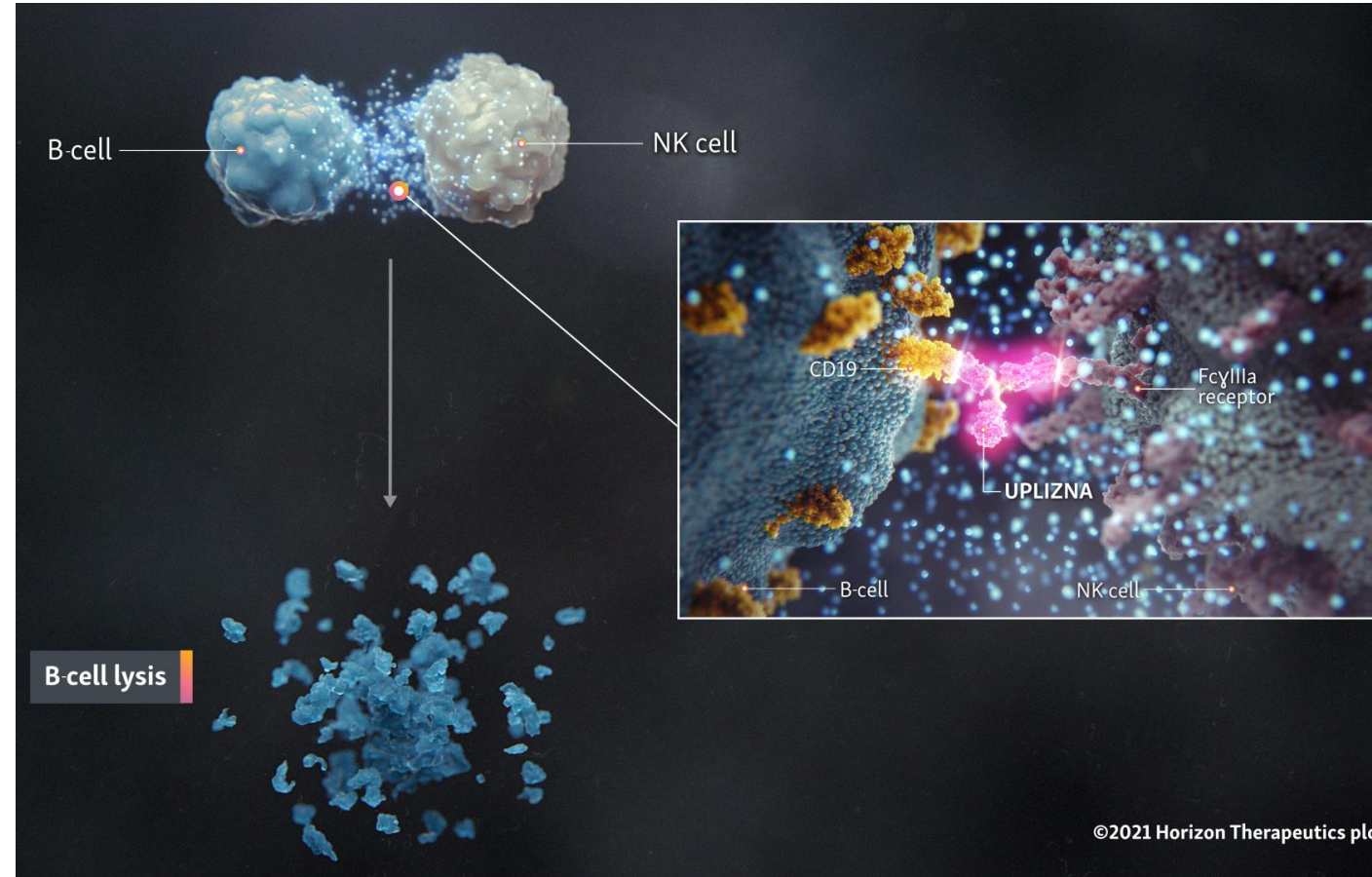


Brain/Brain Stem

# UPLIZNA® Is an Anti-CD19, Humanized Monoclonal Antibody



- CD19 targeted B-cell depleter with potential in multiple autoimmune diseases
  - Depletes a broad array of B-cells, including plasmablasts and certain plasma cells that anti-CD20 therapies do not target
- Provides targeted, rapid, and sustained CD19+ B-cell depletion
- Convenient 6-month dosing interval minimizes patient impact and enables long-term adherence



# UPLIZNA® Is the Fastest Growing Biologic in Neuromyelitis Optica Spectrum Disorder (NMOSD)<sup>1</sup>



- **U.S.: Approved June 2020**
  - ~10K U.S. NMOSD patients; ~8K AQP4+ and are appropriate for UPLIZNA<sup>®2</sup>
  - Drive awareness and understanding of the comprehensive benefits and differentiated clinical profile of UPLIZNA<sup>®</sup>
  - Drive patient initiation and adherence; cultivate a positive patient experience
- **Europe: Approved April 2022 (~8K–10K addressable patients)**
  - Accelerate adoption in EU-4 (France, Germany, Italy, Spain) and launch into remaining parts of Europe
- **Brazil: Approved December 2022 (Brazil's patient population is similar in size to the U.S. or Europe alone)**
  - Rollout of diagnostic programs and engagement with patient advocacy groups to address the high unmet need
- **Canada: Approved January 2024**

AQP4+ = aquaporin-4 positive.

1. Year-to-date by market share

2. Source: Amgen sponsored market research

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# IgG4-Related Disease Is Chronic and Debilitating; Phase 3 Topline Data Expected in H2 2024

## Characteristics and Symptoms

- Chronic, debilitating rare disease characterized by tumor-like inflammatory and fibrotic mass formation in affected organs
  - Affects mostly men (75%)
  - Specific symptoms depend on which organs are affected; multiple organ involvement is typical
  - Major causes for mortality include liver cirrhosis, portal hypertension, retroperitoneal fibrosis, etc.
- U.S. prevalence: ~20K-40K<sup>1</sup>; large variance due to limited epidemiology data
- Significant unmet need; potential to be first FDA-approved therapy

IgG4-RD = Immunoglobulin G4-related disease; FDA = U.S. Food and Drug Administration.  
1. Source: Amgen sponsored market research.

2. Stone JH, Zen Y, Deshpande V. IgG4-related disease. N Engl J Med 2012; 366:539

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## IgG4-Related Disease Is Caused by Multiple Mechanisms of B-Cell Dysfunction



# Phase 3 Trial Design Aims to Reduce gMG-Related Disability in Two Different Patient Populations

- gMG is a chronic, rare autoimmune neuromuscular disorder
  - Two main types of gMG: AChR+ and MuSK+
- Symptoms include weakness in voluntary muscles, especially those that control the eyes, mouth, throat, and limbs
- Prevalence: ~55K in the U.S.<sup>1</sup>
- UPLIZNA<sup>®</sup> provides potential for differentiation based on unique MOA and convenient, predictable 6-month dosing
- Phase 3 topline data expected in H2 2024



**Common gMG Symptom:  
Drooping Eyelids (Ptosis)**

gMG = generalized myasthenia gravis; AChR+ = acetylcholine receptor; MuSK+ = muscle-specific kinase; MOA = mechanism of action.

1. Source: Amgen sponsored market research.

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# We Are Driving UPLIZNA® Growth, With Significant Upside Potential in New Indications



- Uptake driven by patients naïve to biologics, as well as patients switching from competitive biologic therapies
- Drive awareness and understanding of the comprehensive benefits and differentiated clinical profile of UPLIZNA®
- Drive patient initiation and adherence; cultivate a positive patient experience
- Expand internationally, including into Brazil and Europe
- Expansion into IgG4-RD and gMG, with Phase 3 data readouts in H2 2024

IgG4-RD = Immunoglobulin G4-related disease; gMG = generalized myasthenia gravis.

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TAVNEOS®

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# ANCA-Associated Vasculitis Is a Chronic and Progressive Autoimmune Disease that Destroys Vasculature Throughout the Body<sup>1-6</sup>

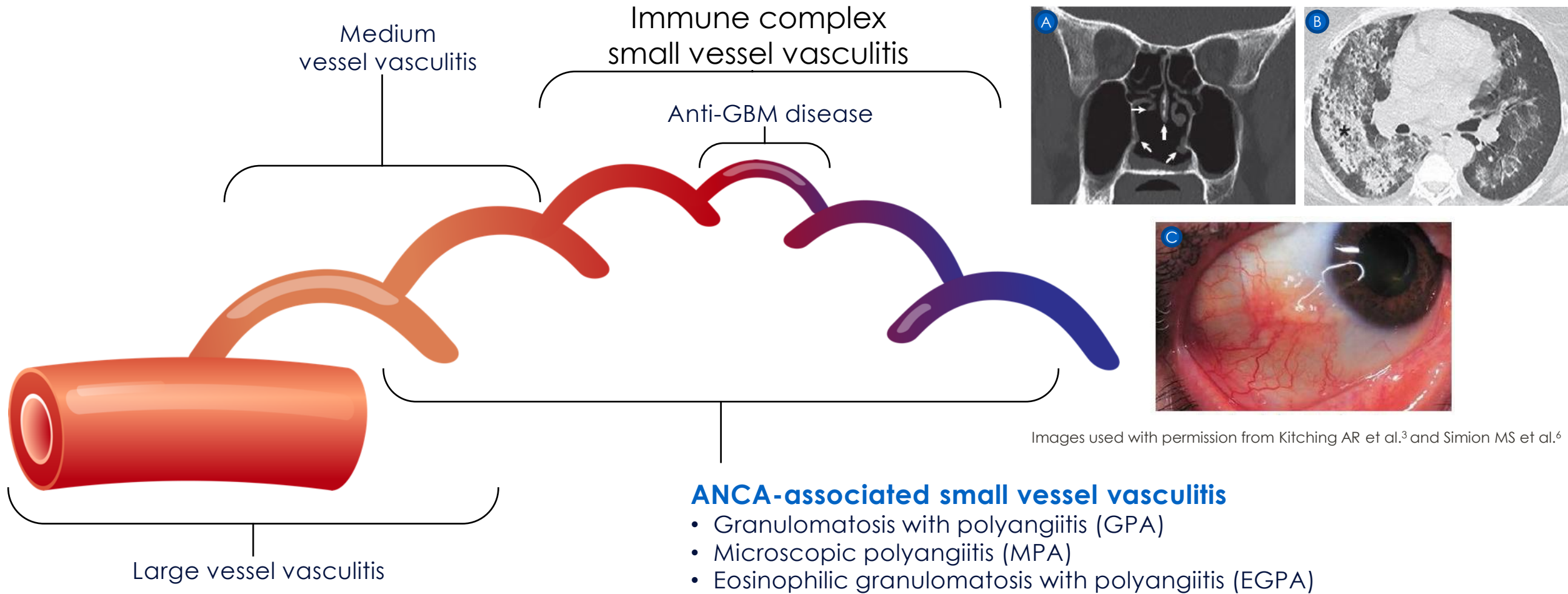


Figure adapted with permission from Jennette JC, et al.<sup>4</sup>

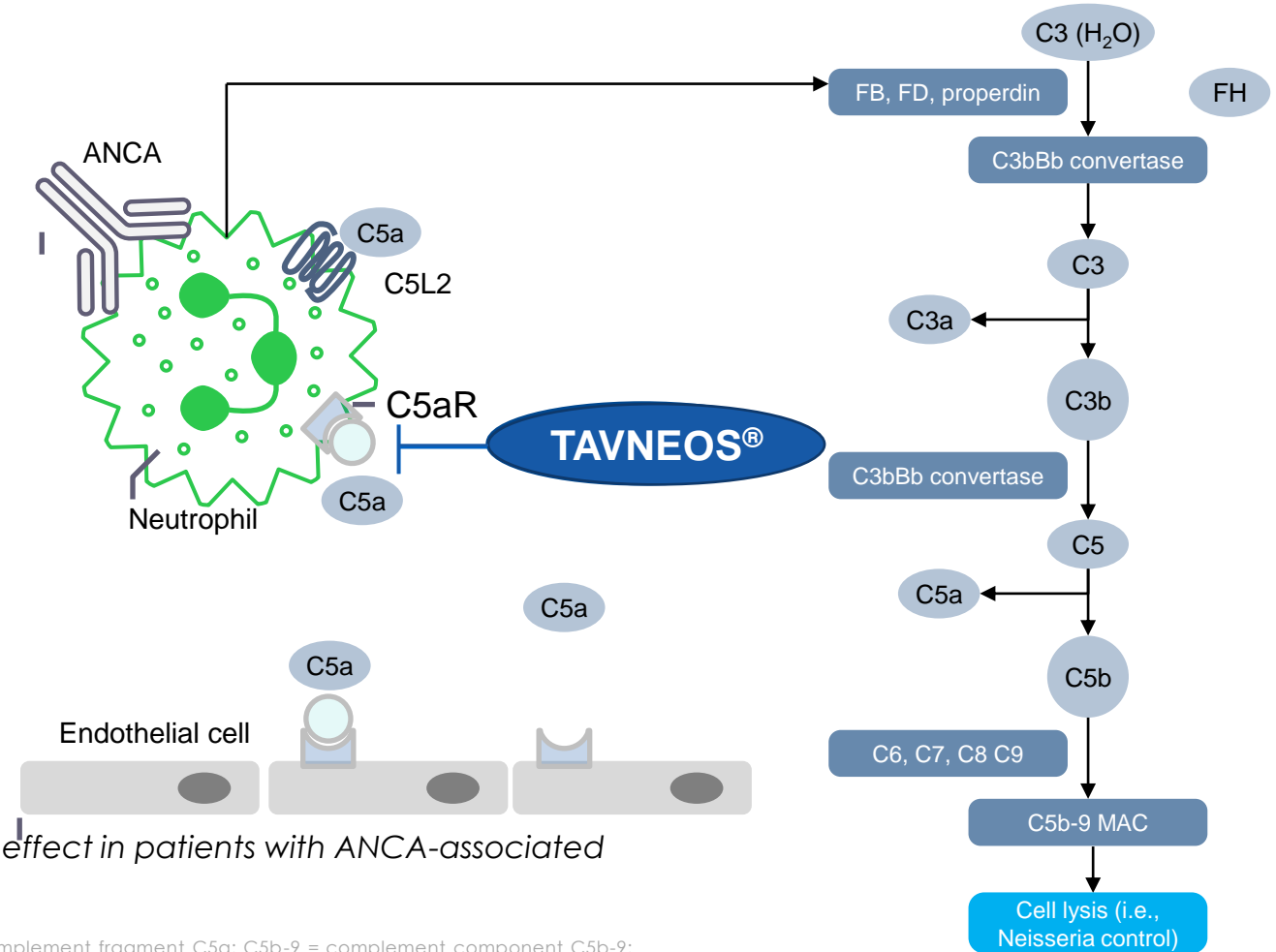
ANCA = anti-neutrophil cytoplasmic antibody; GBM = glomerular basement membrane.

1. Yates M, Watts R. Clin Med (Lond). 2017;17(1):60-64. 2. Al-Hussain T, et al. Adv Anat Pathol. 2017;24(4):226-234. 3. Kitching AR, et al. Nat Rev Dis Primers. 2020;6(1):71. 4. Jennette JC, et al. Arthritis Rheum. 2013;65(1):1-11. 5. King C, et al. Best Pract Res Clin Rheumatol. 2018;32(1):125-136. 6. Simion MS, et al. Rom J Ophthalmol. 2020;64(1):3-7.

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# TAVNEOS® Selectively Antagonizes C5aR and Is Designed to End the Vicious Inflammatory Amplification Loop

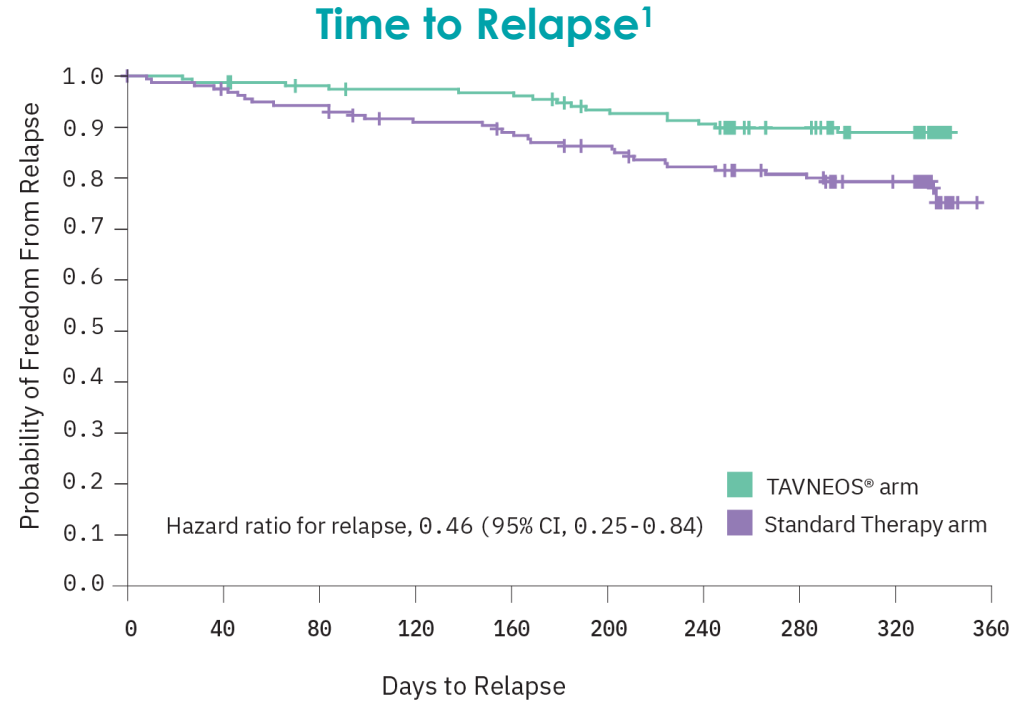
- Blocks neutrophil activation and migration
- Selective inhibition of C5aR leaves the beneficial C5a pathway through the C5L2 receptor functioning normally
- Is believed to not block C5b-9 production; MAC complex remains intact for host defense mechanisms
- Is thought to not interfere with the “upstream” components of the complement cascade



*The precise mechanism by which avacopan exerts a therapeutic effect in patients with ANCA-associated vasculitis has not been definitively established.*

C5aR = C5a receptor; C5a = complement component 5a; C5L2 = transmembrane domain receptor for complement fragment C5a; C5b-9 = complement component C5b-9; MAC = complement membrane attack complex; ANCA = anti-neutrophil cytoplasmic antibody; C3 = complement component C3; FB, FD, properdin = factor B, factor D, and properdin; FH = complement factor H; C3a = complement component C3a; C3b = complement component C3b; C5 = complement component C5; C5b = complement component C5b; C6, C7, C8 C9 = complement components C6, C7, C8, and C9; C5b-9 MAC = C5b-9 membrane attack complex.  
 Provided February 22, 2024, as part of an oral presentation and is qualified by such, contains forward-looking statements, actual results may vary materially; Amgen disclaims any duty to update.

# TAVNEOS® Regimen Reduced the Risk of Relapse of ANCA-associated Vasculitis by Half Compared to Standard Therapy<sup>1</sup>



No. at Risk

	0	40	80	120	160	200	240	280	320	360
<b>TAVNEOS® arm</b>	158	153	149	146	145	133	129	115	92	0
<b>ST arm</b>	157	151	146	137	133	126	119	111	90	0

Figure adapted from Jayne DRW, et al.<sup>1</sup>

**54%**

Estimated relapse risk reduction demonstrated by the TAVNEOS® regimen vs standard therapy<sup>1</sup>

Relapse Rates<sup>1</sup>

**10.1%** TAVNEOS® regimen  
**21%** Standard therapy

**Relapse is defined as the occurrence of one of the following after remission (BVAS of 0) had been achieved:<sup>1</sup>**

- ≥ 1 major item in the BVAS, or

---

- ≥ 3 minor items in the BVAS, or

---

- 1-2 minor items in the BVAS recorded at ≥ 2 consecutive visits

ANCA = anti-neutrophil cytoplasmic antibody; BVAS = Birmingham Vasculitis Activity Score.

1. Jayne DRW, Merkel PA, Schall TJ, Bekker P; ADVOCATE Study Group. Avacopan for the treatment of ANCA-associated vasculitis. *N Engl J Med.* 2021;384(7):599-609

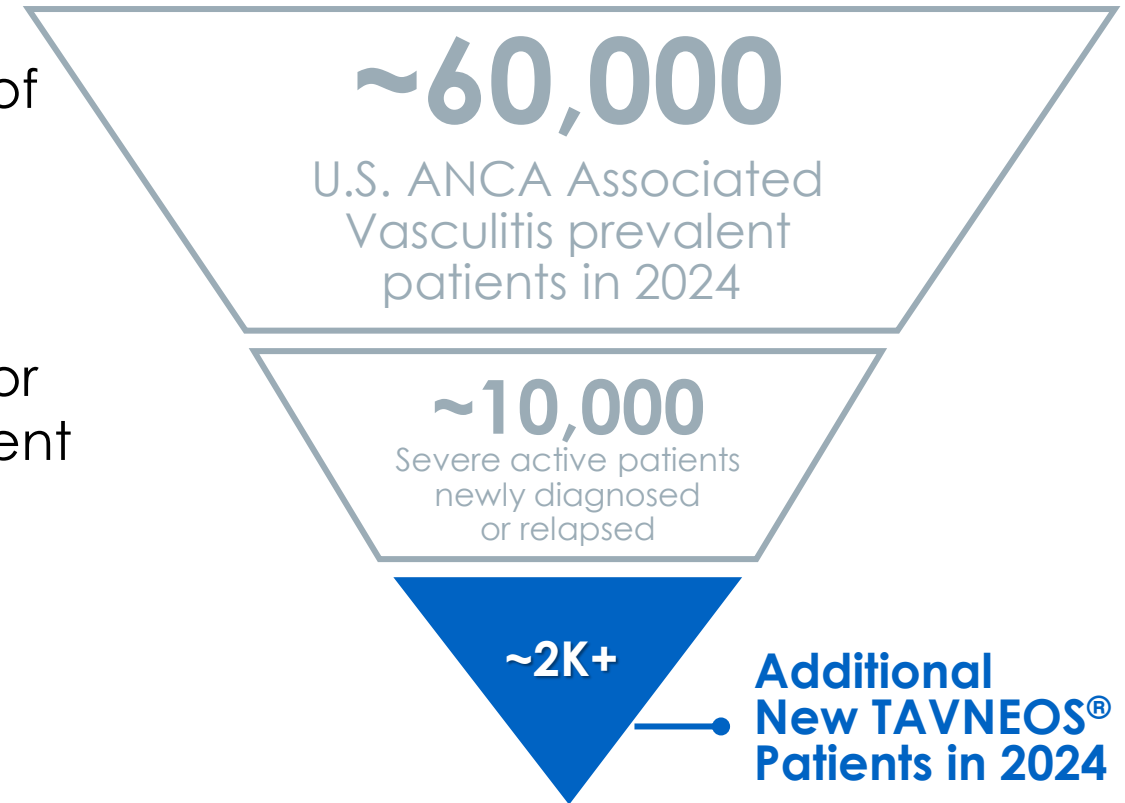
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# Opportunity to Leverage Amgen Leadership in Rheumatology and Nephrology to Drive Growth



- TAVNEOS® is a first-in-class treatment option for patients with severe active disease or relapses of ANCA-associated vasculitis
- Establish TAVNEOS® as the standard of care in severe active GPA and MPA
- Educate stakeholders on data supporting use for patients experiencing new, relapsing, or persistent disease activity
  - Continued real-world evidence generation
  - Using data and AI to locate patients to enable outreach to providers



**IN THE U.S., APPROXIMATELY 2,700 PATIENTS HAVE NOW BEEN TREATED WITH TAVNEOS®**

ANCA = anti-neutrophil cytoplasmic antibody; GPA = granulomatosis with polyangiitis; MPA = microscopic polyangiitis; AI = artificial intelligence.  
Provided February 22, 2024, as part of an oral presentation and is qualified by such, contains forward-looking statements, actual results may vary materially; Amgen disclaims any duty to update.



# We Are Driving Growth Across Our Rare Disease Portfolio



Expand to a broader range of eligible Thyroid Eye Disease (TED) patients, broaden and deepen the prescriber base, generate favorable policy changes, optimize patient experience, and expand internationally



Accelerate the urgency to treat, drive healthcare provider and patient conviction as the treatment of choice, and improve patient experience



Serve more patients with NMOSD in the U.S. and around the world through the differentiated mechanism of action and patient-friendly dosing regimen; Phase 3 data readouts in IgG4-RD and gMG in H2 2024



Establish TAVNEOS<sup>®</sup> as the standard of care in severe active GPA and MPA, supporting its use as an adjunct therapy for patients experiencing new, relapsing, or persistent disease activity

**OUR RARE DISEASE PIPELINE DELIVERS LONG-TERM GROWTH THROUGH  
ADVANCEMENT OF MID- AND LATE-STAGE CLINICAL PROGRAMS**

NMOSD = neuromyelitis optica spectrum disorder; IgG4-RD = Immunoglobulin G4-related disease; gMG = generalized myasthenia gravis; GPA = granulomatosis with polyangiitis; MPA = microscopic polyangiitis. Provided February 22, 2024, as part of an oral presentation and is qualified by such, contains forward-looking statements, actual results may vary materially; Amgen disclaims any duty to update.

# Pipeline

The AMGEN logo is displayed in white, bold, uppercase letters on a blue background. The letters are closely spaced and have a clean, sans-serif font style.

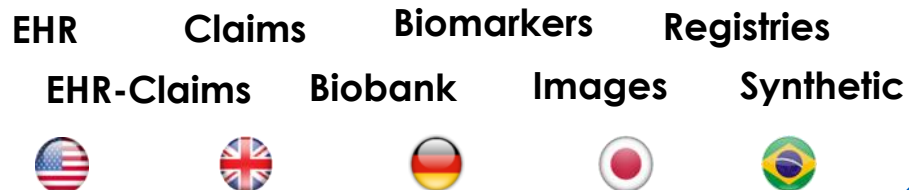
# Advancing Rare Disease R&D Through Amgen's Human Data Platforms and Capabilities

## Center for Observational Research

### Advanced data & analytic capability enables robust RWE generation

- Characterize disease and unmet need with SOC
  - Natural history studies
  - RWE cohorts to enable single-arm registrations
- Patient identification and outcome prediction
- Evaluate benefit/risks of therapeutic intervention

#### Real-World Data Platform (350+M)



## deCODE Genetics & Precision Medicine

### Population-scale datasets enable enhanced understanding of rare disease

- 3.2M genotyped individuals
- 800K whole genome sequences
- 16 populations

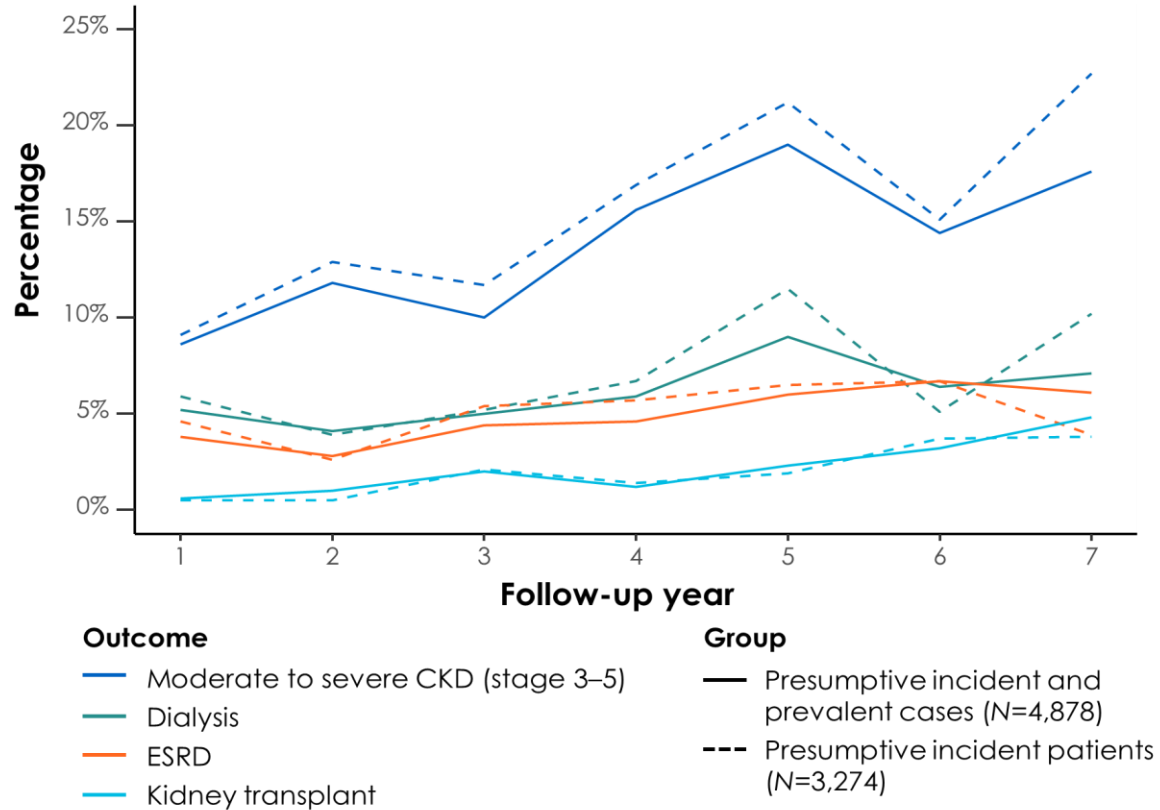
### deCODE has broad applicability

- Understand disease biology
- Target validation
- Protein biomarkers
- Determine likelihood of adverse events
- Broaden the indication to common diseases

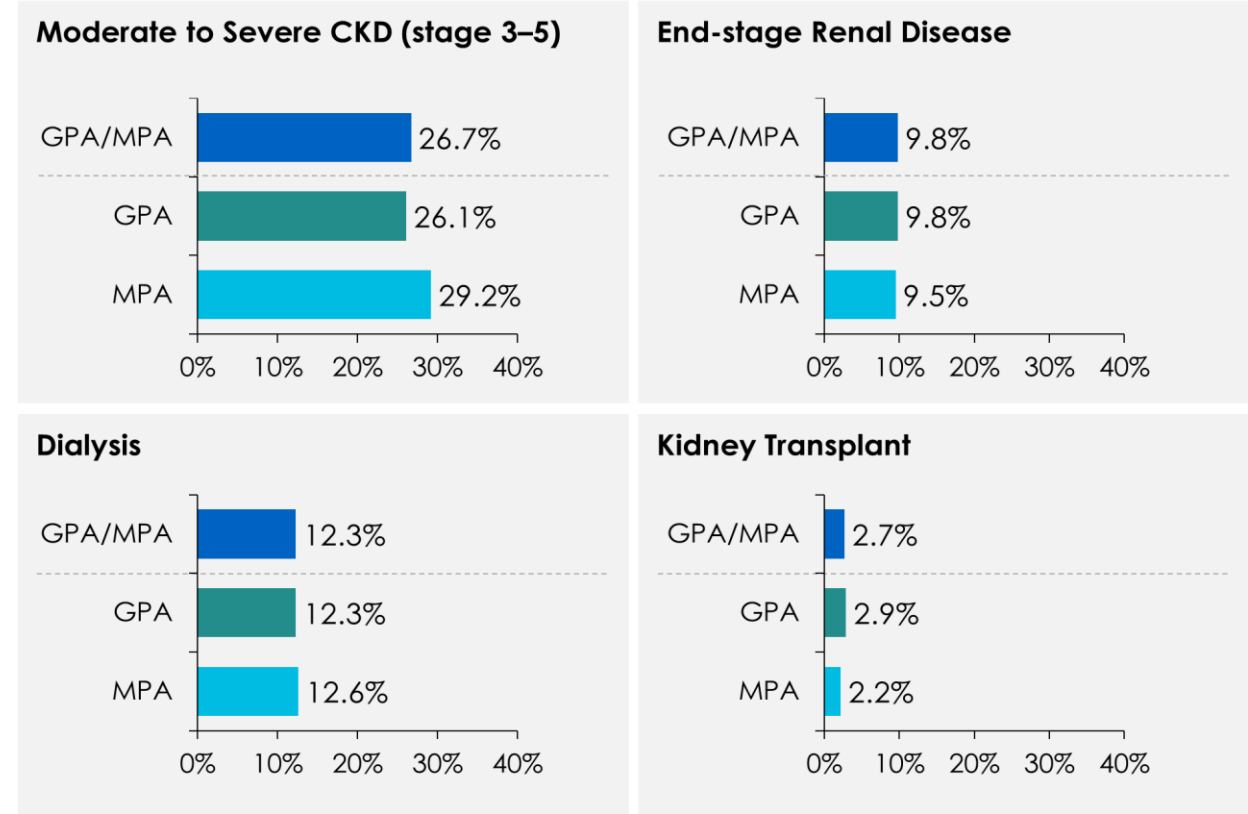


# Generated Real-World Evidence to Understand Burden of Renal Disease Among Patients With GPA or MPA, a Key Focus for TAVNEOS®

Cumulative incidence of renal outcomes by year of follow-up in the US after diagnosis of GPA or MPA



Cumulative incidence of renal outcomes after initiating therapy among patients with presumed incident GPA or MPA



**THE INCIDENCE OF ADVERSE RENAL OUTCOMES IS COMMON AMONG PATIENTS WITH GPA OR MPA**

**THE INCIDENCE OF ADVERSE RENAL OUTCOMES AMONG PATIENTS WITH GPA/MPA IS COMMON DESPITE AVAILABLE THERAPIES**

GPA = granulomatosis with polyangiitis; MPA = microscopic polyangiitis; CKD = chronic kidney disease; ESRD = end-stage renal disease. Presumptive incident GPA or MPA patients defined as patients suspected to have developed GPA or MPA during the study period (October 1, 2015 to January 31, 2023). Provided February 22, 2024, as part of an oral presentation and is qualified by such, contains forward-looking statements, actual results may vary materially; Amgen disclaims any duty to update.

# Multiple Innovative Pipeline Programs With Potential to Reach Additional Patients With High Unmet Need

Medicine/Candidate	Program/Potential Indication	Preclinical	Phase 1	Phase 2	Phase 3
<b>TEPEZZA®</b>	Chronic/Low CAS Thyroid Eye Disease (TED) in Japan	▶			
	Subcutaneous Administration <sup>1</sup>	▶			
<b>UPLIZNA®</b>	Generalized Myasthenia Gravis (gMG)	▶			
	IgG4-Related Disease (IgG4-RD)	▶			
<b>Dazodalibep</b>	Sjögren's Disease <sup>1</sup>	▶			
<b>Daxdilimab</b>	Discoid Lupus Erythematosus (DLE)	▶			
	Dermatomyositis (DM) and Anti-Synthetase Inflammatory Myositis (ASIM)	▶			
<b>Fipaxalparant</b>	Diffuse Cutaneous Systemic Sclerosis (dcSSc)	▶			
	Idiopathic Pulmonary Fibrosis (IPF)	▶			
<b>AMG 329</b>	Sjögren's Disease <sup>1</sup>	▶			

**TWO ADDITIONAL PHASE 4 PROGRAMS: KRSTEXXA® SHORTER INFUSION DURATION AND KRSTEXXA® MONTHLY DOSING**

CAS = clinical activity score.

1. Planned programs; to initiate 1H 24

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# Sjögren's Disease Is a Chronic, Systemic Autoimmune Disease Affecting Exocrine Glands With Overactive CD40-CD40L Pathway

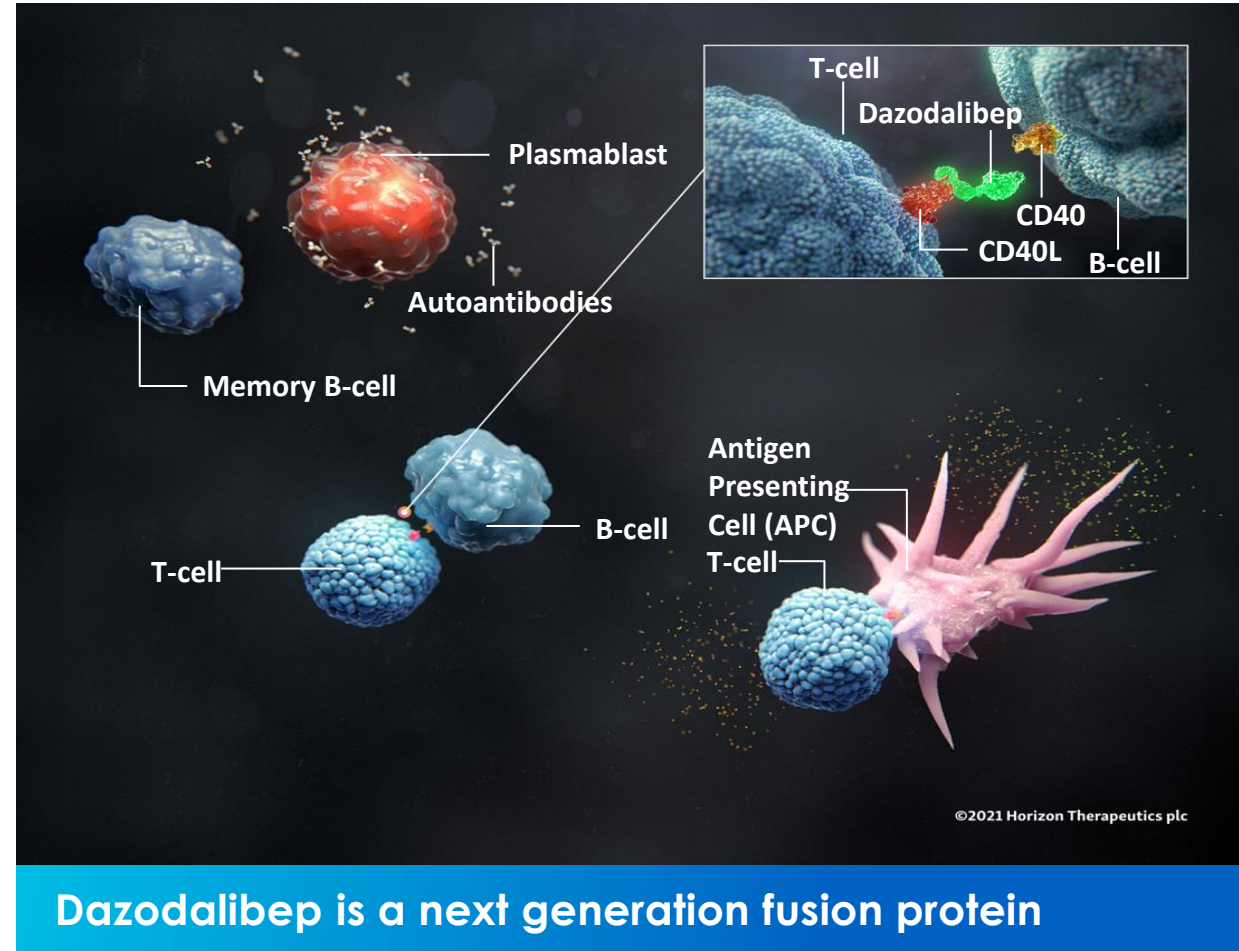
- Attacks exocrine glands; severe cases involve multiple organ systems
- Symptoms include dry eyes and mouth, arthritis, and kidney or lung dysfunction
- CD40/CD40L overexpression observed at sites of inflammation and in circulation
- Prevalence: ~250K-350K patients in the U.S.; OUS prevalence similar in size as U.S.<sup>1</sup>
- No FDA-approved disease modifying treatments



CD40 = cluster of differentiation 40; CD40L = cluster of differentiation 40 ligand; OUS = Defined as prevalence for France, Germany, Italy, Spain, UK and Japan; FDA = Federal Drug Administration.  
1. Maciel G, et al. (2017)  
Provided February 22, 2024, as part of an oral presentation and is qualified by such, contains forward-looking statements, actual results may vary materially; Amgen disclaims any duty to update.

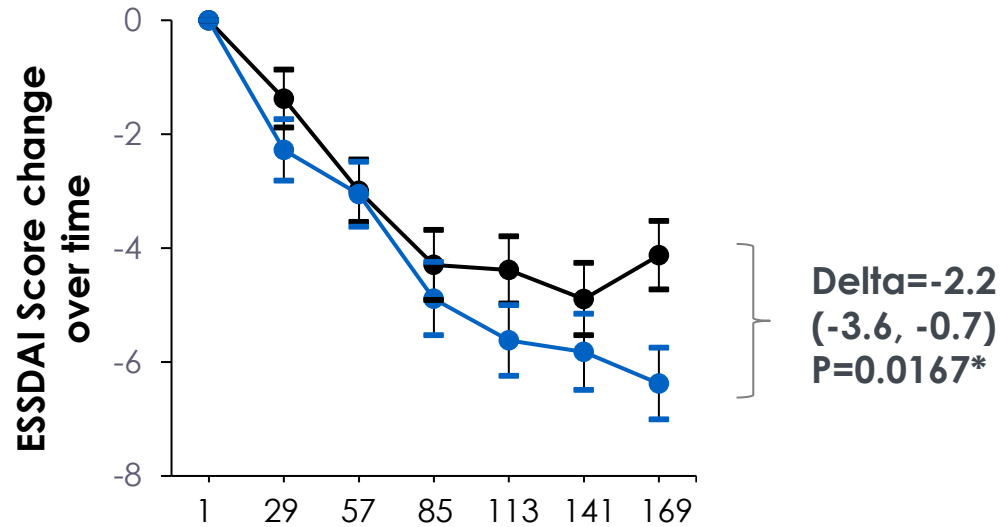
# Dazodalibep Is a CD40L Antagonist in Phase 3 Development for Sjögren's Disease

- Dazodalibep is a next-generation CD40L antagonist that blocks the CD40 pathway and undesired immune responses
- CD40L drives inflammation through CD40R which is expressed on the salivary gland, spleen, kidney, joint, gut, and skin
- The CD40/CD40L pathway is implicated in Sjögren's disease and other autoimmune diseases



# Dazodalibep Demonstrated Statistically Significant Improvement in Sjögren's Disease in a Phase 2 Study

**Population 1: Systemic Sjögren's Moderate-to-High Systemic Disease Activity (ESSDAI  $\geq 5$ )**

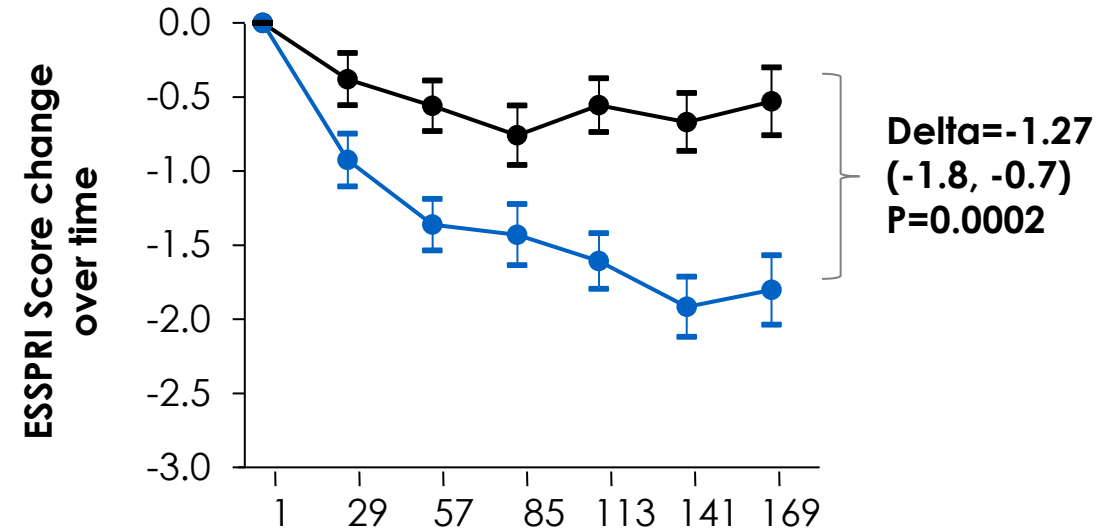


Delta=-2.2  
(-3.6, -0.7)  
P=0.0167\*

	1	29	57	85	113	141	169
Pbo	38	38	36	38	37	36	37
Daz	36	34	33	35	32	33	33

● Placebo  
● Dazodalibep

**Population 2: Symptomatic Sjögren's Moderate-to-Severe Patient-Reported Symptoms (ESSPRI  $\geq 5$ , ESSDAI  $< 5$ )**



Delta=-1.27  
(-1.8, -0.7)  
P=0.0002

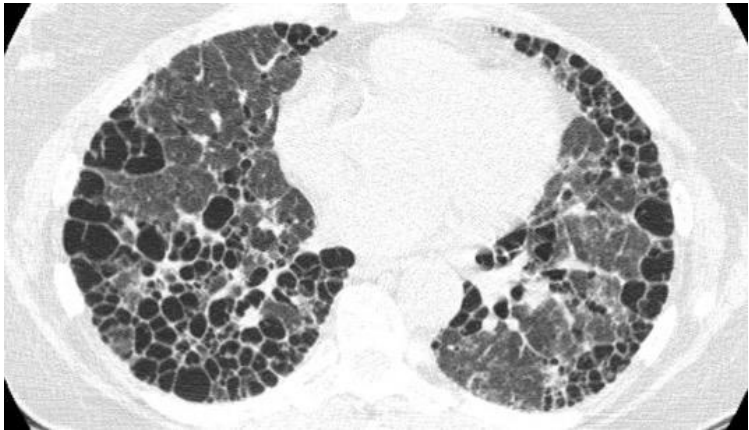
	1	29	57	85	113	141	169
Pbo	55	54	54	54	54	53	53
Daz	54	53	52	51	50	48	51

ESSDAI = EULAR Sjögren's Syndrome Disease Activity Index; ESSPRI = EULAR Sjögren's Syndrome Patient Reported Index. Provided February 22, 2024, as part of an oral presentation and is qualified by such, contains forward-looking statements, actual results may vary materially; Amgen disclaims any duty to update.

# Idiopathic Pulmonary Fibrosis and Diffuse Cutaneous Systemic Sclerosis Are Fibrotic Diseases With Significant Unmet Need

## Idiopathic Pulmonary Fibrosis (IPF)

- Non-systemic interstitial lung disease of unknown cause, associated with interstitial pneumonia
- Prevalence: ~75k–100K patients in the U.S.<sup>1</sup>
- Significant mortality rate with a 2- to 5-year mean survival post diagnosis



## Diffuse Cutaneous Systemic Sclerosis (dcSSc)

- Rare, chronic, autoimmune disease marked by fibrosis or skin thickening
- Rapidly progressive fibrosis of internal organs
- Prevalence: ~35K patients in the U.S.<sup>1</sup>
- No FDA-approved disease modifying treatments; one of the most fatal rheumatologic diseases

Musculoskeletal



Calcinosis



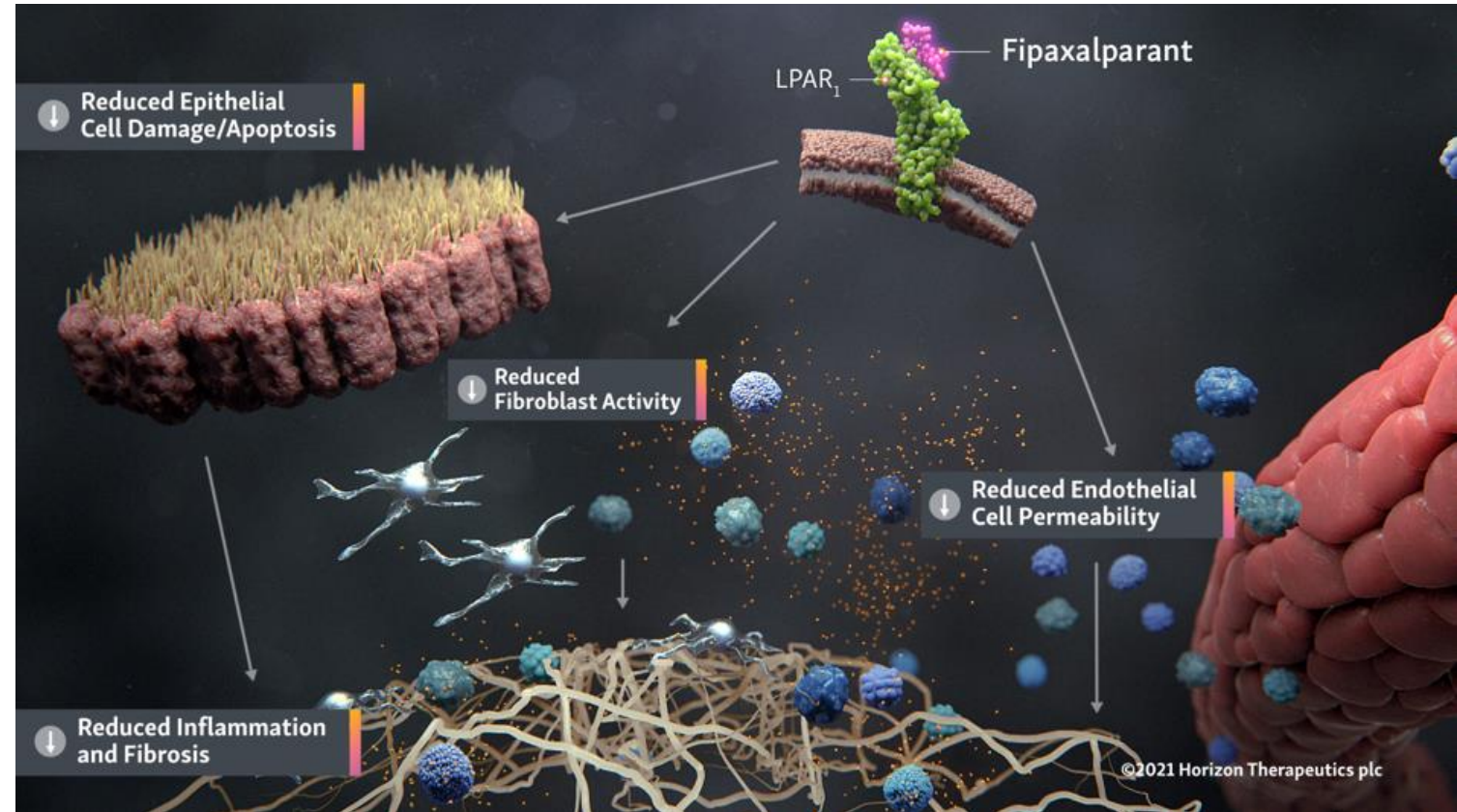
Acro-osteolysis



<sup>1</sup> Bergamasco, Aurore et al. 2019 Prevalence from Epidemiology Assumptions Presentation; FDA = U.S. Food and Drug Administration. Provided February 22, 2024, as part of an oral presentation and is qualified by such, contains forward-looking statements, actual results may vary materially; Amgen disclaims any duty to update.

# Fipaxalparant Is an LPAR1 Antagonist in Phase 2 Development for IPF and dcSSc

- Fipaxalparant is a small molecule designed to block dysregulated LPA signaling via LPAR1
- LPA is a bioactive molecule that works through several receptors (LPAR) on cells
- Dysregulated signaling via LPAR1 can cause leaky blood vessels, inflammation, and fibrosis, leading to many fibrotic diseases
- In Phase 2 development for:
  - Idiopathic pulmonary fibrosis; data readout H2 2024
  - Diffuse cutaneous systemic sclerosis



LPAR1 = Lysophosphatidic acid receptor 1; LPA = lysophosphatidic acid; LPAR = Lysophosphatidic acid receptor; IPF = idiopathic pulmonary fibrosis; dcSSc = diffuse cutaneous systemic sclerosis. Provided February 22, 2024, as part of an oral presentation and is qualified by such, contains forward-looking statements, actual results may vary materially; Amgen disclaims any duty to update.

# Severe Autoimmune Diseases With Significant Unmet Need

## Primary Discoid Lupus Erythematosus

- A chronic, inflammatory skin condition categorized by plaques that develop into permanent atrophic disfiguring scars and alopecia
- Largest segment within cutaneous lupus
- Prevalence: < 40k patients in the U.S.<sup>1</sup>
- No FDA approved, highly effective treatments



## Dermatomyositis & Anti-Synthetase Inflammatory Myositis

- Debilitating autoimmune inflammatory diseases
  - Muscle manifestation: muscle weakness, dysphagia, dysphonia
  - Skin manifestation: papules, plaques, red or purple rash on skin, calcium deposits under skin
  - Systemic manifestations: cardiovascular respiratory, and endocrine
- Prevalence: ~ 40k patients in the U.S.<sup>2</sup>
- Need for new therapies that can target underlying disease



Note: CLASI-A: Cutaneous lupus erythematosus disease area and severity index-activity

FDA = U.S. Food and Drug Administration.

1. Izmirtiy, Peter et al. 2019

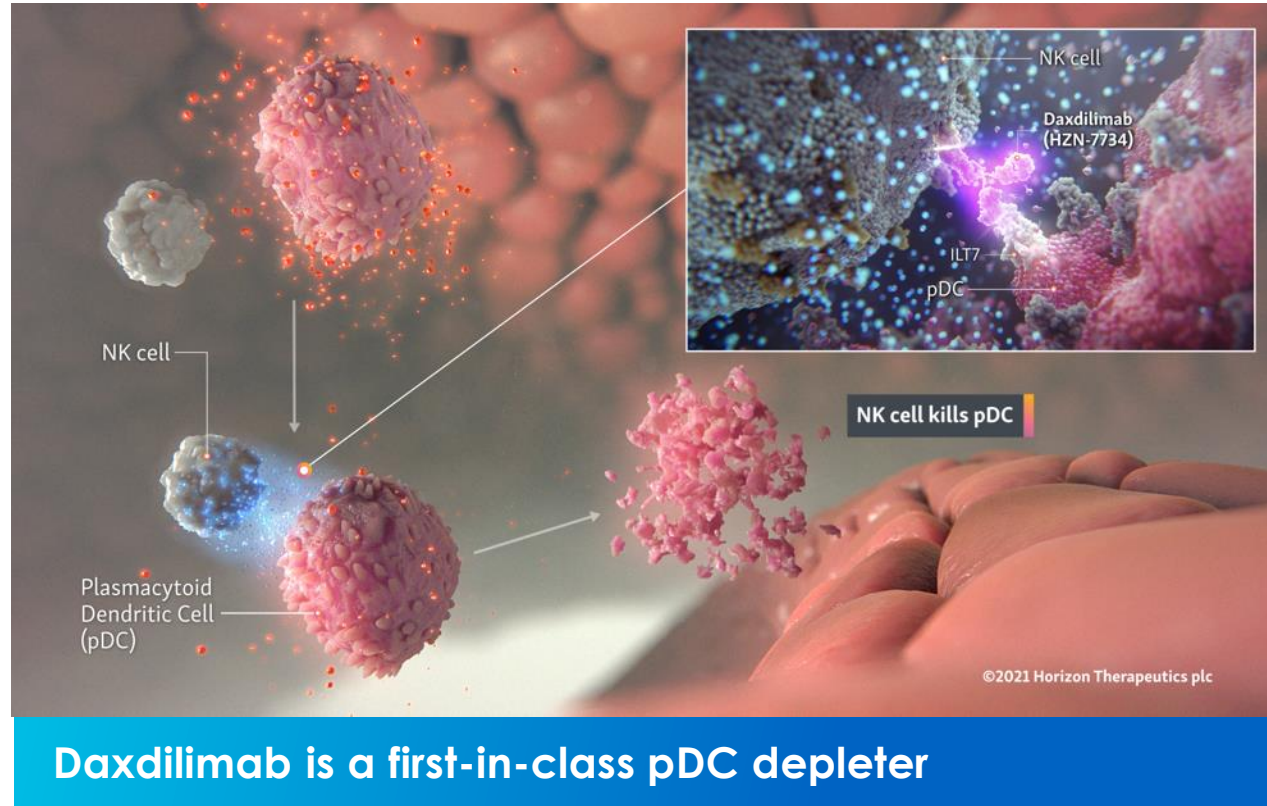
2. Kronzer, Vanessa L et al. 2023

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# Daxdilimab Is a First-in-Class, Plasmacytoid Dendritic Cell Depletor in Phase 2 Development for Primary DLE, DM, and ASIM

- Daxdilimab depletes plasmacytoid dendritic cells
- Plasmacytoid dendritic cells:
  - Present in high numbers
  - Constantly activated in autoimmunity
  - Secrete large amounts of type I interferons
  - Depletion (via targeting ILT7) reduces type I interferon production (and potentially other cytokines and chemokines), controlling inflammation
- In Phase 2 development for:
  - Primary discoid lupus erythematosus
  - Dermatomyositis and anti-synthetase inflammatory myositis



# CONCLUSION

**AMGEN**

# Rare Disease: Amgen's Newest Therapeutic Area Pillar to Drive Long-Term Growth



- Rare Disease establishes a fourth pillar of growth
- Leverages Amgen's decades of experience and leadership in inflammation, world-class manufacturing and process development, and our extensive global footprint and presence
- Additive to long-term revenue growth; accretive in 2024 to non-GAAP earnings per share
- Strong pipeline of in-line and innovative clinical programs to treat rare diseases that will also be additive to long-term growth

**RARE DISEASE PILLAR PROVIDES LONG-TERM GROWTH THROUGH INNOVATIVE MEDICINES THAT ARE EARLY IN THEIR LIFECYCLE WITH MANY WAYS TO EXPAND; PIPELINE IS UPSIDE**

Q&A

**AMGEN**