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Corporate Presentation

SEPTEMBER 2021

Forward Looking Statements

This presentation (together with any other statements or information that we may make in connection herewith) contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 with respect to Kiniksa Pharmaceuticals, Ltd. (and its consolidated subsidiaries, collectively, unless context otherwise requires, "Kiniksa," "we," "us" or "our"). In some cases, you can identify forward looking statements by terms such as "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "goal," "design," "target," "project," "contemplate," "believe," "estimate," "predict," "potential," "strategy," or "continue" or the negative of these terms or other similar expressions, although not all forward-looking statements contain these identifying words. All statements contained in this presentation that do not relate to matters of historical fact should be considered forward-looking statements, including without limitation, statements regarding our commercial and clinical strategy; potential value drivers; potential indications; potential market opportunities and competitive position; ongoing, planned and potential clinical trials and other studies; timing and potential impact of clinical data; regulatory and other submissions, applications and approvals; commercial strategy and commercial activities; expected run rate for our cash, cash equivalents and short-term investments; expected funding of our operating plan; and capital allocation.

These statements involve known and unknown risks, uncertainties, and other important factors that may cause our actual results, performance or achievements to be materially different from those expressed or implied by the forward-looking statements, including, without limitation, potential delays or difficulties with our clinical trials; potential inability to demonstrate safety or efficacy or otherwise producing negative, inconclusive or uncompetitive results; potential for changes in final data from preliminary or interim data; potential inability to replicate in later clinical trials positive results from earlier trials and studies; our reliance on third parties for manufacturing and conducting clinical trials, research and other studies; our ability to source sufficient drug product, as needed, to meet our clinical and commercial requirements; our inability to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities; potential for applicable regulatory authorities to not accept our filings or to delay or deny approval of, or emergency use authorization for, any of our product candidates or to require additional data or trials to support any such approval or authorization; delays, difficulty or inability successfully execute on our commercial strategy for ARCALYST; potential changes in our strategy, clinical trial priority, operating plan and funding requirements; drug substance and/or drug product shortages; substantial new or existing competition; potential impact of the COVID-19 pandemic, and measures taken in response to the pandemic, on our business and operations as well as the business and operations of our manufacturers, CROs upon whom we rely to conduct our clinical trials, and other third parties with whom we conduct business or otherwise engage, including the FDA and other regulatory authorities; and our ability to attract and retain qualified personnel.

These and the important factors discussed in our filings with the U.S. Securities and Exchange Commission, including under the caption "Risk Factors" contained therein, could cause actual results to differ materially from those indicated by the forward-looking statements made in this presentation. These forward-looking statements reflect various assumptions of Kiniksa's management that may or may not prove to be correct. No forward-looking statement is a guarantee of future results, performance, or achievements, and one should avoid placing undue reliance on such statements. Except as otherwise indicated, this presentation speaks as of the date of this presentation. We undertake no obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

This presentation also contains estimates, projections, and/or other information regarding our industry, our business and the markets for certain of our product candidates, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, clinical trials, studies and similar data prepared by market research firms and other third parties, from industry, medical and general publications, and from government data and similar sources. Information that is based on estimates, forecasts, projections, market research, or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information.

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Developing Life-Changing Medicines For The Patients Who Need Them Most

BY THE NUMBERS

1 FDA-approved therapy

3 Clinical-stage assets in multiple indications

3 Orphan Drug designations

2 Breakthrough designations

40 Active and completed global clinical studies to date

200+ Employees and growing

2015 Company founded

2021 Commercial availability of first and only FDA-approved therapy for recurrent pericarditis in the US: ARCALYST® (rilonacept)

LOCATIONS

MORE STRENGTHS

- Passionate employees
- A robust pipeline of product candidates for debilitating diseases
- Find and deliver novel treatments for patients with a significant unmet need
- Focus on immune modulation
- Strong biologic rationale and validated mechanisms
- In-house research team and lab
- Kiniksa manufacturing for early-stage programs

DISEASE AREAS

- Recurrent Pericarditis
- Cryopyrin-Associated Periodic Syndromes (CAPS)
- Deficiency of IL-1 Receptor Antagonist (DIRA)
- COVID-19-Related Acute Respiratory Distress Syndrome (ARDS)
- Giant Cell Arteritis (GCA)
- Prurigo Nodularis
- Rheumatoid Arthritis

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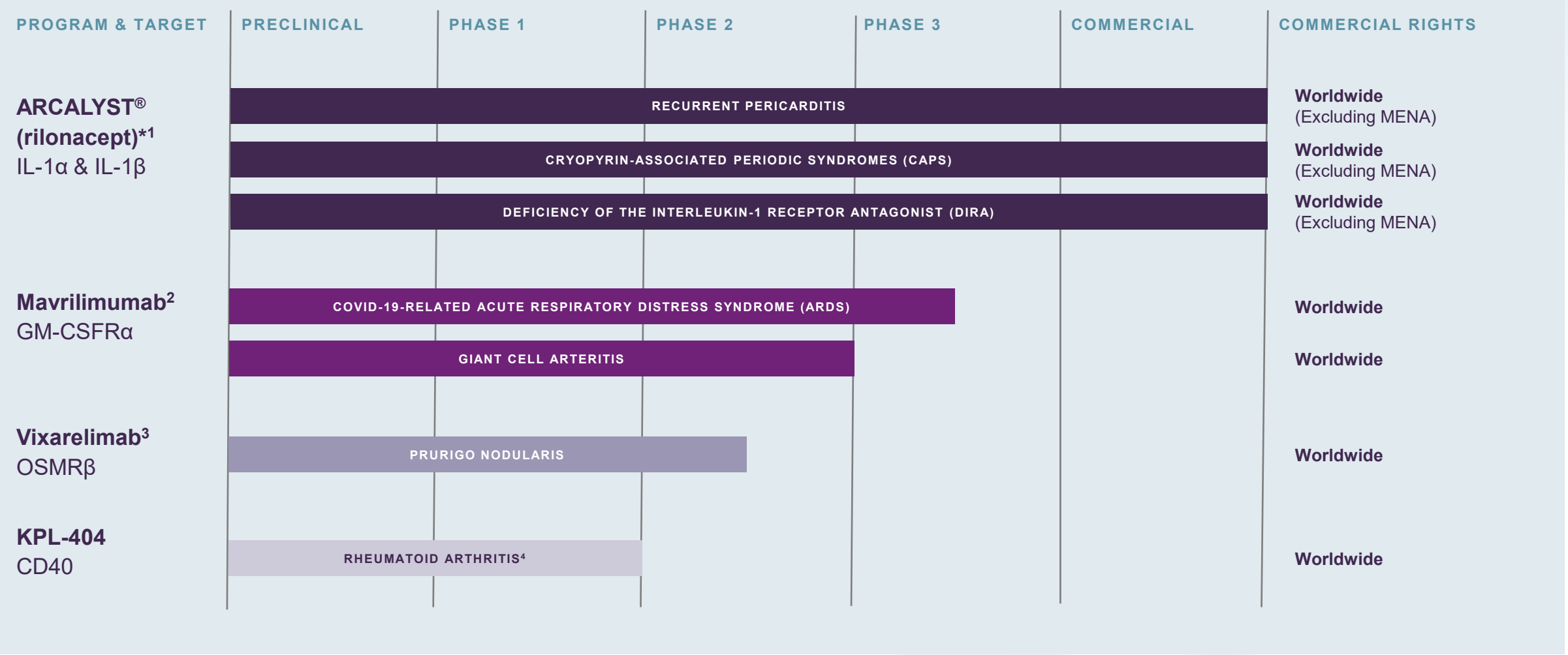
Portfolio of Four Immune-Modulating Assets



* Approved in the U.S.
1) The FDA granted Breakthrough Therapy designation to ARCALYST for recurrent pericarditis in 2019 and Orphan Drug designation to ARCALYST for pericarditis in 2020. The European Commission granted Orphan Drug designation to ARCALYST for the treatment of idiopathic pericarditis in 2020; 2) The FDA granted Orphan Drug designation to mavrilimumab for giant cell arteritis in 2020; 3) The FDA granted Breakthrough Therapy designation to vixarelimab for the treatment of pruritus associated with prurigo nodularis in 2020; 4) Kiniksa plans to initiate a Phase 2 proof-of-concept trial in patients in the fourth quarter of 2021. The planned trial will provide safety and characterization of chronic administration as well as the potential to evaluate KPL-404 across a range of other autoimmune diseases ; IL-1α = interleukin-1α ; IL-1β = interleukin-1β; GM-CSFRα = granulocyte macrophage colony stimulating factor receptor alpha; OSMRβ = oncostatin M receptor beta; MENA = Middle East and North Africa

ARCALYST®

Arcalyst® (rilonacept) For Injection

IL-1α and IL-1β cytokine trap

Disease Area: Recurrent pericarditis[1]; painful and debilitating auto-inflammatory cardiovascular disease

Competition[2]: First and only FDA-approved therapy for recurrent pericarditis

Regulatory: U.S. Orphan Drug designation in pericarditis; U.S. Breakthrough Therapy designation in recurrent pericarditis; European Commission Orphan Drug designation in idiopathic pericarditis

Status: FDA-Approved

Economics: 50/50 profit split on the approved indications in the U.S.

Rights: Kiniksa has the worldwide rights (excluding MENA) to recurrent pericarditis, CAPS and DIRA

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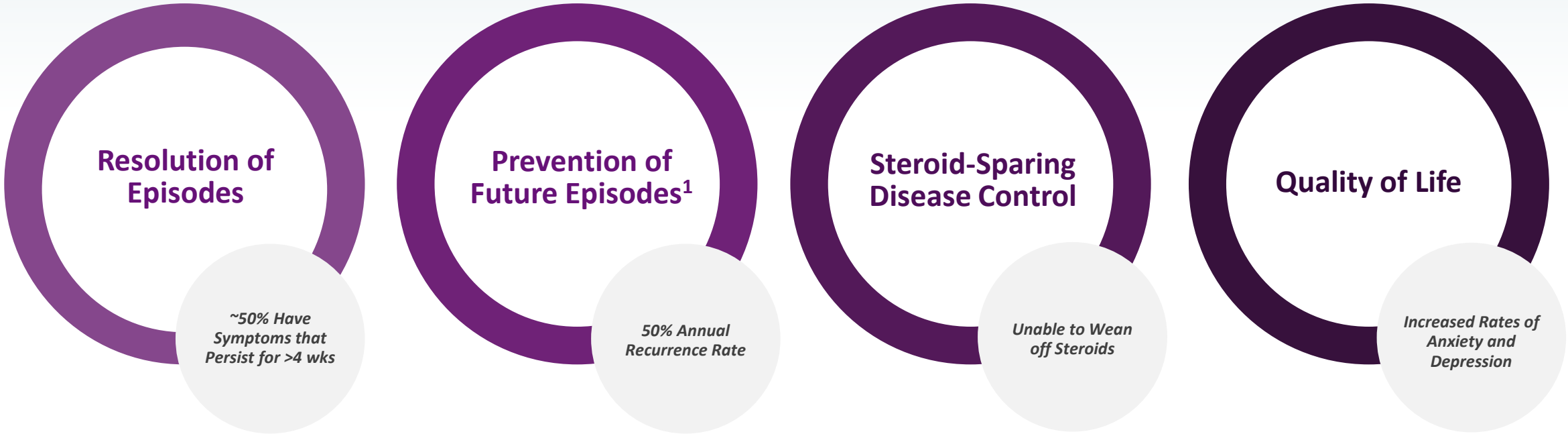
1) ARCALYST is also approved and marketed for Cryopyrin-Associated Periodic Syndromes (CAPS) and maintenance of remission of Deficiency of Interleukin-1 Receptor Antagonist (DIRA) in the United States; 2) Drugs@FDA: Arcalyst Prescribing Information, Ilaris Prescribing Information, Kineret Prescribing Information; Kaiser et al. Rheumatol Int (2012) 32:295–299; Theodoropoulou et al. Pediatric Rheumatology 2015, 13(Suppl 1):P155 ; Fleischmann et al, 2017 ACR/ARHP Abstract 1196; Kosloski et al, J of Clin Pharm 2016, 56 (12) 1582-1590; Cohen et al. Arthritis Research & Therapy 2011, 13:R125; Cardiel et al. Arthritis Research & Therapy 2010, 12:R192; Hong et al. Lancet Oncol 2014, 15: 656-666; IL-1α = interleukin-1α ; IL-1β = interleukin-1β; MENA = Middle East North Africa

Key Areas of Unmet Need in Patients with Recurrent Pericarditis

Recurrent pericarditis episodes: painful, debilitating and disruptive to quality of life



Source: Kiniksa Pharmaceuticals data on file 2019; 1) Prevention of future episodes while on treatment

ARCALYST Label

ARCALYST is a patient-administered once-weekly subcutaneous therapy

ADULTS (18 years and older)	**ADOLESCENTS** (12 to 17 years)
Loading dose: **320 mg** delivered as two 160 mg (2 mL) injections	**Loading dose:** **4.4 mg/kg** delivered up to a maximum of 320 mg, delivered as 1 or 2 injections (not to exceed 2 mL/injection)
Weekly maintenance dose: **160 mg** delivered once weekly as a 2 mL injection	**Weekly maintenance dose:** **2.2 mg/kg** delivered up to a maximum of 160 mg (2 mL) injection, once weekly

The first injection of ARCALYST should be performed under the supervision of a healthcare professional.

ARCALYST is supplied in sterile, single-use, 20-mL glass vials

- Each vial contains 220 mg ARCALYST, a sterile, white to off-white lyophilized powder
- Reconstitution with 2.3 mL of preservative-free Sterile Water for Injection is required prior to subcutaneous administration of the drug
- The reconstituted ARCALYST is a viscous, clear, colorless to pale yellow, free from particulates, 80-mg/mL preservative-free solution

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ARCALYST Use in Clinical Practice

Average Duration of Recurrent Pericarditis is 2 Years[1]

- The presence of certain baseline characteristics may identify patients who may benefit from longer-term treatment
- The mean duration of disease in RHAPSODY in patients prior to enrollment was 2.4 years

Median treatment duration in RHAPSODY was 9 months, with a range up to 14 months, at the close of the randomized period

- ARCALYST treatment was associated with a 96% reduction in risk for pericarditis recurrence
- Patients on ARCALYST experienced no/minimal pericarditis pain for 92% of trial days[2]
- 74/75 patients continued into LTE for longer-term therapy, demonstrating a desire to continue to a duration of up to 24 months

Data support treatment duration tailored to duration of autoinflammation

- Registry data indicate patients treated for 6 months have worse outcomes compared to patients treated for 9 months[3]
- The only events in the ARCALYST arm in the randomized period of RHAPSODY took place in the setting of temporary drug interruptions of 1-3 doses
- Continued ARCALYST treatment resulted in continued treatment response.

Additional data anticipated from LTE, in which patients are assessed at 18 months (including imaging) for possible treatment cessation under observation[4]

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1) D. Lin, et al.; Recurrence Burden in Recurrent Pericarditis: A US-Based Retrospective Study of Administrative Healthcare Claims; Quality of Care and Outcomes Research (QCOR) 2020 Scientific Sessions; 2) Compared to 40% of trial days in patients treated with placebo; 3) M. Imazo, et al.; Anakinra for corticosteroid-dependent and colchicine-resistant pericarditis: The IRAP (International Registry of Anakinra for Pericarditis) study. European Journal of Preventative Cardiology 2019; 4) A. Klein, et al.; 2020 AHJ Reference for Phase 3 design; LTE = long-term extension

ARCALYST: First and Only FDA-Approved Therapy for Recurrent Pericarditis

Third indication for ARCALYST underscores utility in IL-1 mediated diseases

Arcalyst® (rilonacept) Injection for Subcutaneous Use

Arcalyst® (rilonacept) For Injection

2008	2020	2021
CAPS FDA Approved	DIRA FDA Approved	Recurrent Pericarditis FDA Approved

KINIKSA oneconnect™ support made simple.

CAPS = Cryopyrin-Associated Periodic Syndromes ; DIRA = Deficiency of IL-1 Receptor Antagonist

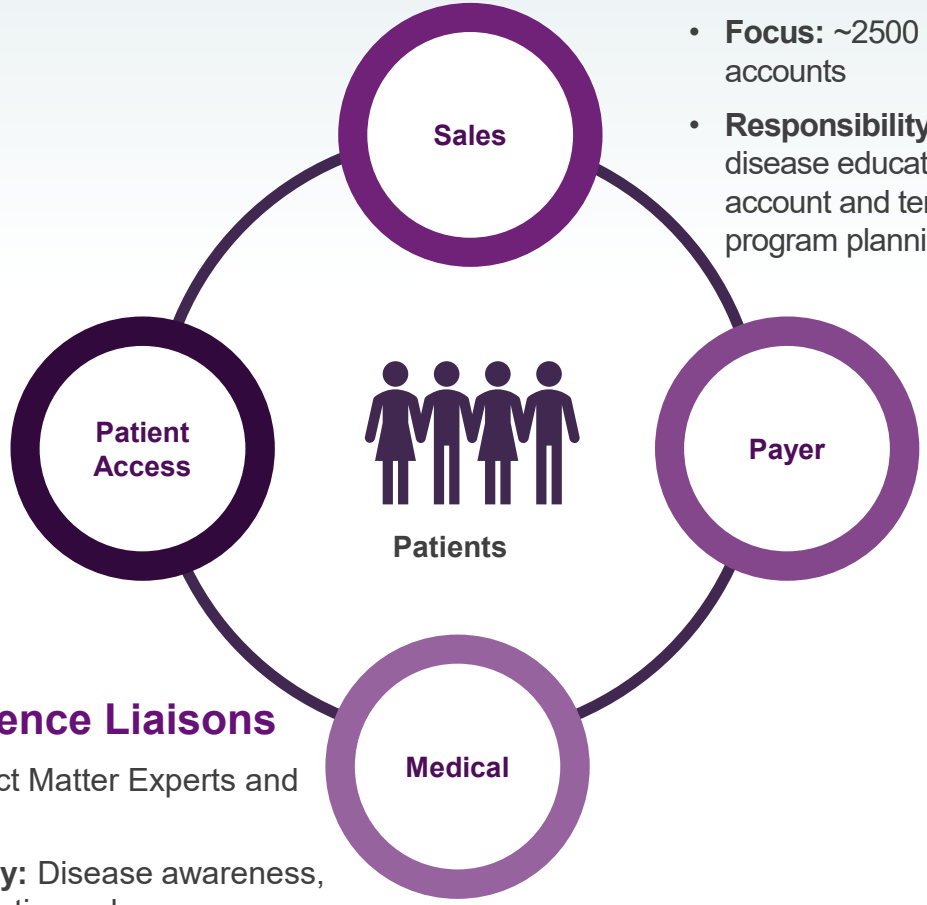
Collaborative Field Force to Drive Awareness, Overcome Access Barriers and Help Ensure Positive Patient and Physician Experience

Clinical Sales Specialists

- **Focus:** ~2500 HCPs across ~800 accounts
- **Responsibility:** Physician accounts, disease education, Arcalyst promotion, account and territory plans, speaker program planning

Patient Access Leads

- **Focus**: Patients and caregivers, HCPs seeking reimbursement support for their patients
- **Responsibility:** Optimize patient and customer experience with Arcalyst and Kiniksa, provide seamless initiation, reimbursement, and adherence support



Strategic Accounts

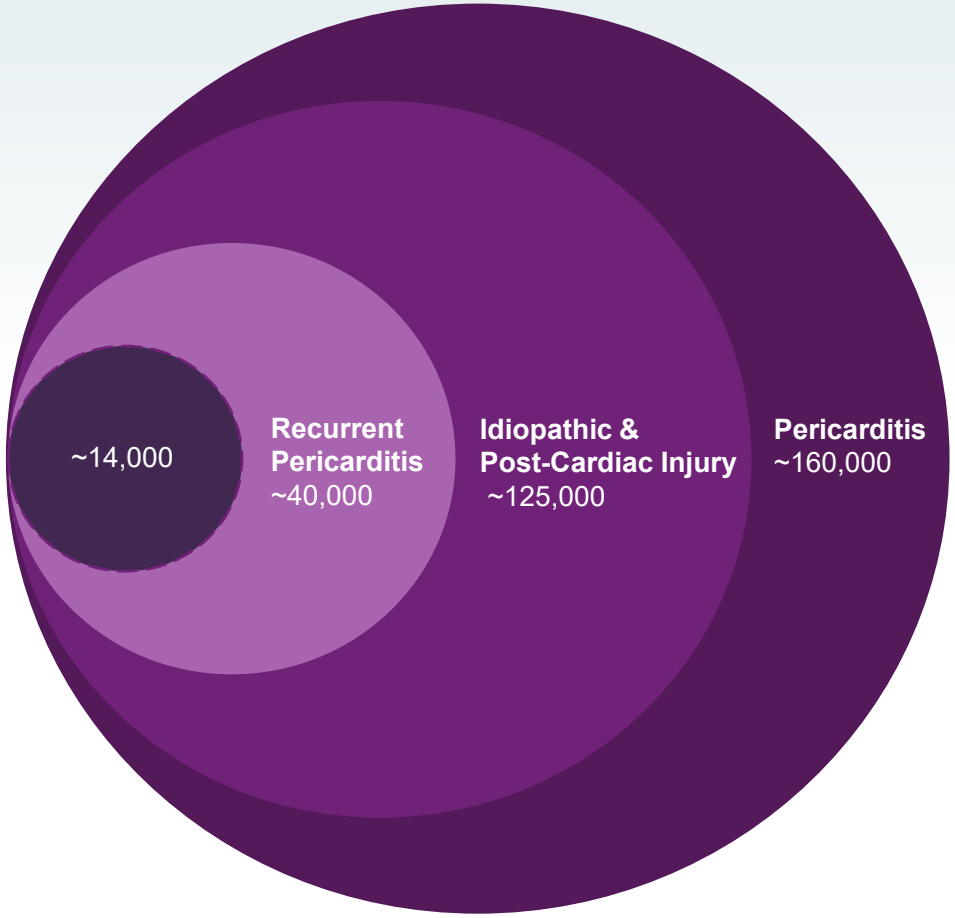
- **Focus:** ~350 payers and 5 Specialty Pharmacies
- **Responsibility:** Payer/specialty pharmacy relationship, strategic account planning, support sales team

Medical Science Liaisons

- **Focus:** Subject Matter Experts and HCPs
- **Responsibility:** Disease awareness, data dissemination, advocacy development, account and payer support, speaker management

HCP = health care provider

Pericarditis Epidemiology



All figures annual period prevalence

Approximately 14,000 recurrent pericarditis patients suffer from persistent underlying disease, with multiple recurrences and inadequate response to conventional therapy[1]

- **~ 160,000:** Epidemiological analysis using large national surveillance databases to calculate the pooled annualized prevalence of pericarditis ***(Basis for Orphan Drug Designation approval)[2]***
- **~125,000:** Approximately 75-80% are considered idiopathic (thought to be post-viral) and post cardiac injury[3-5]
- **~40,000:** Up to 30% experience at least one recurrence; some recur over multiple years[6,7]
- **~14,000:** Nearly 50% annual turnover with ~7,000 patients coming into the pool each year[8]

1) Cremer et al. American Journal of Cardiology. 2016;2311-2328; 2) DOF, Kiniksa Pharmaceuticals, Ltd.; 3) Brucato A, Maestroni S, Cumetti D, et al. Autoimmun Rev. 2008; 8:44-47; 4) Lange R, Hills L. N Engl J Med. 2004; 351: 2195-2202; 5) Imazio M, Cecchi E, Demichelis B, et al. Circulation. 2007; 115: 2739-2744; 6) Imazio et al. Circulation. 2005;112:2012-2016; 7) Adler et al. Circulation. 1998;97:2183-2185; 8) DOF, Kiniksa Pharmaceuticals, Ltd.

Recurrent Pericarditis U.S. Prevalence Estimated to be ~40K Patients

~14K patients with inadequate response to conventional therapy and persistent underlying disease

Clear Call to Action: ~14K Patients

~8K	~5K	~1K
Refractory[1,2]	Multiple Relapsing[1,2]	Steroid-Dependent[1,2]

Potential to Broaden Utilization Over Time

~3K
First Recurrence, High Risk[1,2]

1) Klein A, Cremer P, Kontzias A, Furqan M, Tubman R, Roy M, Magestro M. Annals of Epidemiology. 2019;36:71; 2) Lin D, Majeski C, DerSarkissian M, Magestro M, Cavanaugh C, Laliberte F, Lejune D, Mahendran M, Duh M, Klein A, Cremer P, Kontzias A, Furqan M, Tubman R, Roy M, Mage. (Nov, 2019). Real-World Clinical Characteristics and Recurrence Burden of Patients Diagnosed with Recurrent Pericarditis in the United States. Poster session presented at the American Heart Association, Philadelphia, PA.; 3) ClearView Forecasting Analysis 2019 Q1

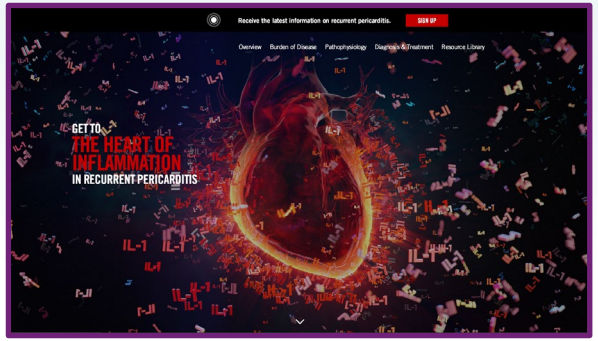
Specialty Cardiology Salesforce Expected to Reach ~70% of U.S. Recurrent Pericarditis Patients

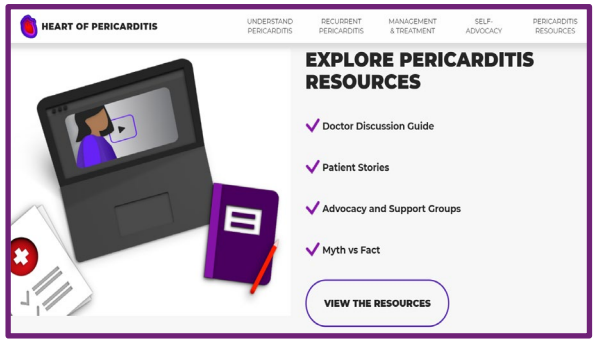
Focused & Targeted Sales Execution

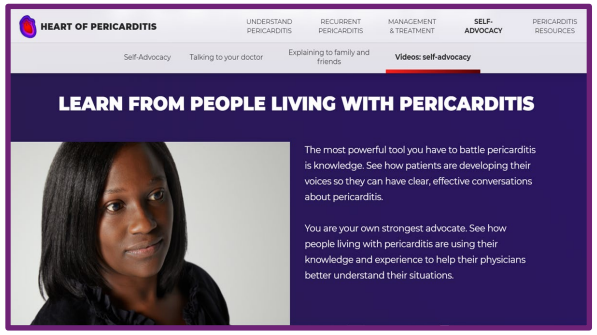
National	Territory Level	
Initial launch focus on top tier accounts **~45%** of RP patients nationally **~350** accounts nationally	**Early Launch**	**Mid-Term Expansion**
Following adoption, moving into next deciles to **~70%** of RP patients nationally **~800** accounts nationally (20% of total accounts)	**10-15** accounts **~60** high value HCPs	**30** accounts **~100** high value HCPs

Specialty cardiology sales force of ~30 reps

Disease Awareness and ARCALYST promotion







Patient Advocacy Support

PERICARDITIS ALLIANCE
AUTOINFLAMMATORY ALLIANCE formerly known as The NOMID Alliance
MYOCARDITIS FOUNDATION

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Pricing, Access and Distribution Considerations

Pricing

- Kiniksa maintains the already established list price for ARCALYST **of $20,000 per month**

  Based on first and only FDA-approved therapy for recurrent pericarditis, in-line with specialty biologics with Breakthrough Therapy and Orphan Drug designation.

- Helping to ensure patient affordability and access to treatment is one of our core principles and to this end, we offer a suite of programs to support affordability to eligible patients who are prescribed ARCALYST.

Access

- Kiniksa's goal is to enable rapid and broad access to ARCALYST for patients with Recurrent Pericarditis, CAPS, and DIRA.
- Payer mix for ARCALYST is largely **commercial (60%) and Medicare (25%)**.
- Early payer engagement has increased awareness of recurrent pericarditis and the differentiated value of ARCALYST (145 meetings and 24 clinical presentations)*
- **Kiniksa OneConnect™** is a personalized treatment support program for patients prescribed ARCALYST

Distribution

- ARCALYST is distributed through a closed network of **5 specialty pharmacies and the Veterans Affairs**.
- The distribution network for ARCALYST was developed to provide a high and consistent level of patient support with broad access. Network pharmacies provide customized services to support patients.

*Estimated through end of March
CAPS = Cryopyrin-Associated Periodic Syndromes ; DIRA = Deficiency of IL-1 Receptor Antagonist

Comprehensive Support for Patients Through Kiniksa OneConnect™

The Patient Access Leads provide one-on-one support, including:

- Insurance coverage determination
- Explanation of benefits verification
- Assistance with prior authorizations and appeals
- Injection training support and education with ARCALYST Nurse Educators
- Identification of possible sources of financial assistance
- Help with ARCALYST shipment and delivery

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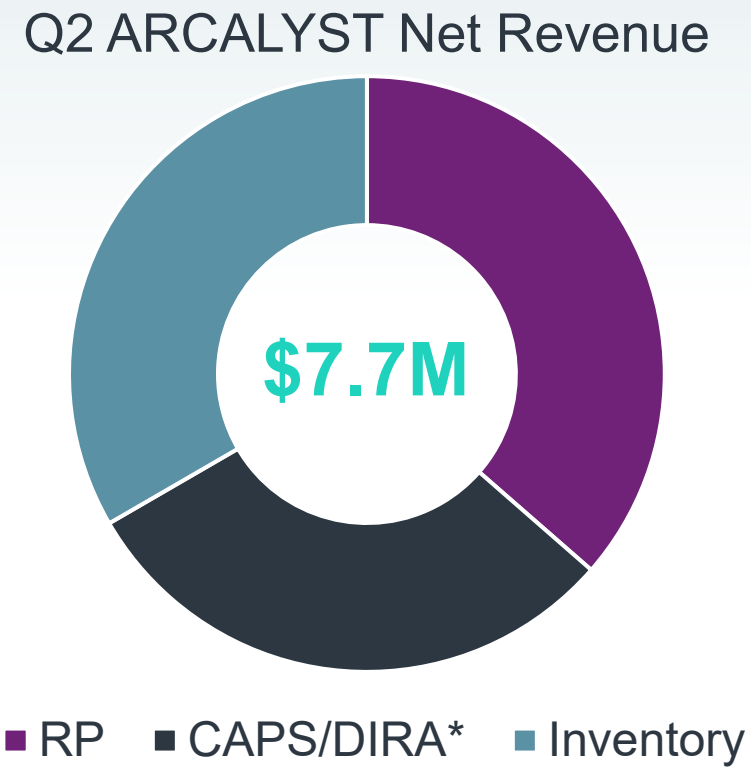
First Launch Quarter Resulted in the Successful Transition of Existing Patients and Strong Demand in Recurrent Pericarditis (RP)

Net Revenue

- $7.7 million

Revenue Drivers

- Q2 revenue relatively evenly split between RP, CAPS/DIRA, and initial channel inventory build
- Solid execution led to robust CAPS and DIRA patient continuation of therapy with demand at/near historical levels
- Q2 ending inventory weeks on hand was higher than is expected in subsequent quarters
- Strong RP demand is the primary growth driver with high conversion rate of RHAPSODY patients and new to brand patients

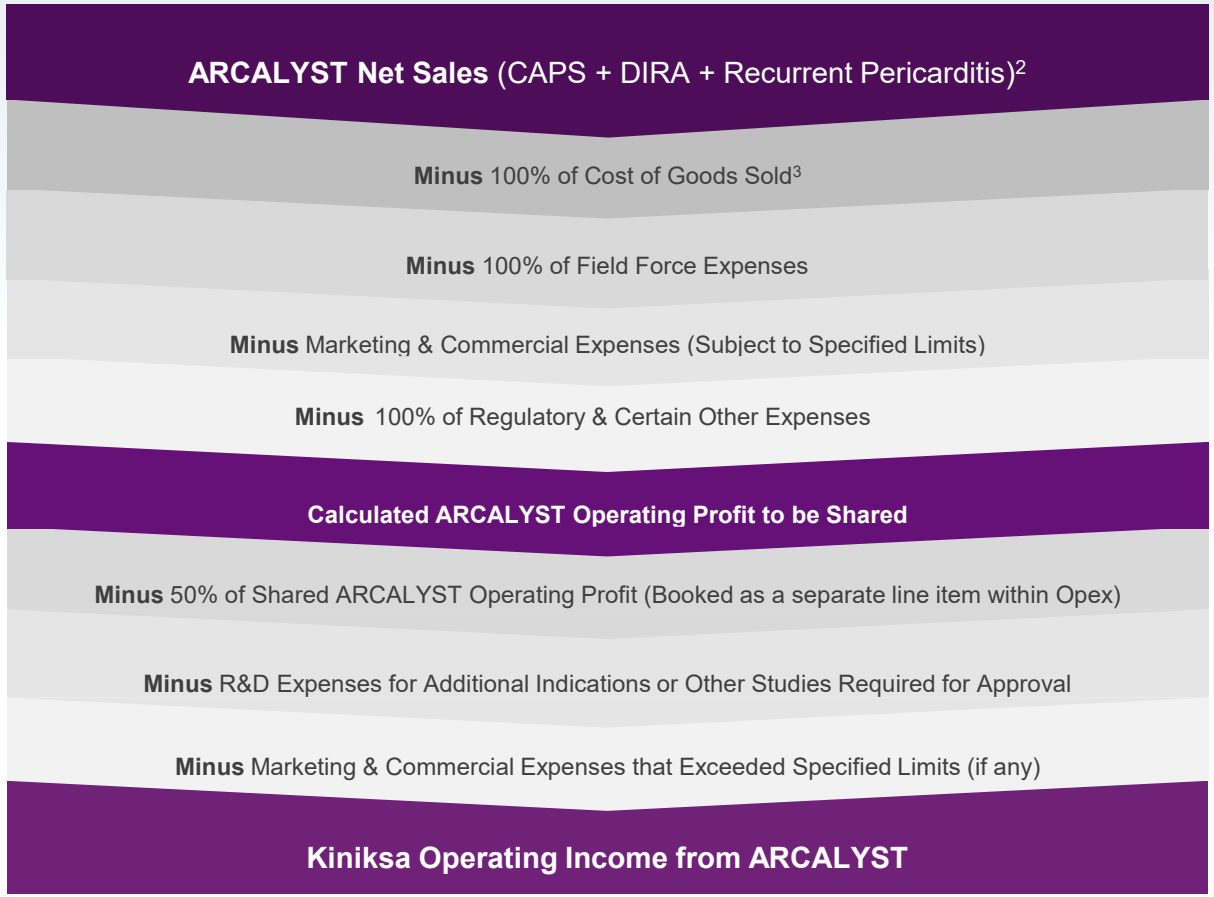


Kiniksa is expecting Q3 ARCALYST revenue of $9.0-10.0M

Driven by robust anticipated growth in RP demand

*Includes prescriptions for other indications

Summary of ARCALYST Profit Share Arrangement with Regeneron[1]



- Kiniksa is responsible for sales and distribution of ARCALYST in all approved indications in the United States.
- Kiniksa's license to ARCALYST includes worldwide rights, excluding the Middle East and North Africa, for all applications other than those in oncology and local administration to the eye or ear.
- Kiniksa covers 100% of development expenses related to approval of additional indications.
- We evenly split profits on sales with Regeneron, where profits are determined after deducting certain commercialization expenses, subject to specified limits, from ARCALYST sales.

1) Subject to description contained in definitive agreement; 2) Global net sales for CAPS, DIRA and recurrent pericarditis recognized as revenue on Kiniksa's income statement; 3) Including cost of product purchased from Regeneron as well as relevant Kiniksa overhead; CAPS = Cryopyrin-Associated Periodic Syndromes; DIRA = Deficiency of the Interleukin-1 Receptor Antagonist

MAVRILIMUMAB

Monoclonal antibody inhibitor targeting GM-CSFRα

Disease Area: COVID-19-related acute respiratory distress syndrome (ARDS); Giant Cell Arteritis (GCA): chronic inflammatory disease of medium-to-large arteries

Competition[1]: Only one FDA-approved therapy for GCA, but unmet needs remain

Regulatory: U.S. Orphan Drug designation in GCA

Status: Positive Phase 2 data in GCA reported in Q4 2020; Data from Phase 3 trial in severe COVID-19-related ARDS expected in Q1 2022

Economics: Clinical, regulatory and sales milestones; tiered royalty on annual net sales

Rights: Worldwide

1) Cortellis,;UpToDate; Correspondence, Trial of Tocilizumab in Giant-Cell Arteritis, NEJM, 2017; GM-CSFRα = granulocyte macrophage colony stimulating factor receptor alpha

Potential Broad Utility

Mavrilimumab Data Across 3 Indications:

COVID-19-related ARDS

Phase 2 trial in non-mechanically-ventilated patients with COVID-19 achieved its primary efficacy endpoint of the proportion of patients alive and free of mechanical ventilation at Day 29

Giant Cell Arteritis

Phase 2 trial of mavrilimumab in giant cell arteritis achieved both the primary and secondary efficacy endpoints with statistical significance

Rheumatoid Arthritis

Mavrilimumab was dosed in over 550 patients with rheumatoid arthritis through Phase 2b clinical studies in Europe and achieved prospectively-defined primary and secondary efficacy endpoints

Mavrilimumab has been shown to be well-tolerated in giant cell arteritis, severe COVID-19-related ARDS, and rheumatoid arthritis clinical trials

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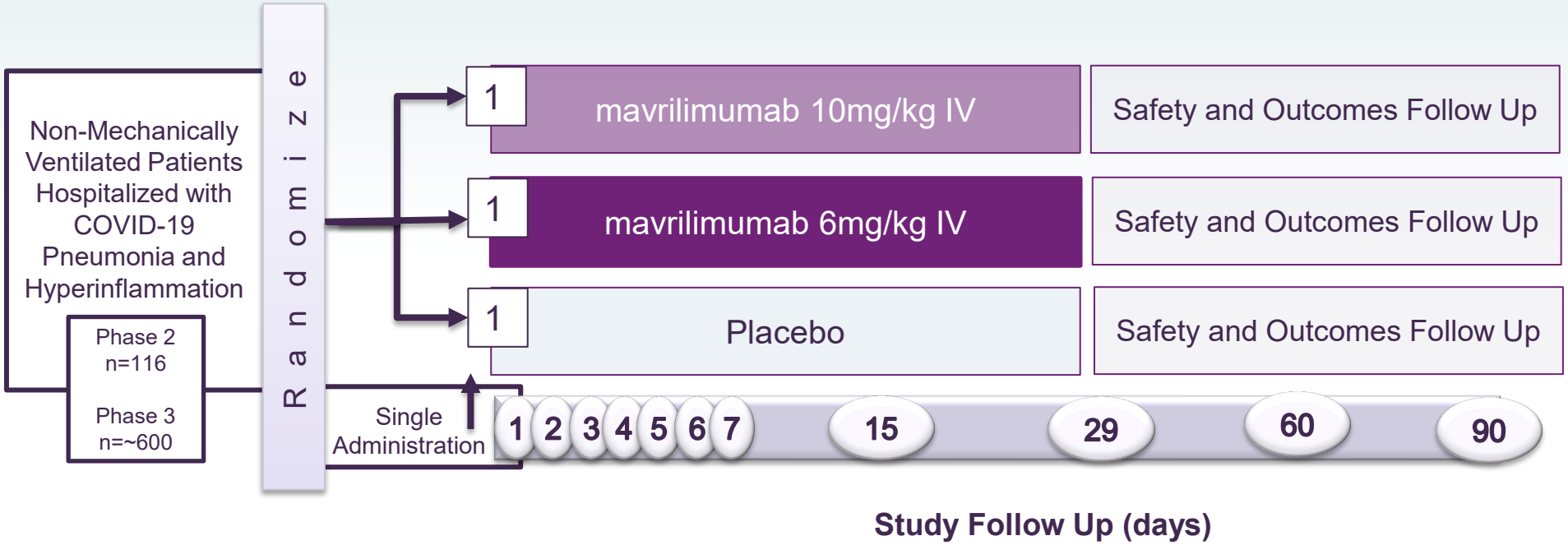
Seamless Design Phase 2/3 Clinical Trial of Mavrilimumab in COVID-19-Related ARDS

Key Inclusion Criteria:

- Positive COVID-19 test within 14 days prior to randomization
- Hospitalized for COVID-19
- Bilateral pneumonia on chest x-ray or computed tomography
- Active fever or recently documented fever within 72 hours prior to randomization
- Clinical laboratory results indicative of hyper-inflammation
- Non-ventilated; requiring supplemental oxygen to maintain oxygen saturation (SpO2) ≥ 92% and not-intubated
- All patients should receive best standard of care, including steroids and antivirals, according to investigator judgement



Primary Efficacy Endpoint:

- Proportion of patients alive and without mechanical ventilation at Day 29.

Secondary Efficacy Endpoints:

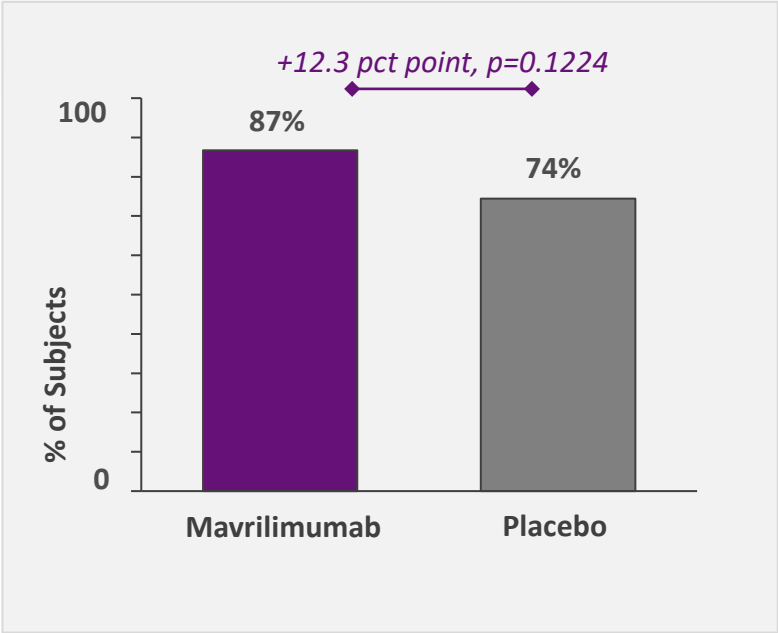
- Mortality rate at Day 29
- Ventilation-free survival (time to ventilation or death) by Day 29
- Overall survival by Day 29

ARDS = acute respiratory distress syndrome

Non-Mechanically Ventilated Patients Treated with Mavrilimumab Demonstrated a Reduction in Mechanical Ventilation and Death at Day 29 Pooled Across Dose Levels

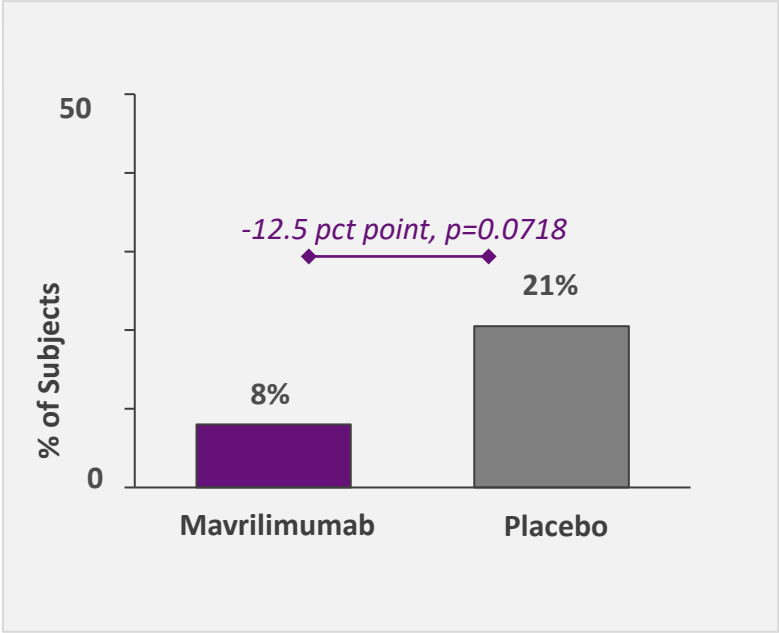
Phase 2 Data from the Phase 2/3 trial of Mavrilimumab in COVID-19-related ARDS

Primary Endpoint: Proportion of Patients Alive and Free of Mechanical Ventilation at Day 29



Mavrilimumab recipients experienced a 65% reduction in the risk of mechanical ventilation or death (Hazard Ratio (HR) = 0.35; p=0.0175).

Key Secondary Endpoint: Mortality at Day 29



Mavrilimumab recipients experienced a 61% reduction in the risk of death (HR= 0.39; p=0.0726).

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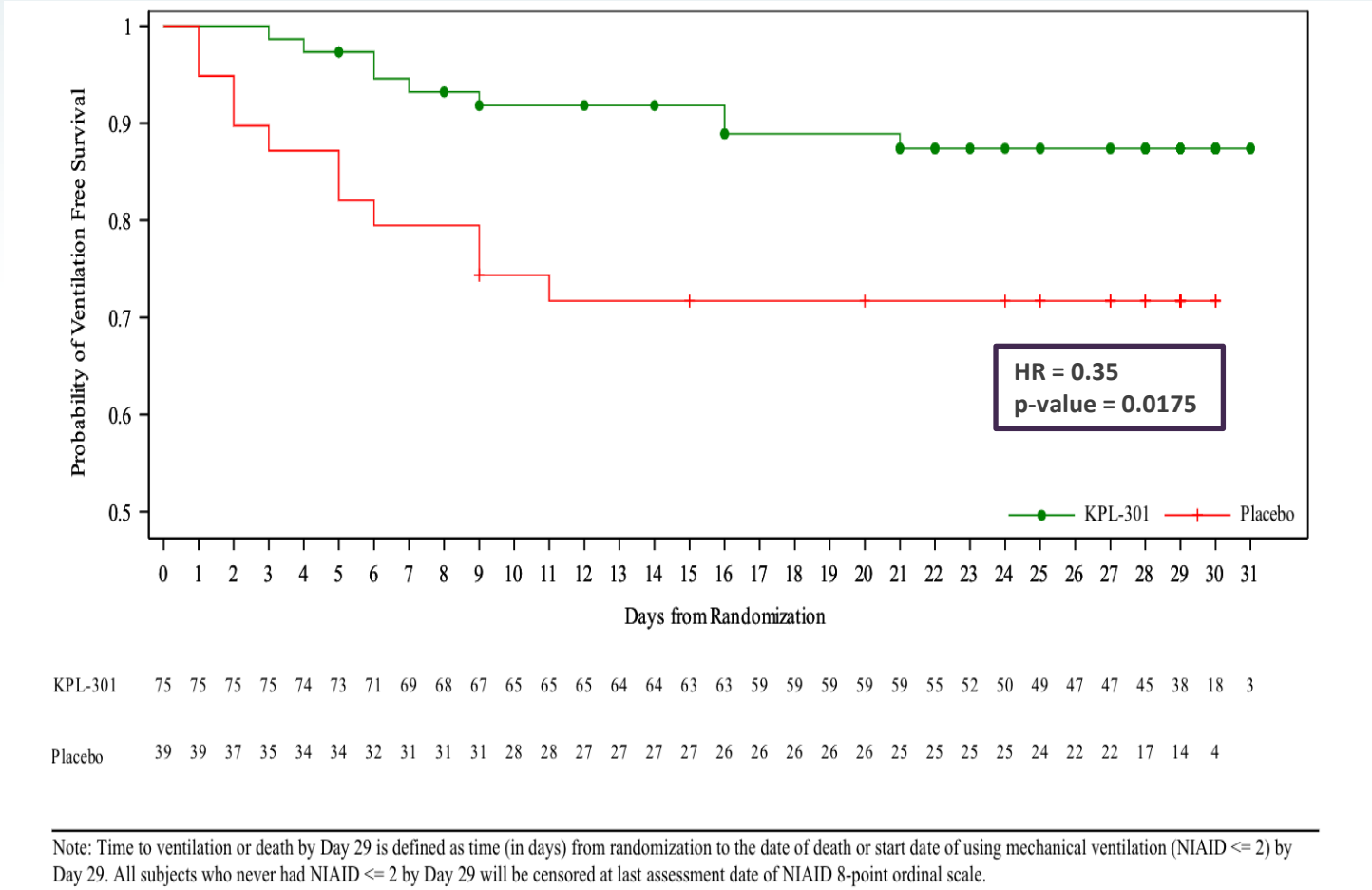
The prespecified evidentiary standard for Phase 2 endpoints was a 2-sided alpha value of 0.2, without adjustment for multiplicity.

Mavrilimumab Reduced the Risk of Mechanical Ventilation or Death by 65% Versus Placebo at Day 29 Pooled Across Dose Levels

Phase 2 data from the Phase 2/3 trial of Mavrilimumab in COVID-19-related ARDS

Baseline Demographics & Characteristics:

- 43% non-whites, 57% males enrolled
- 96% received corticosteroids/dexamethasone
- 29% received antivirals/remdesivir
- Randomized number of patients by country
  - Brazil (37.72%)
  - United States (31.58%)
  - South Africa (27.19%)
  - Peru (2.63%)
  - Chile (0.88%)

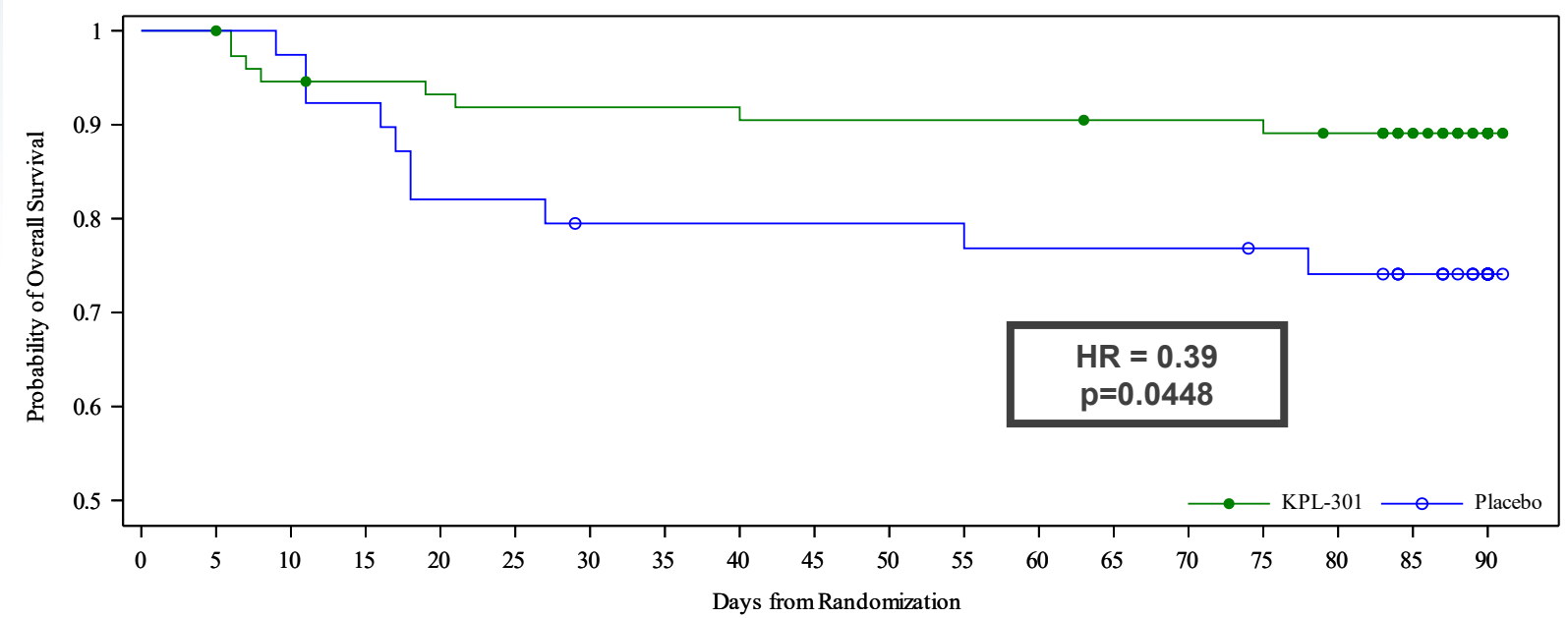


Note: Time to ventilation or death by Day 29 is defined as time (in days) from randomization to the date of death or start date of using mechanical ventilation (NIAID <= 2) by Day 29. All subjects who never had NIAID <= 2 by Day 29 will be censored at last assessment date of NIAID 8-point ordinal scale.

L Pupim et al, (2021). Mavrilimumab improves outcomes in Phase 2 trial in non-mechanically ventilated patients with severe COVID-19 pneumonia and systemic hyperinflammation, *Annals of Rheumatic Disease* 80 (Issue Suppl 1). http://dx.doi.org/10.1136/annrheumdis-2021-eular.5012

Mavrilimumab Demonstrated Persistent Clinical Effect Through Day 90

Phase 2 data from the Phase 2/3 trial of Mavrilimumab in COVID-19-related ARDS



KPL-301	75	75	70	69	68	67	67	67	67	66	66	66	66	65	65	65	63	55	43
Placebo	39	39	38	36	32	32	30	30	30	30	30	30	29	29	29	28	27	23	16

Overview of Clinical Evaluation of Mavrilimumab in COVID-19

Seamless clinical trial experience and on-going clinical development

March-April 2020	May-September 2020	July 2020-February 2021	December 2020 - Active
Italy Investigator-led Protocol (Open-label, Single-center)	**U.S. Investigator-Initiated Studies (Double-blind, Multi-center)**	**Global Phase 2 (Double-blind, Multi-center)**	**Global Phase 3 (Double-blind, Multi-center)**
Earlier and improved clinical outcomes compared to contemporary control-group N = 39 patients (13 in treated cohort)	*Trends toward lower mortality and shorter duration of mechanical ventilation in mavrilimumab treated compared to placebo N=40 patients, 52% non-white*	*65% reduction in mechanical ventilation and mortality at Day 29 in mavrilimumab treated compared to placebo N = 116 patients, 43% non-white*	*Currently enrolling with data anticipated later this year (n=600 patients)*
THE LANCET Rheumatology	THE LANCET Rheumatology	Annals of the Rheumatic Diseases	
De Luca et al, *Lancet Rheumatol*. 2020 Aug: 2(8): e465-e478	Cremer et al, *Lancet Rheumatol*. 2021 Jun: 3(6) e410-e418	Pupim et al, *Ann Rheum Dis*. Scientific Abstracts of EULAR 2021	

- Data from a Phase 2 study in a diverse population of non-mechanically-ventilated patients with severe COVID-19 pneumonia suggest that mavrilimumab may be a potential **best-in-class** in reducing risk of death in patients with severe COVID-19-related ARDS
- In the context of other treatments being evaluated, Kiniksa is particularly encouraged by the benefit/risk of **GM-CSF receptor inhibition** with mavrilimumab given the **sustained treatment effect demonstrated throughout the 90-day observation period** after a **single administration,** and the well-tolerated safety profile to-date
- Kiniksa believes the way mavrilimumab blocks the body's counterproductive inflammatory reaction is **agnostic to coronavirus variant**

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Mavrilimumab Reduced Mortality in Non-mechanically Ventilated Patients at Day 29 Pooled Across Dose Levels (Phase 2 Data)

Program	Mavrilimumab[1] *GM-CSFRα Antagonist*	Plonmarlimab[6] *Anti-GM-CSF*	Anakinra[2] *Anti-IL-1α/β*	Tofacitinib[3] *Pan-JAK Inhibitor*	Baricitinib + Remdesivir[4] *JAK 1/2 Inhibitor*	Lenzilumab[5] *Anti-GM-CSF*	Tocilizumab[7] *IL-6R Antagonist*	Dexamethasone[8] *Corticosteroid*
Population	Non-IMV subjects on top of standard of care	Non-IMV subjects on top of standard of care	Non-IMV subjects with suPAR > 6 ng ml^{-1} & pO2/FiO2 > 150 mmHg on top of corticosteroids	Non-IMV subjects on top of corticosteroids	Non-IMV subjects on top of standard of care	Non-IMV subjects on top of corticosteroids	Non-IMV subjects on top of standard of care	Non-IMV subjects on top of standard of care
Decreased Risk of Death at ~1mo Relative (Absolute)	**61%** (12.5%)	**63%** (8.4%)	**54%** (3.7%)	**49%** (2.7%)	**35%**** (2.7%)	**30.9%** (4.3%)	**21%** (1.8%)	**11%** (2.8%)
Trial Details	Kiniksa-sponsored Phase 2 (n=114)	I-Mab-sponsored interim Phase 2 (n=91 interim)[6] Planned P3 enrollment Ph2/3 n=384[9])	Investigator-Initiated (n=594)	Investigator-Initiated (n=289)	Investigator-Initiated (n=1,033)	Humanigen-sponsored Phase 3 (n=520)	Investigator-Initiated (n=>4,000)	Investigator-Initiated (n=>6,000)
Status	Enrolling patients in a Phase 3 trial; data expected in Q1 2022	Continuing the Phase 2/3 clinical study in the U.S.	Completed Investigator-Initiated study	Completed Investigator-Initiated study	Completed Investigator-Initiated study	FDA declined Emergency Use Authorization Request; Phase 2/3 NIH-sponsored study ongoing	Completed Investigator-Initiated study	Completed Investigator-Initiated study
Administration	Single intravenous (IV) Infusion	Single intravenous (IV) Infusion	Once daily subcutaneous for 10 days	Oral twice daily for up to 14 days	Oral/IV once daily For up to 14 days	Three (3) IV infusions separated by 8 hours over 24-hours	Single IV infusion; possible second dose	Once daily oral or IV for up to 10 days

*Relative risk reduction in death or VFS defined as (Rate in Control –Rate in Active) / Rate in Control at ~1 month; relies on cross-trial comparisons that may be complicated by varying patient populations, study designs, etc. Not intended to be head-to-head comparisons.
** At D15; no monthly data available
ND = comparable data not disclosed

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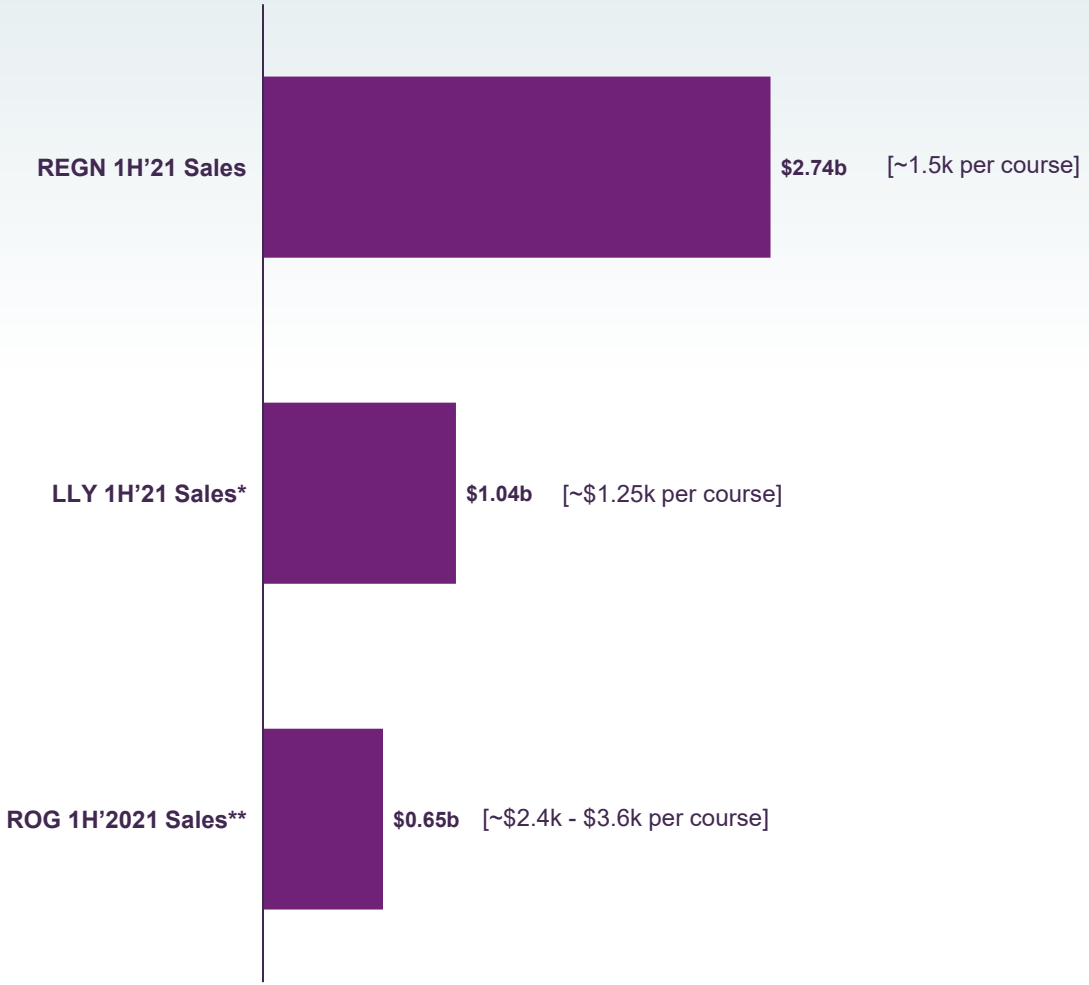
1) Kiniksa Press Release April 12, 2021; 2) Kyriazopoulou, E., Poulakou, G., Milionis, H. et al. Early treatment of COVID-19 with anakinra guided by soluble urokinase plasminogen receptor plasma levels: a double-blind, randomized controlled phase 3 trial. Nat Med (2021). https://doi.org/10.1038/s41591-021-01499-z; 3) Guimarães PO, Quirk D, Furtado RH, et al. Tofacitinib in Patients Hospitalized with Covid-19 Pneumonia. N Engl J Med. 2021;385(5):406-415. doi:10.1056/NEJMoa2101643; 4) Kalil et al., NEJM 2021; 384:795-807; 5) Humanigen Press Release March 29, 2021; 6) I-Mab Press Release August 31, 2021; 7) https://www.nejm.org/doi/full/10.1056/NEJMoa2030340 8) The RECOVERY Collaborative Group, NEJM 2021 384:693-704; 9) CT.gov NCT04341116

Significant Market Opportunity for COVID-19 Treatments



"Regeneron's COVID-19 antibodies rake in $2.6B, reflecting their market dominance and blowing away estimates" – Fierce Pharma 8/5/2021

"Eli Lilly Profit Rises, Helped by COVID-19 Drug Sales" – The Wall Street Journal 1/29/2021

"Roche warns of global Actemra shortage as delta variant drives huge spike in demand for COVID-19 patients – Fierce Pharma 8/17/2021

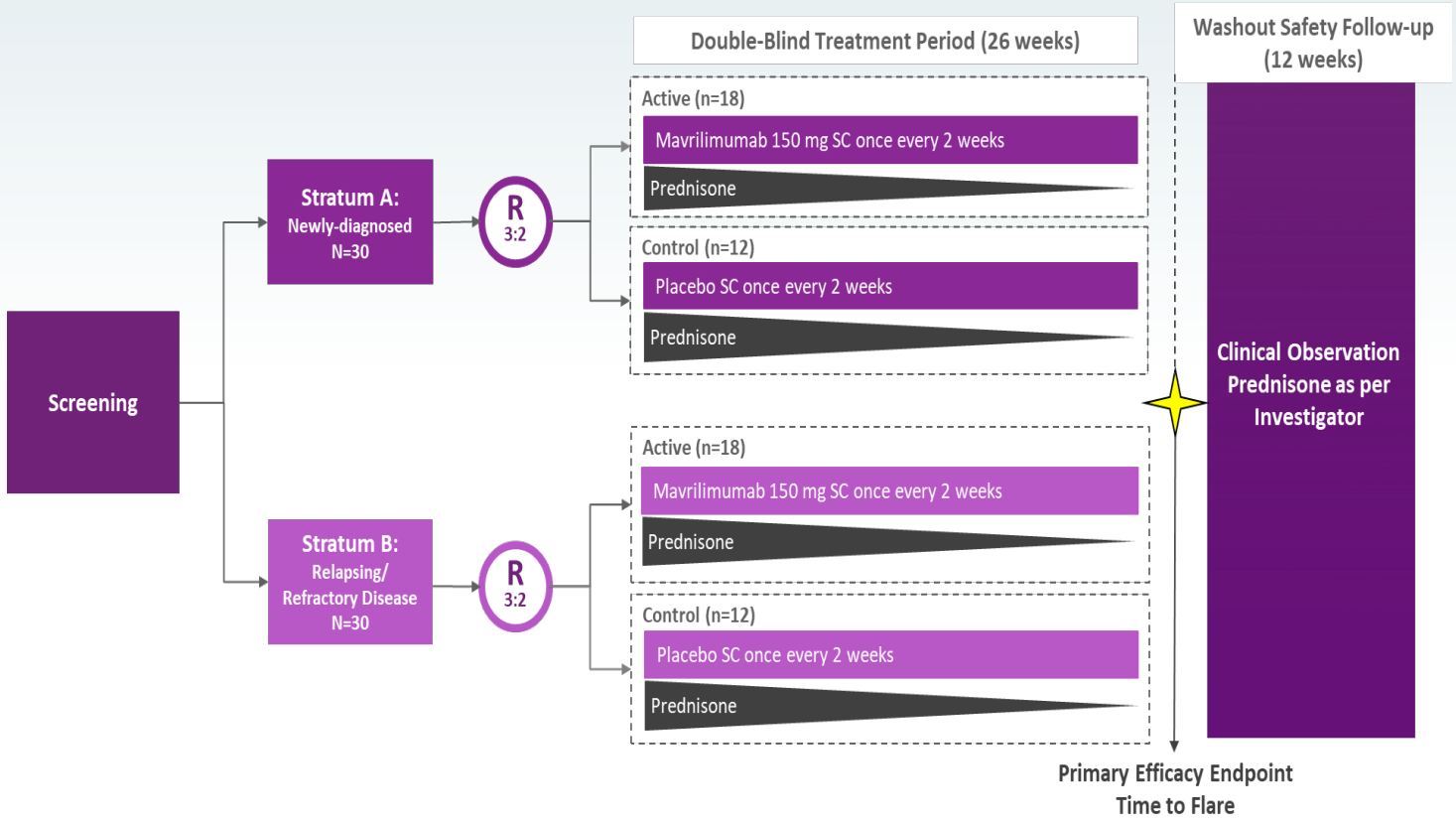
* LLY Q2 2021 sales dropped to ~$180m owing to lack of efficacy of antibody cocktail against delta variant. Baricitinib EUA approval was end of Q2
** Estimate based on reported growth of 30% YoY in 2020 and 22% YoY for 2Q 2021

Phase 2 Clinical Trial of Mavrilimumab in GCA

Key Inclusion Criteria:
- Age > 50 to 85 years
- Diagnosis of new-onset or relapsing/refractory GCA event within 6 wks prior to randomization (Biomarkers, Signs/Symptoms, imaging/biopsy)

Screening: Patients receive prednisone (or equivalent) at any dose required to induce remission at/before Randomization (resolution of symptoms and CRP < 20 mm in first hour)

Design Advances vs. GiACTA:
- Clinical remission at randomization adds precision to time-to-event endpoint
- 26 wk vs 52 wks shortens trial duration
- Adjudicated events require biomarkers and Signs/Symptoms/Imaging
- Adequately powered for 20-40% relative/absolute delta vs PBO in time-to-event in pooled population (trends in disease subgroups)



Treatment Period:
- Randomization 3:2 to mavrilimumab (150 mg) vs PBO SC q2wk)
- Prednisone (20-60 mg/day at Randomization) tapered over 26 weeks according to protocol-defined schedule

Efficacy Endpoints:
- Primary: Time to adjudicated GCA flare by Week 26
- Secondary: Sustained remission rate at Week 26

GCA Flare Definition (Adjudicated):
- Re-increase of CRP from normal to ≥1mg/dL and/or of ESR from <20 mm to ≥30 mm

-and-

- At least one of the following signs/symptoms attributed by the Investigator to be new, worsening, or recurrent GCA:
  - Cranial symptoms (new-onset localized headache, scalp or temporal artery pain or tenderness, ischemia-related vision loss, or otherwise unexplained mouth or jaw pain upon mastication)
  - Extracranial symptoms (symptoms of polymyalgia rheumatica, claudication of the extremities)
  - Imaging (new or worsening angiographic abnormalities detected via MRI, CT/CTA, or PET-CT of the aorta or other great vessels or via ultrasound of the temporal arteries

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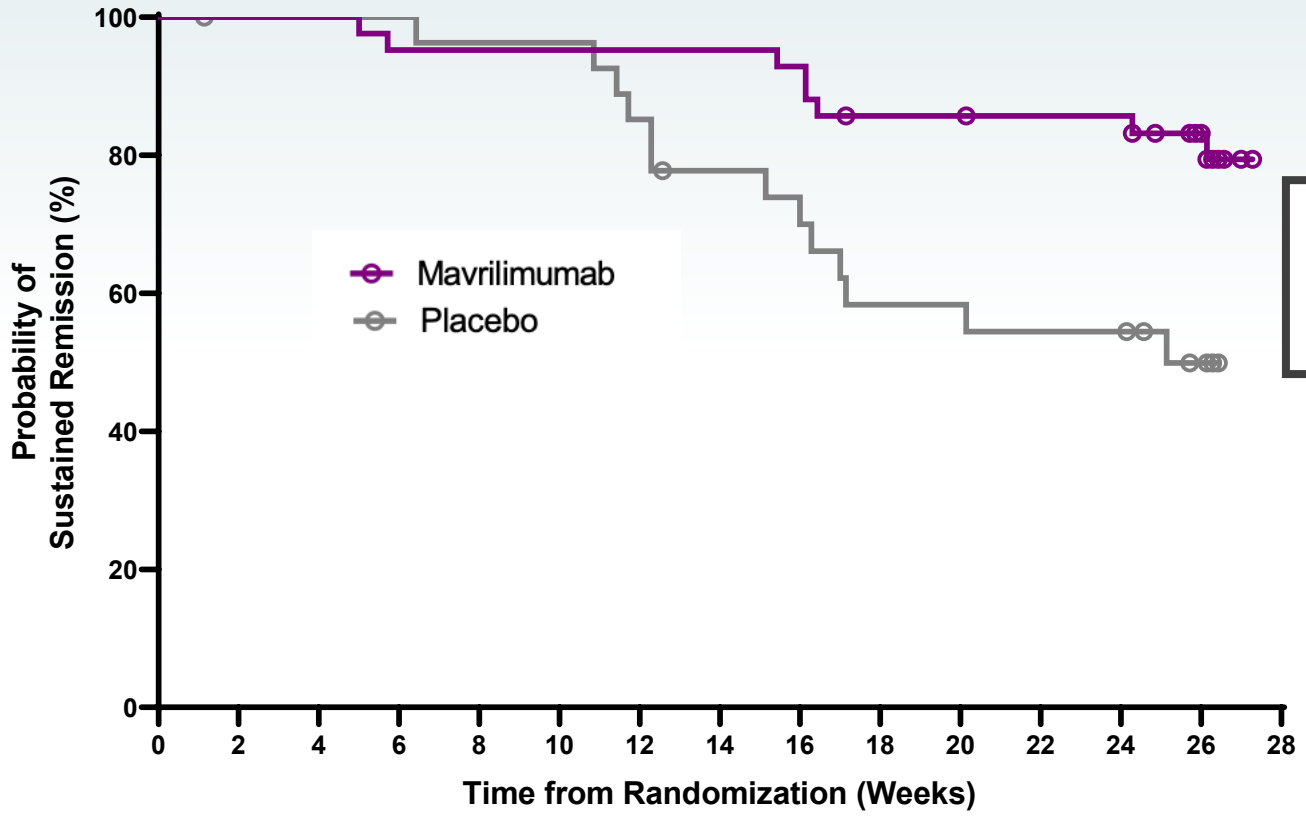
Primary Efficacy Endpoint: Time-to-First Adjudicated GCA Flare by Week 26

Mavrilimumab Phase 2 giant cell arteritis data



HR = 0.38
Risk Reduction = 62%
p=0.0263

	Mavrilimumab (N=42)	Placebo (N=28)
Patients with Flare by Week 26, n (%)	8 (19)	13 (46.4)

Median time-to-flare by Week 26 could not be estimated in mavrilimumab recipients due to the low number of flares in the mavrilimumab treatment arm. The median time-to-flare for placebo recipients was 25.1 weeks. There was a 62% lower risk of flare in mavrilimumab recipients compared to placebo recipients.

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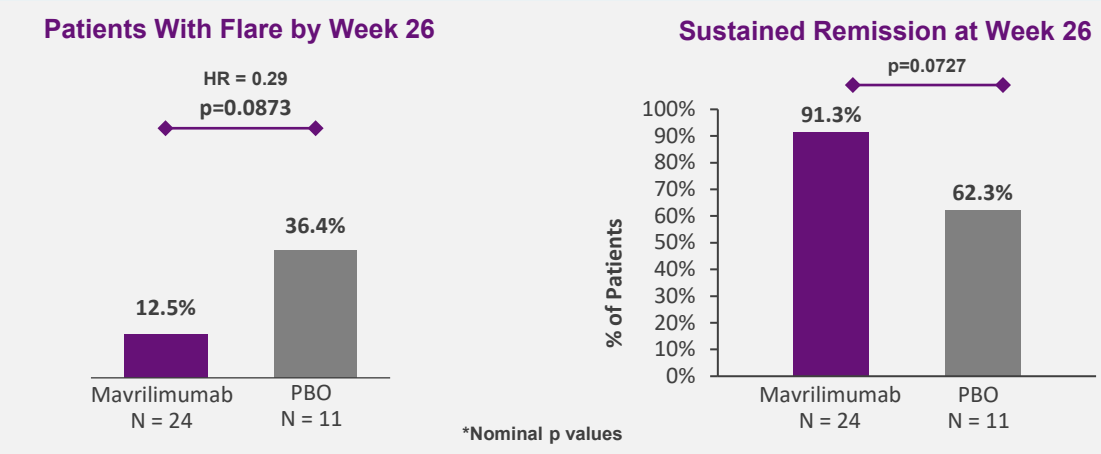
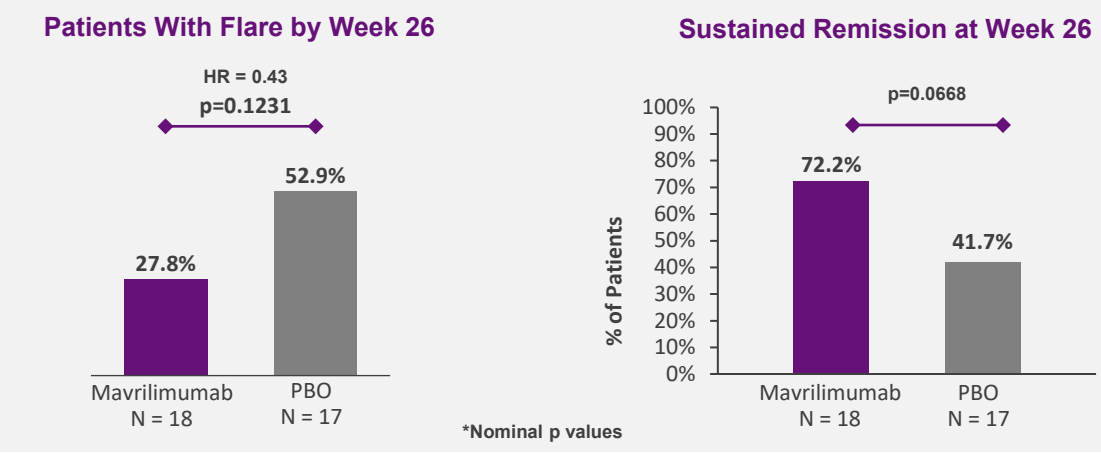
Unmet Need and Commercial Opportunity for Safe and Effective GCA Therapies

Mavrilimumab Phase 2 giant cell arteritis data[1]

New-Onset GCA



Relapsing/Refractory GCA



REMAINING UNMET NEED

- Cumulative U.S. GCA prevalence expected to grow 50% by 2035[2]
- ~50% of relapse/refractory patients are unable to achieve sustained remission within one year of starting treatment with approved biologics[3]
- Mechanistic (GM-CSFRα vs IL-6) and administrative (Q2WK vs QWK) differentiation
- Well-tolerated safety profile particularly important given large elderly patient population

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1) Statistically significant primary (p=0.0263) and secondary endpoint (p=0.0038); consistent trend of efficacy in relapsing/refractory cohort; 2) Chandran AK, Udayakumar PD, Crowson CS, Warrington KJ, Matteson EL. The incidence of giant cell arteritis in Olmsted County, Minnesota, over a 60-year period 1950–2009. Scand J Rheumatol. 2015; 44(3):215–8.; Labarca C, Koster MJ, Crowson CS, et al. Predictors of relapse and treatment outcomes in biopsy-proven giant cell arteritis: a retrospective cohort study. Rheumatology (Oxford). 2016;55(2):347-356.; Medcape; Trinity Lifesciences primary market research; Trinity Lifesciences analysis of Integrated 2016-2019 Medicare FFS & 2016-2019 IBM MarketScan Commercial & Medicare Supplemental data; 3) Trinity Partners Primary Market Research; Stone et al., NEJM 2017

VIXARELIMAB

Monoclonal antibody inhibitor targeting OSMRβ

Disease Area: Prurigo Nodularis (PN); chronic inflammatory skin disease with pruritic nodules

Competition[1]: No FDA-approved therapies for PN

Regulatory: U.S. Breakthrough Therapy designation for the treatment of pruritus associated with prurigo nodularis

Status: Enrolling and dosing in a Phase 2b clinical trial, evaluating a range of once-monthly dose regimens

Economics: Clinical, regulatory and sales milestones; tiered royalty on annual net sales

Rights: Worldwide

1) Journal of the American Academy of Dermatology - Analysis of Real-World Treatment Patterns in Patients with Prurigo Nodularis: https://www.jaad.org/article/S0190-9622(19)32744-6/pdf ; OSMRβ = oncostatin M receptor beta

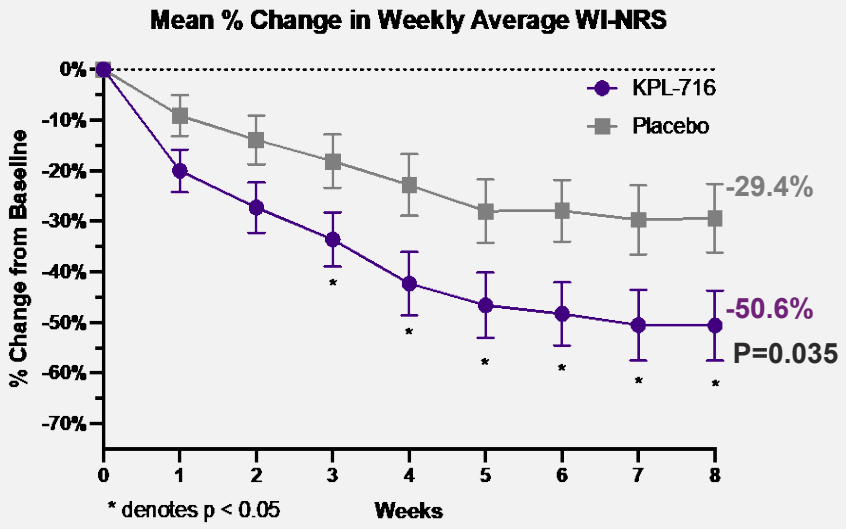
Dual Mechanism Offers Potential Pruritus Relief and Nodule Improvement

Vixarelimab Phase 2a prurigo nodularis data

Vixarelimab is the only mAb targeting OSMRβ, which mediates signaling of key cytokines (IL-31 & OSM)

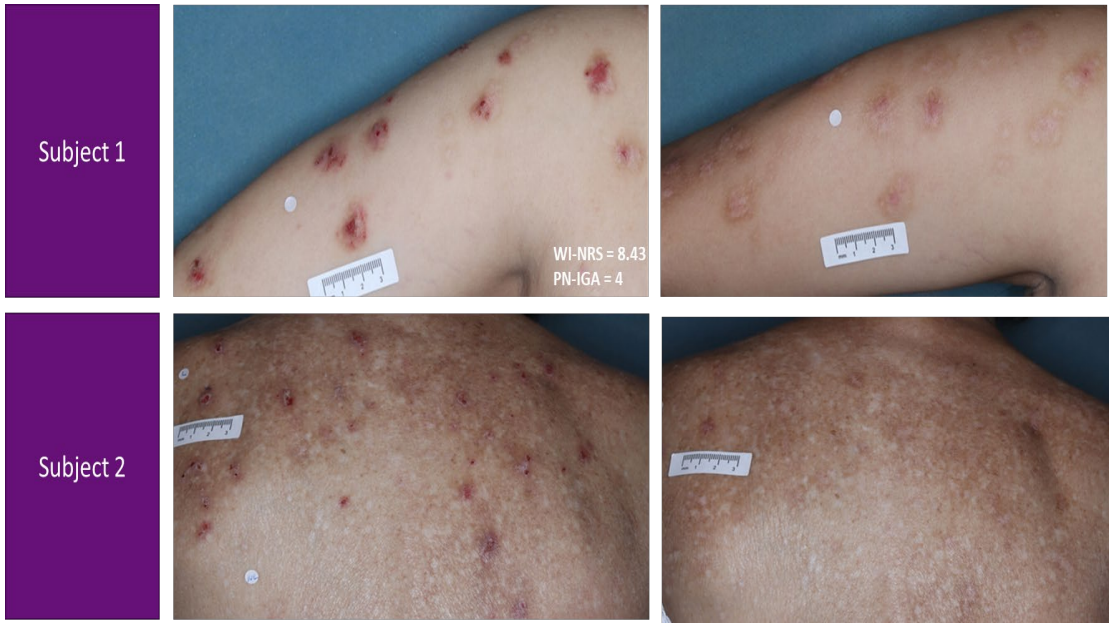
Primary Efficacy Endpoint

Mean change in weekly-average WI-NRS at Week 8 was -50.6% in vixarelimab recipients compared to -29.4% in placebo recipients (p=0.035).



Secondary Efficacy Endpoint

30.4% of vixarelimab recipients achieved a PN-IGA score of 0/1 at Week 8 compared to 7.7% of placebo recipients (p=0.032).



Representative Treatment Response

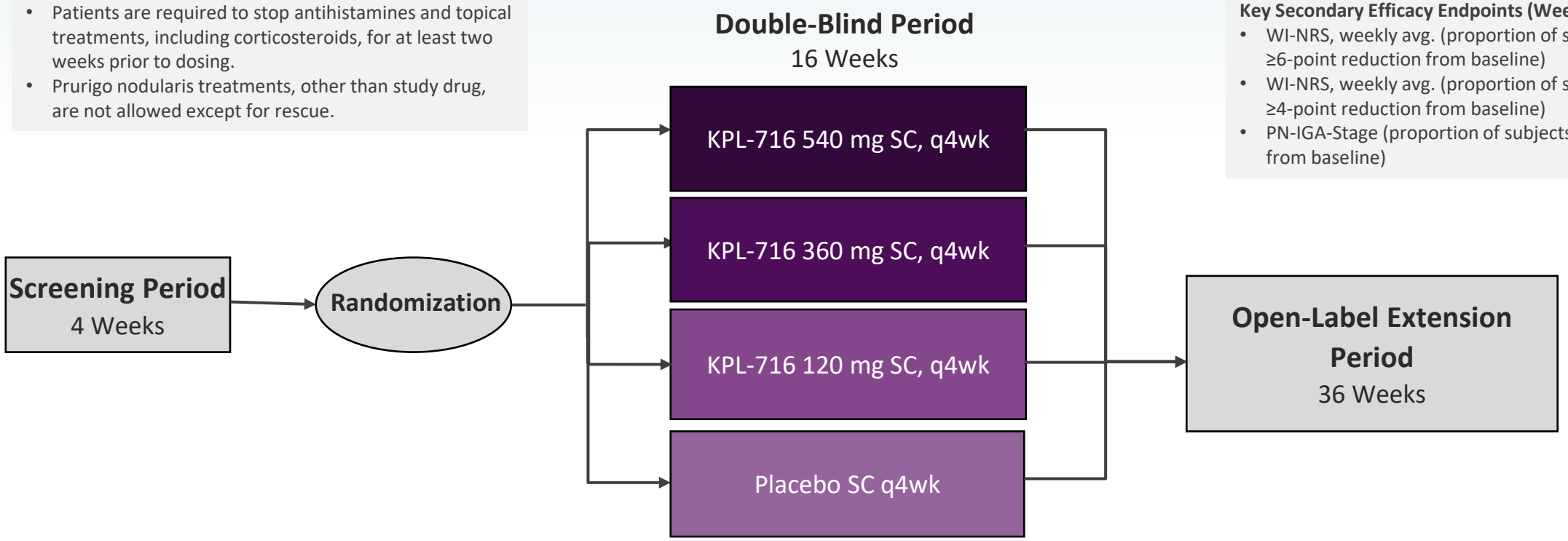
mAb = monoclonal antibody; OSMRβ = oncostatin M receptor beta; IL-31 = interleukin-31; OSM = oncostatin M; WI-NRS = Worst-Itch Numeric Rating Scale; PN-IGA = prurigo nodularis-investigator's global assessment

Vixarelimab Phase 2b Dose-Ranging Study in Prurigo Nodularis

Enrollment and dosing of patients commenced in Q4 2020

Expected to enroll approximately 180 patients

- Moderate-to-severe prurigo nodularis experiencing severe pruritus.
- Patients are required to stop antihistamines and topical treatments, including corticosteroids, for at least two weeks prior to dosing.
- Prurigo nodularis treatments, other than study drug, are not allowed except for rescue.



Primary Efficacy Endpoint (Week 16):

- WI-NRS (% change from baseline in weekly average)

Key Secondary Efficacy Endpoints (Week 16):

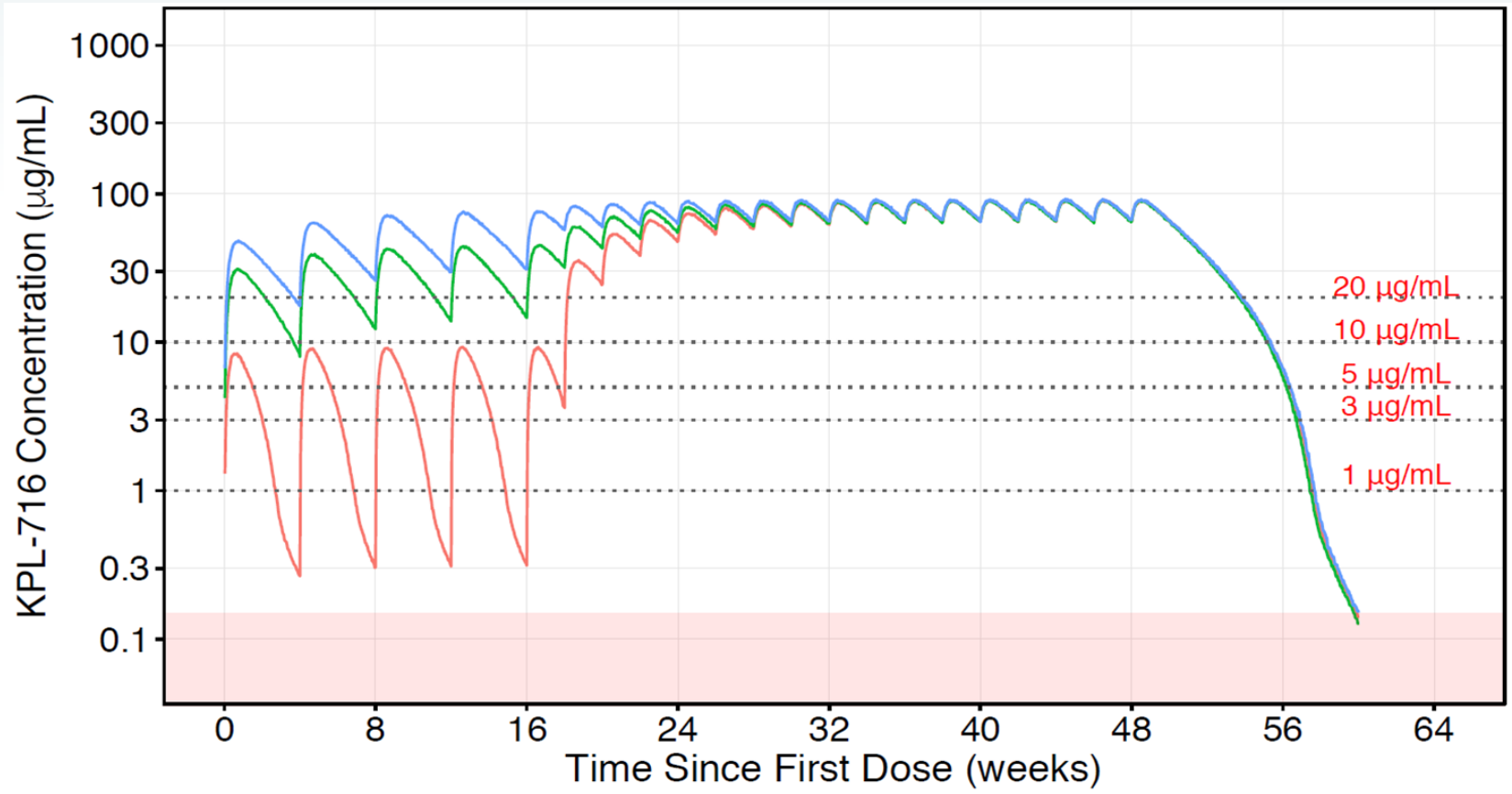
- WI-NRS, weekly avg. (proportion of subjects achieving ≥6-point reduction from baseline)
- WI-NRS, weekly avg. (proportion of subjects achieving ≥4-point reduction from baseline)
- PN-IGA-Stage (proportion of subjects achieving 0 or 1 from baseline)

WI-NRS = Worst-Itch Numeric Rating Scale; PN-IGA = prurigo nodularis-investigator's global assessment

Vixarelimab Dose-Ranging Phase 2b Study in Prurigo Nodularis

Pharmacokinetic Simulation

Supraphysiologic doses of IL-31 in a non-human primate IL-31 challenge model suggest a C_{eff} of 5-8ug/ml
Data from studies of vixarelimab in prurigo nodularis and chronic pruritic diseases support a potential C_{eff} of approximately 5-8ug/ml



KPL-404

Monoclonal antibody inhibitor interaction between CD40 and CD40L

Disease Area: Rheumatoid Arthritis; a chronic inflammatory disorder affecting many joints; External proof-of-concept previously established in broad range of autoimmune diseases: Sjogren's disease, systemic lupus, solid organ transplant and Graves' disease[1]

Scientific Rationale[2,3]: Attractive target for blocking T-cell dependent, B-cell–mediated autoimmunity

Status: Phase 1 single-ascending-dose study in healthy volunteers completed and supports further development in patients with optionality for testing SC and/or IV dosing; Expect to initiate Phase 2 proof-of concept trial in patients in Q4 2021

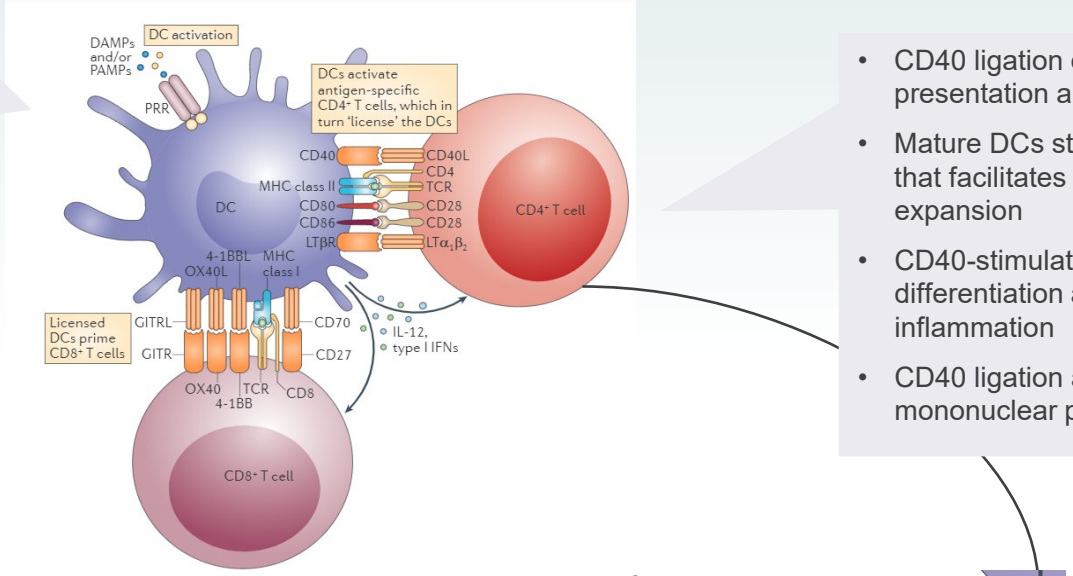
Economics: Clinical and regulatory milestones and royalty on annual net sales

Rights: Worldwide

1) Poster presentation at the Keystone Symposia: Antibodies as Drugs: New Horizons in the Therapeutic Use of Engineered Antibodies: KPL-404, a CD40 antagonist, blocked antigen-specific antibody responses in an in vivo NHP model and demonstrated strong PK/PD correlation; 2) Elgueta, et al. Immunol Rev 2009, 229 (1), 152-172; 3) Peters, et al. Semin Immunol 2009, 21 (5) 293-300; CD40L = CD40 ligand; RO = receptor occupancy; TDAR = T-cell Dependent Antibody Response

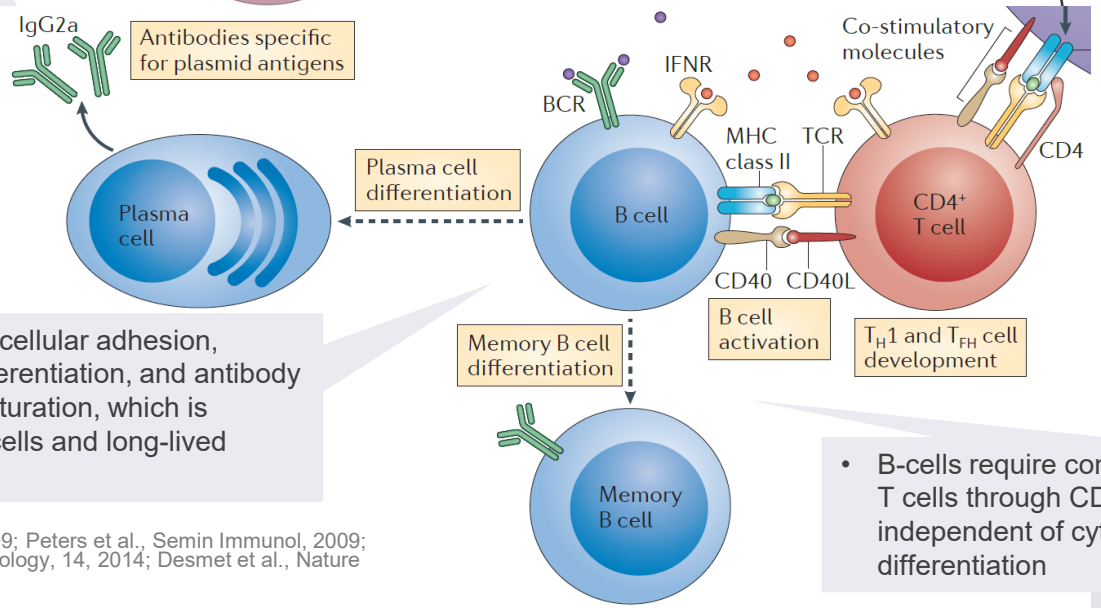
CD40/CD40L is an Essential Immune Pathway for T-Cell Priming and T-Cell Dependent B-Cell Responses

- CD40 is expressed on the surface of dendritic cells, B-cells, antigen-presenting cells and non-immune cell types
- Its ligand, CD40L (CD154), is expressed by activated T-cells, platelets, and other cell types



- CD40 ligation on DCs induces cell maturation by promoting antigen presentation and enhancing their costimulatory activity
- Mature DCs stimulate activated T-cells to increase IL-2 production that facilitates T-helper cells (Th) and cytolytic T-Lymphocyte (CTL) expansion
- CD40-stimulated DCs also secrete cytokines favoring Th1 cell differentiation and promoting Th cell migration to sites of inflammation
- CD40 ligation also provides a pro-inflammatory signal within the mononuclear phagocyte system

- Humoral immunity is dependent on a thriving B cell population and activation by Th cells; blockade of CD40/CD40L interaction has been shown to completely ablate primary and secondary TDAR response



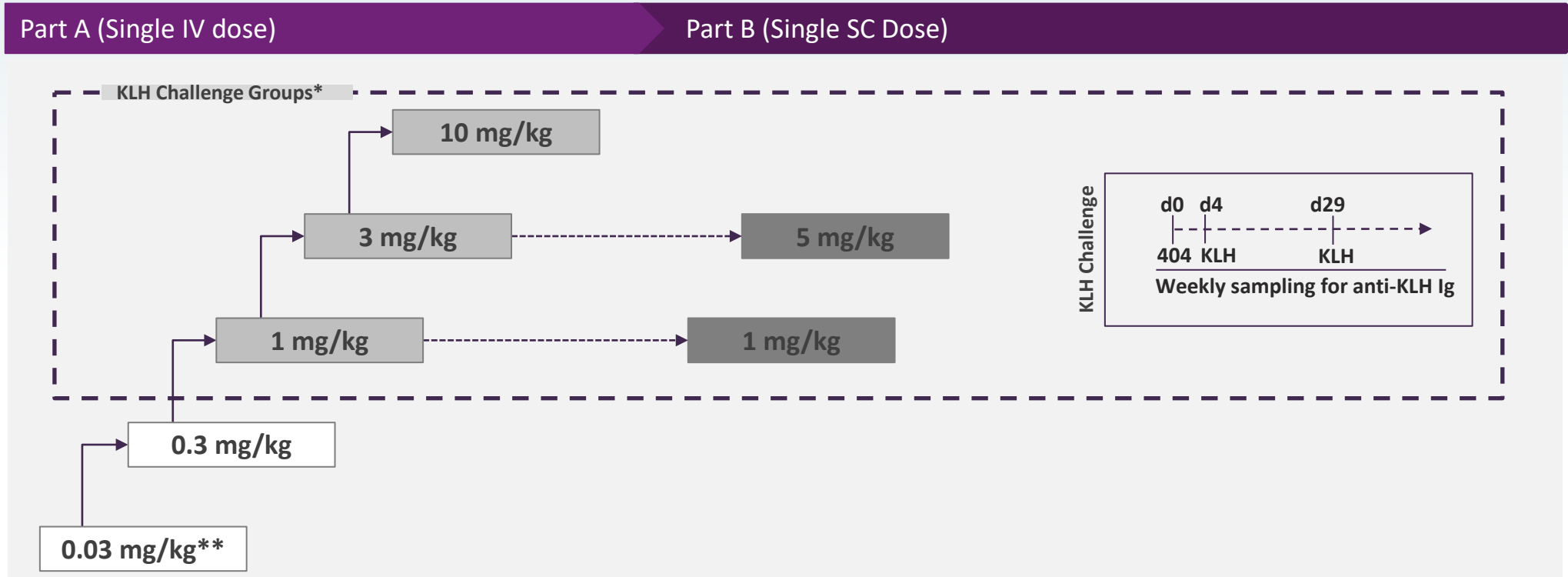
- CD40 engagement triggers B-cell intercellular adhesion, sustained proliferation, expansion, differentiation, and antibody isotype switching leading to affinity maturation, which is essential for generation of memory B cells and long-lived plasma cells

- B-cells require contact-dependent stimulus from T cells through CD40/CD40L interaction independent of cytokines to trigger growth and differentiation

1Sources: Elgueta et al., Immunol Rev, 2009; Peters et al., Semin Immunol, 2009; Kambayashi et al., Nature Reviews: Immunology, 14, 2014; Desmet et al., Nature Reviews: Immunology, 12, 2012

KPL-404 Single-Ascending-Dose Phase 1 Study

First-in-human study to provide safety data and pharmacokinetics as well as receptor occupancy and TDAR



- **Primary endpoints:** Safety and Tolerability
- **Secondary endpoints:** PK and ADA / CD40 RO in blood / Serum anti-KLH Ig levels
- **Exploratory endpoints:** Serum CXCL13 levels

Notes: Unless otherwise noted dose groups included 6 active/2 placebo subjects; *1° KLH challenge for all SAD dose groups except 0.03 and 0.3 mg/kg, 2° KLH re-challenge only in 1, 3, and 10 mg/kg IV; ** Cohort included 2 active and 2 placebo subjects

SAD = single-ascending-dose; TDAR = T-cell dependent antibody response; KLH = keyhole limpet hemocyanin; RO = receptor occupancy; ADA = anti-drug antibodies

Final Data from KPL-404 Single-Ascending-Dose Phase 1 Study

The randomized, double-blind, placebo-controlled first-in-human (FIH) study is designed to investigate the safety, tolerability, PK and PD properties of single-ascending intravenous (IV) and subcutaneous (SC) doses of KPL-404 in healthy subjects.

- 2 single-ascending-dose arms (SAD):
  - Single-dose KPL-404 0.03 mg/kg, 0.3 mg/kg, 1 mg/kg, 3 mg/kg or 10 mg/kg IV and
  - Single-dose KPL-404 1 mg/kg or 5 mg/kg SC

Primary Endpoint: Safety and tolerability of single ascending intravenous (IV) and subcutaneous (SC) doses of KPL-404 in healthy subjects.

- KLH challenge in 1 mg/kg, 3 mg/kg, and 10 mg/kg IV and 1 mg/kg and 5 mg/kg SC cohort

Secondary Endpoints: Pharmacokinetics and anti-drug antibody response following single IV and SC doses of KPL-404 in healthy subjects, serum anti- keyhole limpet hemocyanin (KLH) IgG levels

Exploratory Endpoint: Receptor occupancy of KPL-404 on CD40 in healthy subjects

Preliminary Data:

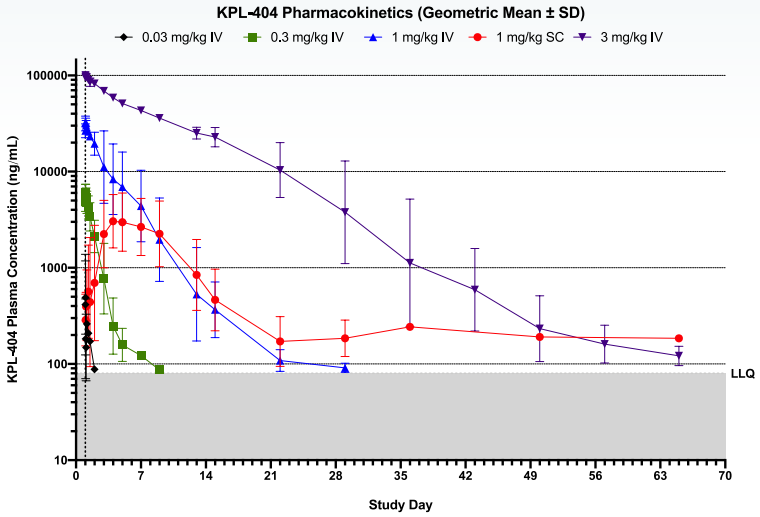
- All dose escalations occurred as per protocol with no dose limiting safety findings. All 6 subjects dosed with KPL-404 3 mg/kg IV showed full receptor occupancy through Day 29, which corresponded with complete suppression of the T-cell Dependent Antibody Response (TDAR) to KLH through Day 29. Consistent dose relatedness was shown in the lower dose level cohorts, including 0.03 mg/kg, 0.3 mg/kg, 1 mg/kg IV and 1 mg/kg SC. Data collection for the higher dose level cohorts, 10 mg/kg IV and 5 mg/kg SC, is ongoing.
- The data to-date support subsequent study in patients, including potential IV or SC monthly administration.

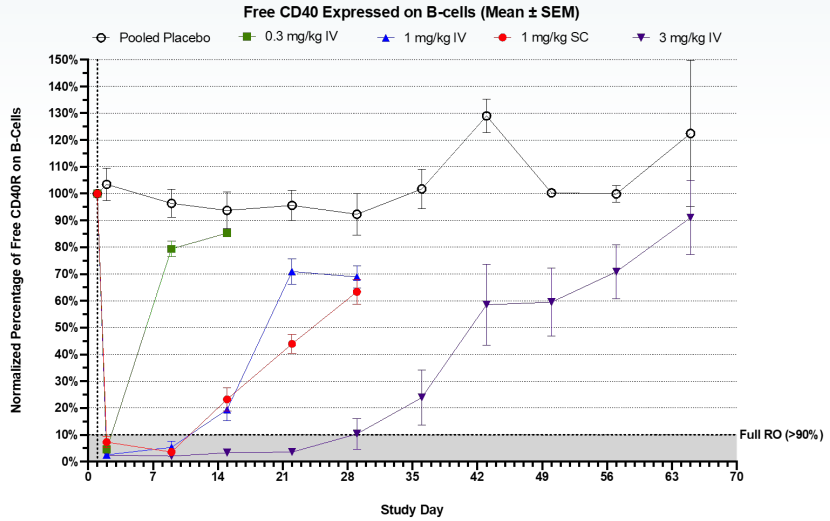
Final Data:

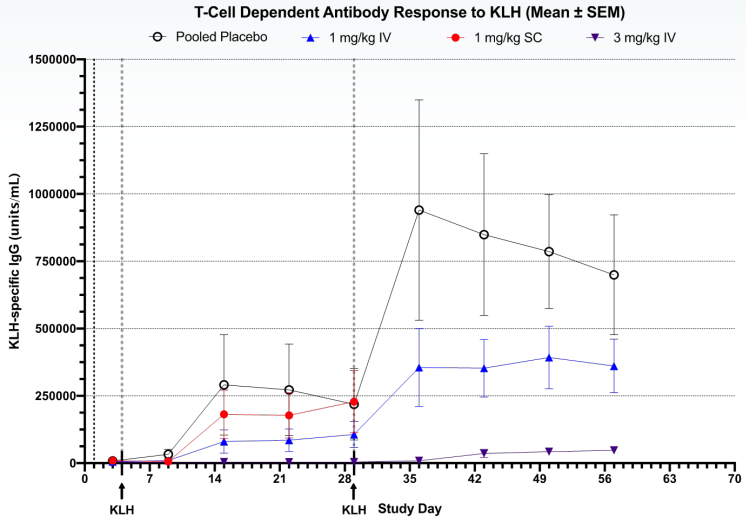
- KPL-404 showed dose-dependent increases in concentration across cohorts. All dose escalations occurred as per protocol with no dose-limiting safety findings.
- KPL-404 was well-tolerated, and there were no serious adverse events.
- Subjects dosed with KPL-404 10 mg/kg IV showed full RO through at least Day 71 and complete suppression of TDAR after KLH challenge and re-challenge through at least Day 57.
- Subjects dosed with KPL-404 5 mg/kg SC showed full RO through Day 43 and suppression of TDAR after KLH challenge through at least Day 29. These data confirm and extend previously-reported 3 mg/kg IV cohort data, in which RO and suppression of TDAR after KLH challenge were demonstrated through Day 29.
- The 3 mg/kg IV dose level had previously demonstrated complete suppression of memory TDAR response to a re-challenge on Day 29.
- Anti-drug antibodies to KPL-404 were suppressed for at least 57 days at 10 mg/kg IV; the suppression of antibody responses to the drug itself is an independent indicator of target engagement and pharmacodynamic effect

RO and TDAR Suppression Shown Through Day 29 at 3mg/kg IV

Preliminary KPL-404 Phase 1 data



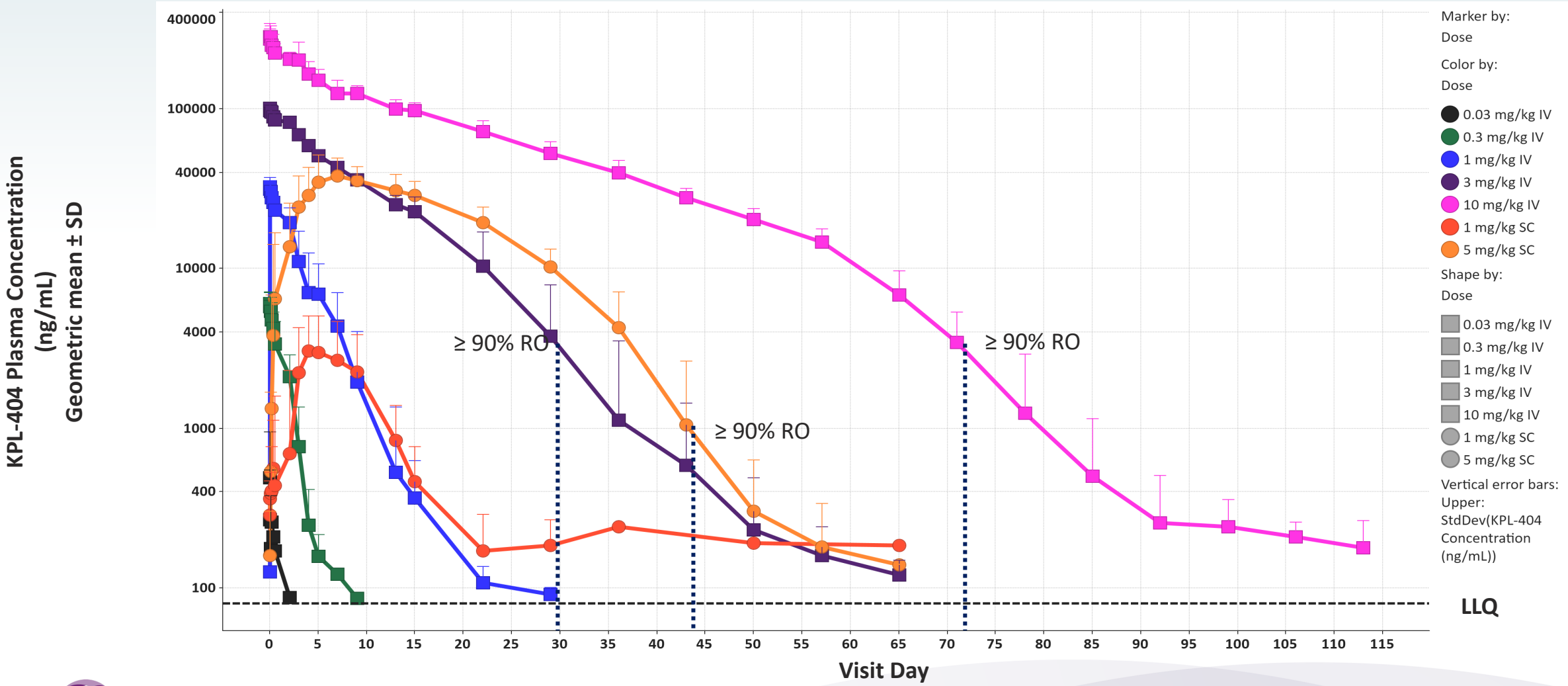




1) Free CD40R = inverse of receptor occupancy; RO = receptor occupancy; KLH = keyhole limpet hemocyanin; TDAR = T-cell dependent antibody response ; IV = intravenous

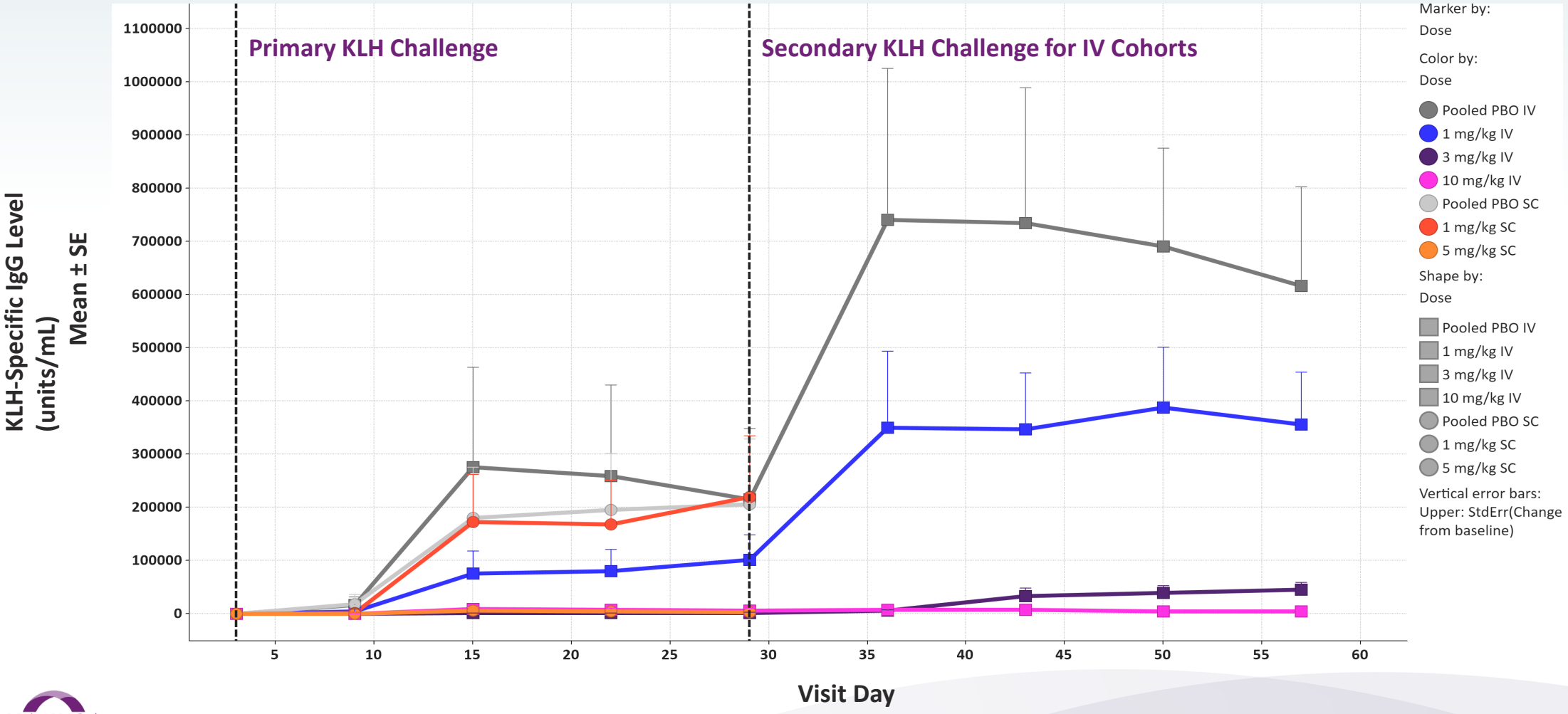
Final Data from KPL-404 Single-Ascending-Dose Phase 1 Study

Pharmacokinetic profiles for KPL-404



Final Data from KPL-404 Single-Ascending-Dose Phase 1 Study

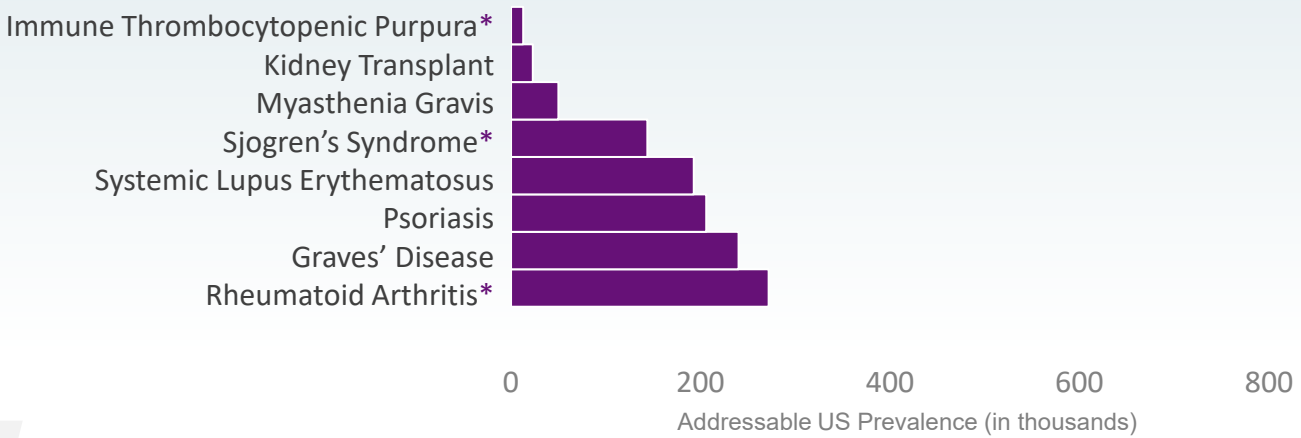
T-Cell Dependent Antibody Response (TDAR) for KLH antigen challenge



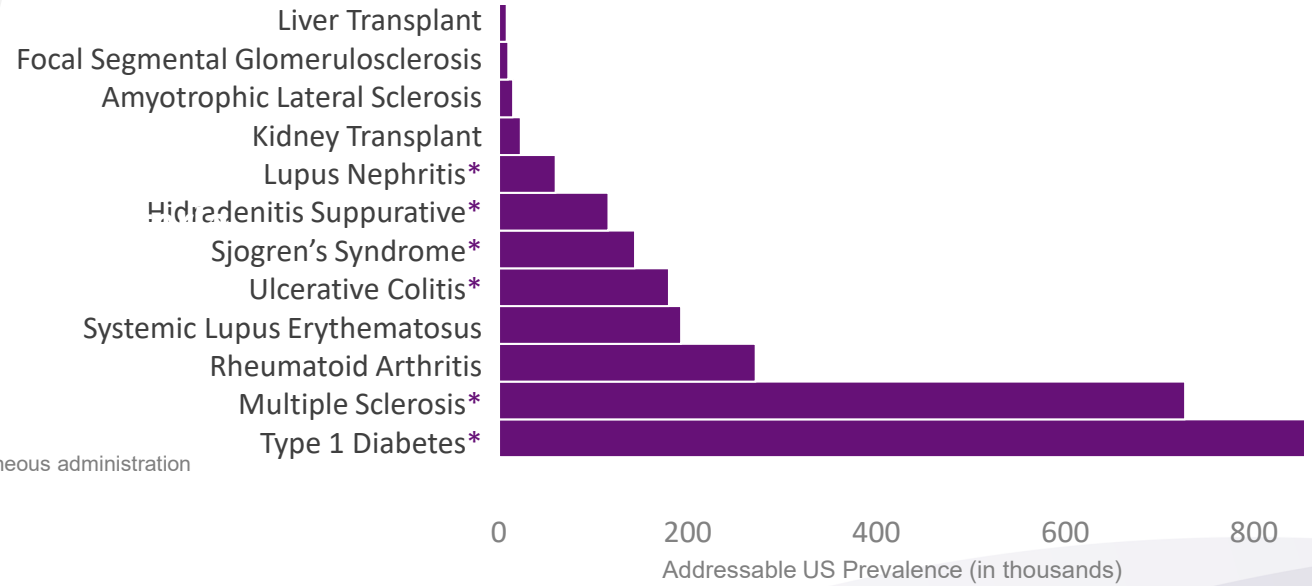
KLH = keyhole limpet hemocyanin

Potential for Evaluation of KPL-404 in a Broad Range of Autoimmune Diseases

Indications with Published Data[1]



Indications with Pending Data & Trials Ongoing[1]



*Indications evaluated with subcutaneous administration
1) With the CD40 mechanism

INDICATION SELECTION CRITERIA

- Robust Data or proof-of-concept supporting mechanism
- Differentiation vs. Competitors
- Commercial Attractiveness

Sources: 2019 numbers: https://unos.org/data/transplant-trends/; Hunter et al. Prevalence of rheumatoid arthritis in the United States adult population in healthcare claims databases, 2004-2014; Rheumatol Int. 2017 Sep;37(9):1551-1557; Overall Prevalence: Maciel et al, Arthritis Care Res (Hoboken) 2017; Qin et al, Ann Rheum Dis 2015; UpToDate; Baldini et al. Prevalence of Severe Extra-Glandular Manifestations in a Large Cohort of Patients with Primary Sjögren's Syndrome; 2012 ACR/ARHP Annual Meeting, ABSTRACT NUMBER: 2185; Wallin et al. The prevalence of MS in the United States A population-based estimate using health claims data, Neurology, March 5, 2019; Somers et al.; Prevalence of Systemic Lupus Erythematosus in the United States: Preliminary Estimates from a Meta-Analysis of the Centers for Disease Control and Prevention Lupus Registries; 2019 ACR/ARP Annual Meeting ABSTRACT NUMBER: 2886; Garg et al. JAMA Dermatol. 2017;153(8):760-764. doi:10.1001/jamadermatol.2017.0201 Sex- and Age-Adjusted Population Analysis of Prevalence Estimates for Hidradenitis Suppurativa in the United States; MayoClinic.org; Yale J Biol Med. 2013 Jun; 86(2): 255–260. N Engl J Med 2016;375:2570-81; https://www.diabetesresearch.org/diabetes-statistics; Nephcure.org; Kitiyakara C, Eggers P, Kopp JB. Twenty-one-year trend in ESRD due to focal segmental glomerulosclerosis in the United States. Am J Kidney Dis. 2004 Nov;44(5):815-25; Rachakonda et al. J Am Acad Dermatol . 2014 Mar;70(3):512-6. doi: 10.1016/j.jaad.2013.11.013. Epub 2014 Jan 2. Psoriasis prevalence among adults in the United States; Yeung et al. Psoriasis severity and the prevalence of major medical co-morbidities: a population-based study; JAMA Dermatol. 2013 Oct 1; 149(10): 1173–1179; Hoover etal. Kidney Int. 2016 Sep; 90(3): 487–492. Insights into the Epidemiology and Management of Lupus Nephritis from the U.S. Rheumatologist's Perspective.

Building Value at Kiniksa

Corporate Priorities

ARCALYST

Commercial launch in recurrent pericarditis (April 2021)

MAVRILIMUMAB

Phase 3 COVID-19-related ARDS data expected Q1 2022

VIXARELIMAB

Phase 2b study in prurigo nodularis evaluating a range of once-monthly dose regimens

KPL-404

Final Phase 1 data (May 2021); plan to initiate Phase 2 proof-of-concept trial in rheumatoid arthritis in Q4 2021

Financials
Second Quarter 2021

Q2 2021 Financial Results

Income Statement	Three Months Ended June 30,	
	2021	2020
Total Revenue	$7.7M	N/A
Cost of Goods Sold	$2.5M	N/A
Research and Development Expenses	$23.9M	$22.3M
Selling, General and Administrative Expenses	$21.8M	$9.5M
Total Operating Expenses	$48.3M	$31.9M
Net Loss	($41.6M)	($37.5M)

Balance Sheet	June 30, 2021	December 31, 2020
Cash, Cash Equivalents and Short-term Investments	$225.9M	$323.5M

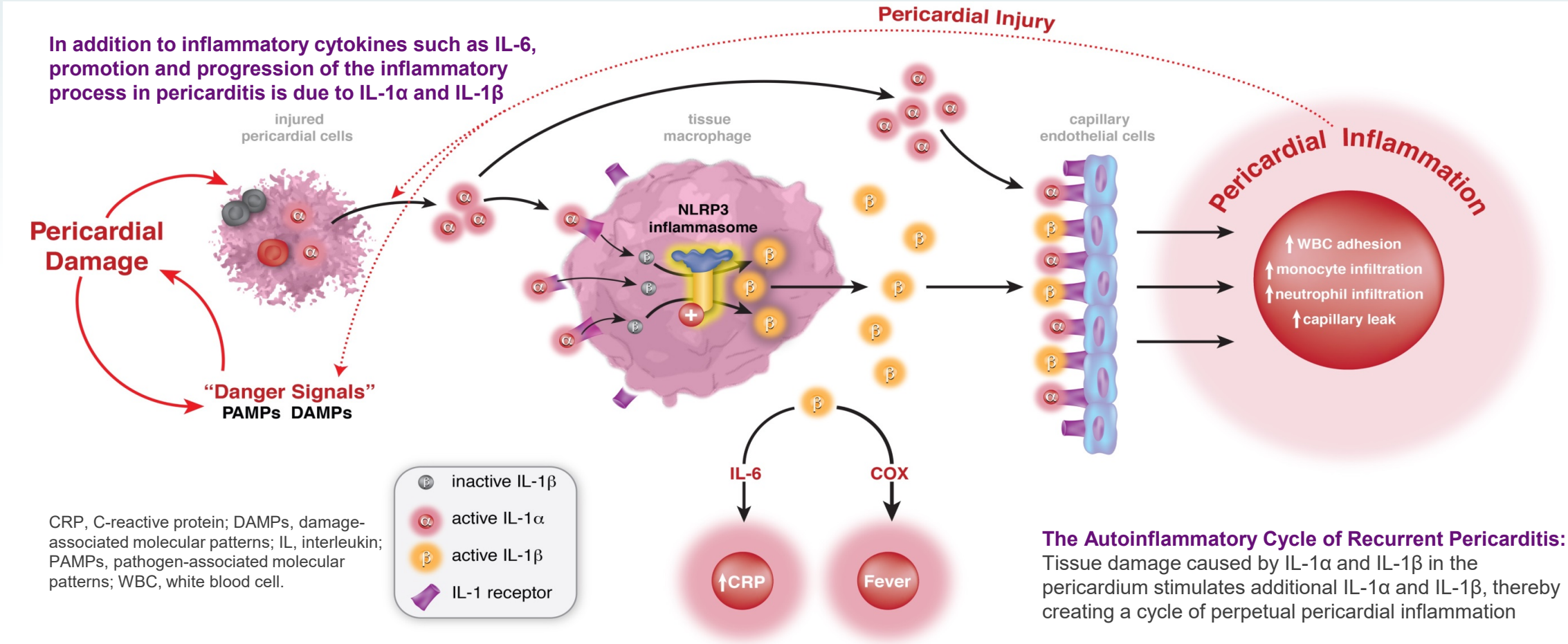
Q2 2021 Cash Reserves Expected to Fund Current Operating Plan into 2023

KINIKSA

Appendix

ARCALYST® (rilonacept)

Role of IL-1α and IL-1β in the Autoinflammatory Cycle of Recurrent Pericarditis



CRP, C-reactive protein; DAMPs, damage-associated molecular patterns; IL, interleukin; PAMPs, pathogen-associated molecular patterns; WBC, white blood cell.

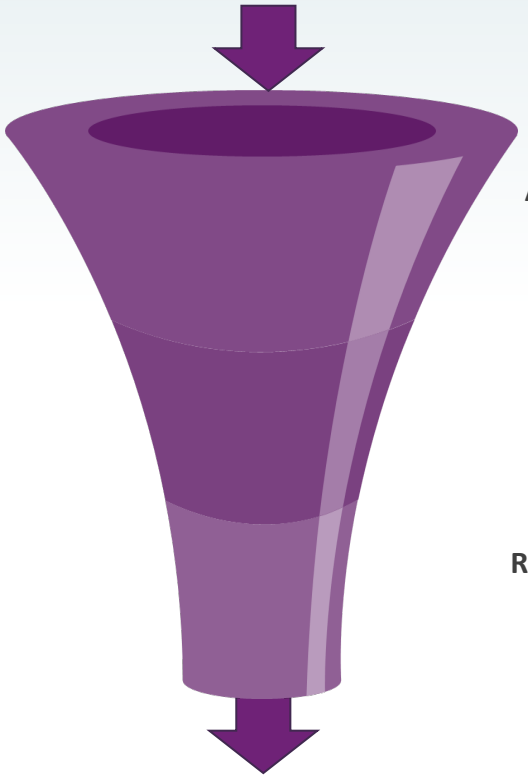
The Autoinflammatory Cycle of Recurrent Pericarditis: Tissue damage caused by IL-1α and IL-1β in the pericardium stimulates additional IL-1α and IL-1β, thereby creating a cycle of perpetual pericardial inflammation

Brucato A, et al. Int Emerg Med 2018 https://doi.org/10.1007/s11739-018-1907-x
Dinarello CA, et al. Nat Rev Drug Discov 2012;11:633-652

KINIKSA

Addressable U.S. Opportunity of ARCALYST Estimated to be ~14K Patients

~7K new patients with multiple recurrences enter target pool annually



Annual pericarditis incidence ~117K

1st recurrence ~26K

Repeat Recurrences

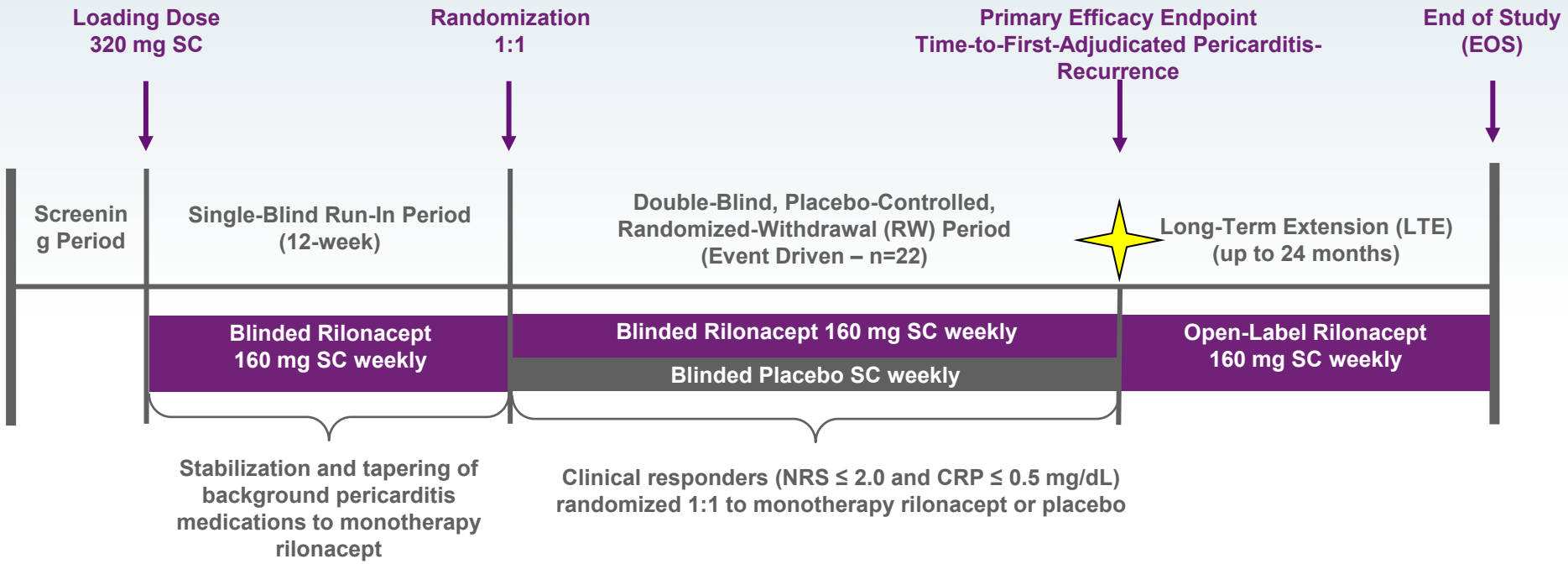
- **~7K new patients with repeat recurrences annually**
- **~14K total patients with repeat recurrences annually at any point**

Year	-4	-3	-2	-1	0
Incident case of acute pericarditis (1st episode)[1]	117K	117K	117K	117K	117K
Incidence of initial RP patients (1st recurrence)[2]	26K	26K	26K	26K	26K
Ongoing recurrent from year-1[3]					7K
Ongoing recurrent from year-2[3]				7K	3.5K
Ongoing recurrent from year-3[3]			7K	3.5K	1.8K
Ongoing recurrent from year-4[3]		7K	3.5K	1.8K	0.9K
Ongoing recurrent from year-5[3]	7K	3.5K	1.8K	0.9K	0.5K
Ongoing recurrent from year-6[3]	3.5K	1.8K	0.9K	0.5K	0.2K
Ongoing recurrent from year-7[3]	1.8K	0.9K	0.5K	0.2K	0.1k

Addressable Opportunity in U.S.

1: Prevalence estimate from Imazio, et al. (2008); includes all etiologies (~80% idiopathic)
2: Mid point of 15-30% of initial recurrence rate published in ESC Guidelines given higher colchicine use today
3: Estimate for recurrence rate of subsequent recurrences from ESC Guidelines and Claims Analysis

Pivotal Phase 3 Trial of ARCALYST in Recurrent Pericarditis



Inclusion Criteria:

- All etiologies except infection and malignancy
- Present at screening with at least a third pericarditis episode, defined as at least 1 day with **NRS pain of ≥ 4** and **CRP value ≥ 1 mg/dL** within the 7-day period prior to first study drug administration
- Concomitant NSAIDs and/or colchicine and/or oral corticosteroid treatment in any combination

Primary Efficacy Endpoint :

- Time-to-first-adjudicated pericarditis-recurrence in the RW period

Major Secondary Efficacy Endpoints (16-weeks):

- Proportion of subjects who maintained Clinical Response
- Percentage of days with no or minimal pain
- Proportion of subjects with absent or minimal pericarditis symptoms

CEC Adjudication Criteria:

- Typical pericarditis pain (≥ 1 pain **NRS recording ≥4**) AND elevated **CRP (≥1.0 mg/dL)**, same day or ≤ 7 days
- Typical pericarditis pain (≥ 1 pain **NRS recording ≥4**) AND abnormal **CRP (>0.5 mg/dL),** same day or ≤ 7 days AND ≥ **1 supportive evidence** of pericarditis
- Typical pericarditis pain (BUT pain **NRS recording ≤ 4**) AND elevated **CRP (≥1.0 mg/dL)**, AND ≥ **1 supportive evidence** of pericarditis

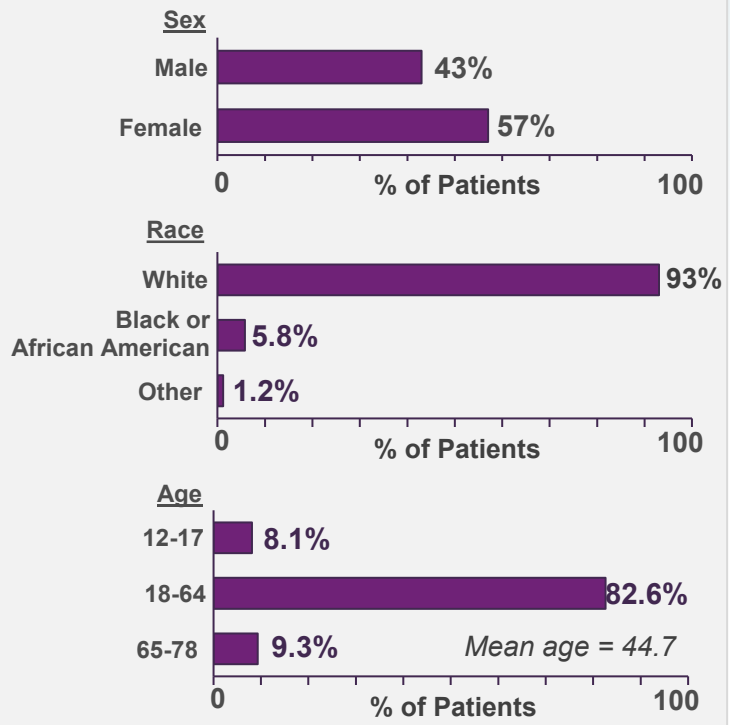
CRP = C-reactive protein; NRS = Numerical Rating Scale; NSAIDs = nonsteroidal anti-inflammatory drugs; CEC = Clinical Endpoint Committee

Klein AL, Imazio M, Cremer P, et al. Phase 3 trial of interleukin-1 trap rilonacept in recurrent pericarditis. N Engl J Med. 2021;384(1):31-41.

Baseline Demographics and Clinical Characteristics

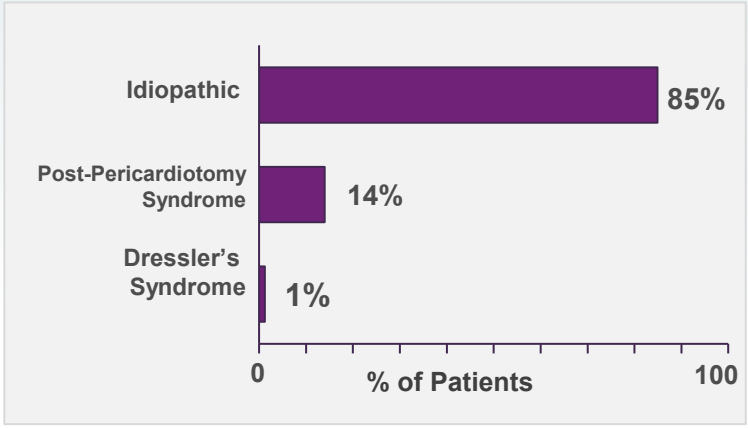
Pivotal Phase 3 Rilonacept Data

Baseline Demographics (n=86)

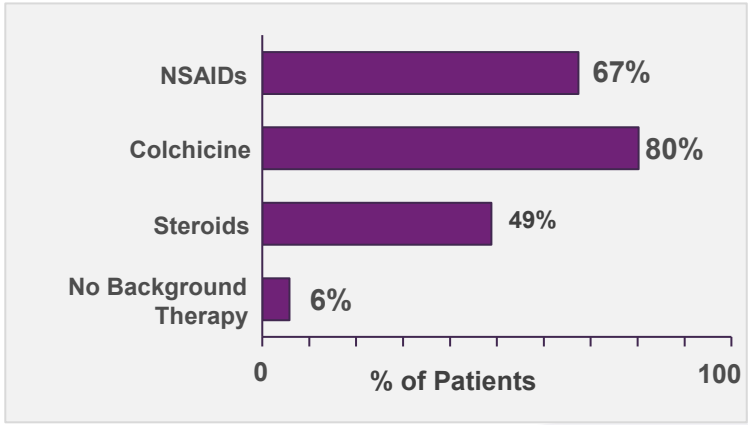


Total Number of Episodes Including Index and Qualifying Episodes	Run-in Period (n=86)
Mean	4.7

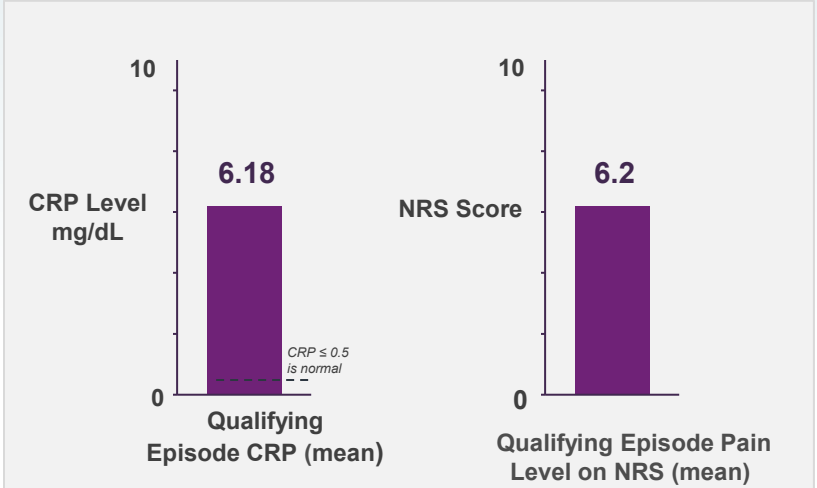
Prior Pericarditis History at Baseline (n=86)



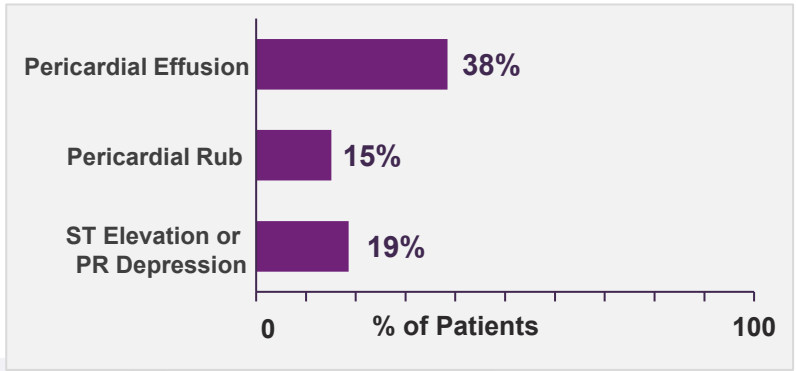
SoC Received at Qualifying Episode (n=86)



Qualifying Episode CRP & NRS (n=86)



Pericarditis Manifestations at Qualifying Episode (n=86)

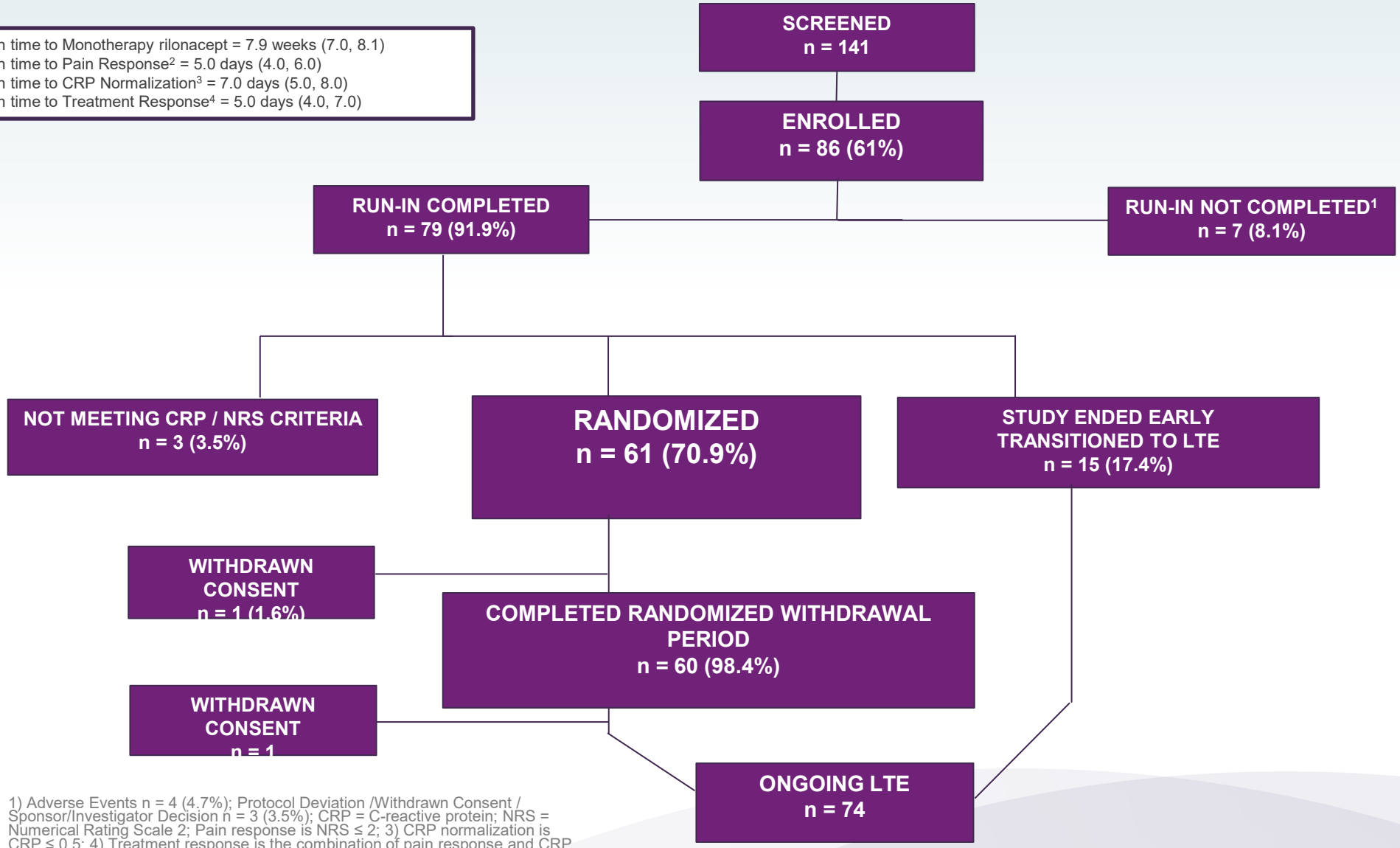


CRP = C-reactive protein; NRS = Numerical Rating Scale; SoC = Standard of Care; NSAIDs = nonsteroidal anti-inflammatory drugs

Subject Disposition

Pivotal Phase 3 Rilonacept Data

Median time to Monotherapy rilonacept = 7.9 weeks (7.0, 8.1)
Median time to Pain Response[2] = 5.0 days (4.0, 6.0)
Median time to CRP Normalization[3] = 7.0 days (5.0, 8.0)
Median time to Treatment Response[4] = 5.0 days (4.0, 7.0)



1) Adverse Events n = 4 (4.7%); Protocol Deviation /Withdrawn Consent / Sponsor/Investigator Decision n = 3 (3.5%); CRP = C-reactive protein; NRS = Numerical Rating Scale 2; Pain response is NRS ≤ 2; 3) CRP normalization is CRP ≤ 0.5; 4) Treatment response is the combination of pain response and CRP normalization

ARCALYST Initiation Resulted in Rapid Resolution of Pericarditis Episodes

Pivotal Phase 3 RHAPSODY Data

Rapid and sustained reductions in both reported pain and inflammation as early as after the first dose of ARCALYST

Median time to pain response = 5.0 days; Median time to CRP normalization = 7.0 days

Secondary endpoints that were assessed during the run-in period

5 days

Time to treatment response (median; 95% CI: 4, 7)*

97%

Treatment response* rate

7.9 weeks

Time to ARCALYST monotherapy (median; 95% CI: 7, 8)

*Time to treatment response was defined as the time from the first dose to the first day when pericardial pain was NRS ≤2 and CRP ≤0.5 mg/dL (measured within 7 days before or after the pain response). During the 12-week run-in period, 77 of 79 patients demonstrated a treatment response.

Klein AL, Imazio M, Cremer P, et al. Phase 3 trial of interleukin-1 trap rilonacept in recurrent pericarditis. N Engl J Med. 2021;384(1):31-41.
ARCALYST (rilonacept) prescribing information 2021

ARCALYST Demonstrated a Steroid-Sparing Treatment Effect

Pivotal Phase 3 RHAPSODY Data

Patients treated with ARCALYST discontinued corticosteroids

In the run-in period of the Phase 3 trial RHAPSODY, patients receiving corticosteroids at baseline were transitioned to ARCALYST monotherapy in 7.9 weeks

Each patient treated with corticosteroids at baseline achieved clinical response with ARCALYST monotherapy

- 49% (27 of 86) of patients received corticosteroids at baseline
- None of the patients treated with corticosteroids at baseline and randomized to ARCALYST monotherapy experienced a recurrence while on therapy

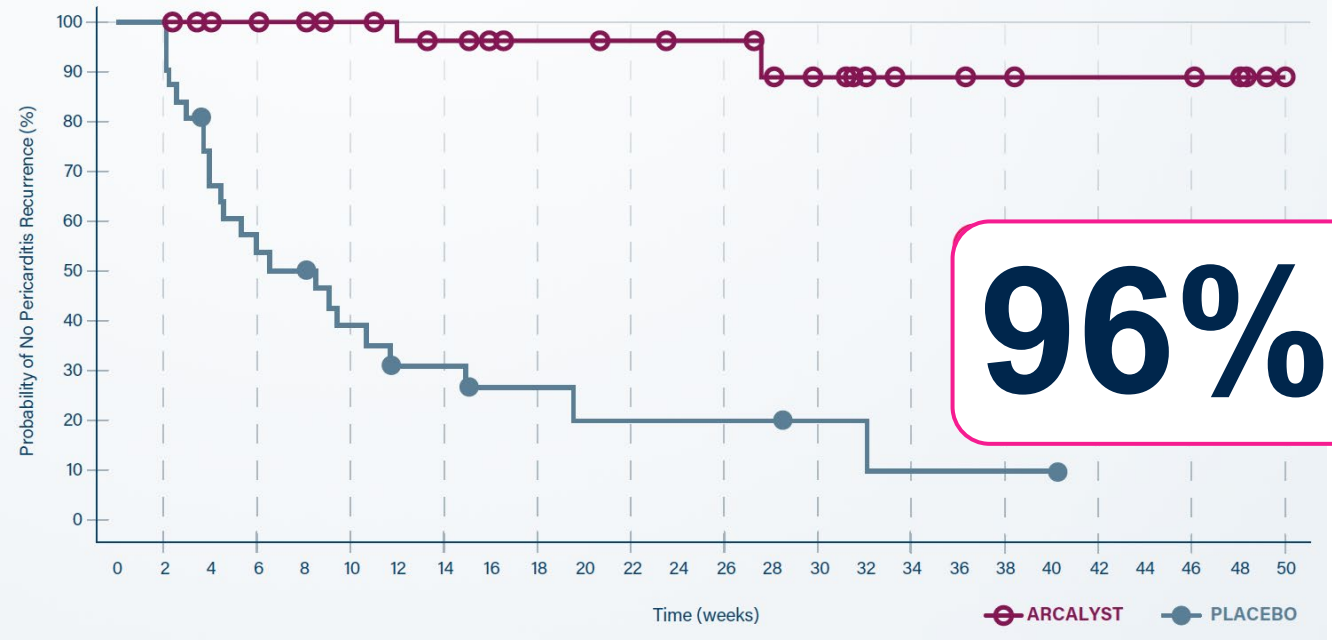
Klein AL, Imazio M, Cremer P, et al. Phase 3 trial of interleukin-1 trap rilonacept in recurrent pericarditis. N Engl J Med. 2021;384(1):31-41.
ARCALYST (rilonacept) prescribing information 2021

96% Reduction in Risk of Pericarditis Recurrence

Pivotal Phase 3 RHAPSODY Data

ARCALYST reduced the risk of pericarditis recurrence

The primary efficacy endpoint was time to first adjudicated pericarditis recurrence in the randomized withdrawal period.



The median time to recurrence on ARCALYST could not be estimated due to the low number of recurrences

- 2 of 30 of patients treated with ARCALYST had a recurrence
- The 2 pericarditis recurrences with ARCALYST occurred during temporary interruptions of 1 to 3 doses of ARCALYST

96% **reduction in the risk of recurrent pericarditis (hazard ratio: 0.04; *p*<0.0001)**

The median time to recurrence on placebo was 8.6 weeks (95% CI: 4.0, 11.7)

- 74% (23 of 31) of patients treated with placebo experienced a recurrence at the time that the event-driven portion of the trial was closed
- Consistent with the expected washout pharmacokinetics of once-weekly ARCALYST at steady state

Klein AL, Imazio M, Cremer P, et al. Phase 3 trial of interleukin-1 trap rilonacept in recurrent pericarditis. N Engl J Med. 2021;384(1):31-41.
ARCALYST (rilonacept) prescribing information 2021

92% of Trial Days of No/Minimal Pain

Pivotal Phase 3 RHAPSODY Data

Patients on ARCALYST had significantly more trial days with no/minimal pain vs placebo

Secondary efficacy endpoint was assessed during the randomized withdrawal period

92% **of days**

Patients reported no/minimal (NRS≤2) pericarditis pain

Compared with 40% of trial days in patients on placebo ($p<0.0001$) at the secondary endpoint assessed at Week 16 of the randomized withdrawal period.

At Week 16 of the randomized withdrawal period:

- A majority (81%) of patients maintained a clinical response measured at Week 16 of the randomized withdrawal period compared with 20% of patients on placebo ($p=0.0002$)

KINIKSA

Klein AL, Imazio M, Cremer P, et al. Phase 3 trial of interleukin-1 trap rilonacept in recurrent pericarditis. N Engl J Med. 2021;384(1):31-41.
ARCALYST (rilonacept) prescribing information 2021

Most Common ARCALYST Adverse Reactions:

Injection-site reactions and upper respiratory tract infections

Adverse experiences in RHAPSODY

	RUN-IN PERIOD	RANDOMIZED-WITHDRAWAL PERIOD				TOTAL (N=86)
EVENT	Rilonacept (N=86)	Rilonacept, Including Bailout (N=30)	Placebo, Including Bailout (N=31)	Rilonacept, Before Bailout (N=30)	Placebo, Before Bailout (N=31)	
	number of patients with event (percent)					
Any adverse event	69 (80)	24 (80)	22 (71)	24 (80)	13 (42)	74 (86)
Adverse events according to maximum severity†						
Mild	52 (60)	16 (53)	17 (55)	16 (53)	9 (29)	47 (55)
Moderate	15 (17)	8 (27)	5 (16)	8 (27)	4 (13)	25 (29)
Severe	2 (2)	0	0	0	0	2 (2)
Serious adverse event	1 (1)	1 (3)	3 (10)	1 (3)	1 (3)	5 (6)
Adverse event leading to death	0	0	0	0	0	0
Adverse event leading to dose interruption	0	1 (3)	0	1 (3)	0	1 (1)
Adverse event leading to discontinuation of rilonacept or placebo	4 (5)	0	0	0	0	4 (5)
Cancer‡	0	1 (3)	0	1 (3)	0	1 (1)
Injection-site reaction	28 (33)	6 (20)	2 (6)	5 (17)	0	29 (34)
Infection or infestation	14 (16)	12 (40)	7 (23)	12 (40)	3 (10)	29 (34)
Upper respiratory tract infection	12 (14)	7 (23)	2 (6)	7 (23)	0	19 (22)

*Patients with multiple events were counted once in each appropriate category

†Counted once, according to the maximum severity of the adverse event.

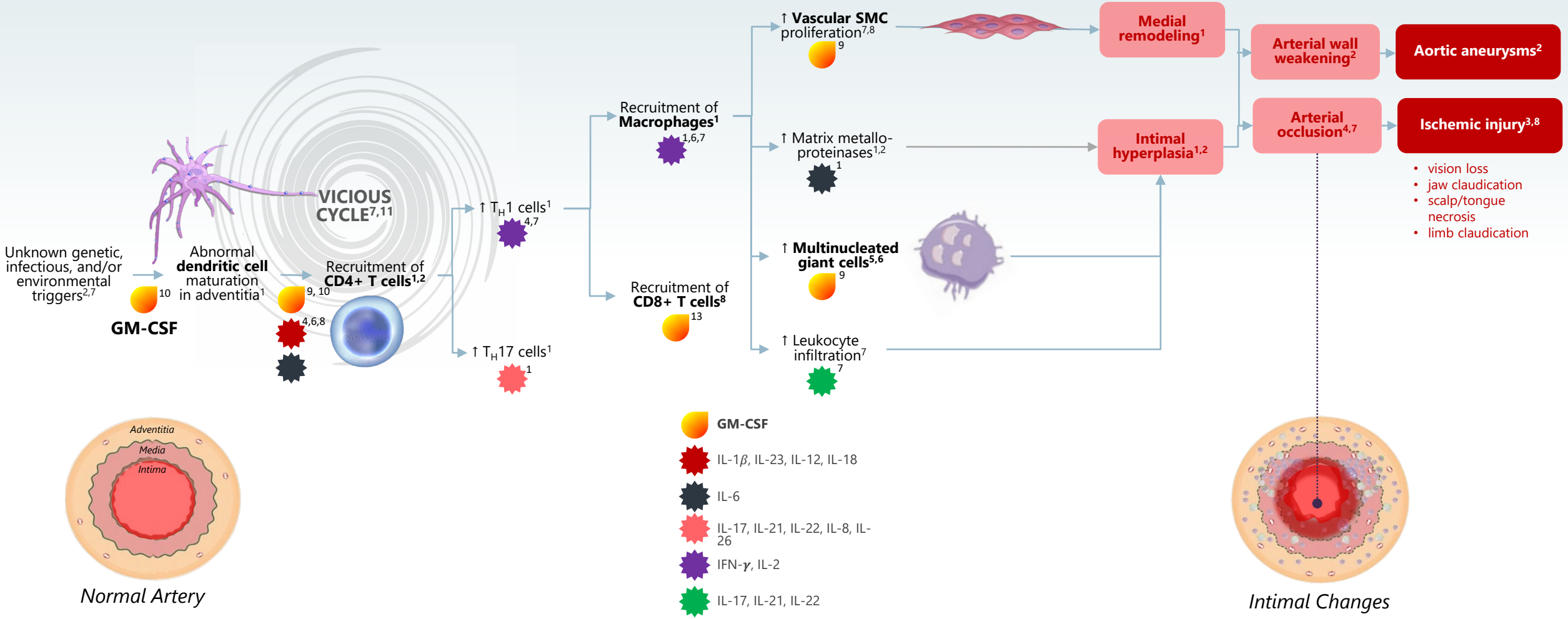
‡Cancer was an event of special interest.

KINIKSA

1Klein AL, Imazio M, Cremer P, et al. Phase 3 trial of interleukin-1 trap rilonacept in recurrent pericarditis. N Engl J Med. 2021;384(1):31-41.

Appendix
MAVRILIMUMAB

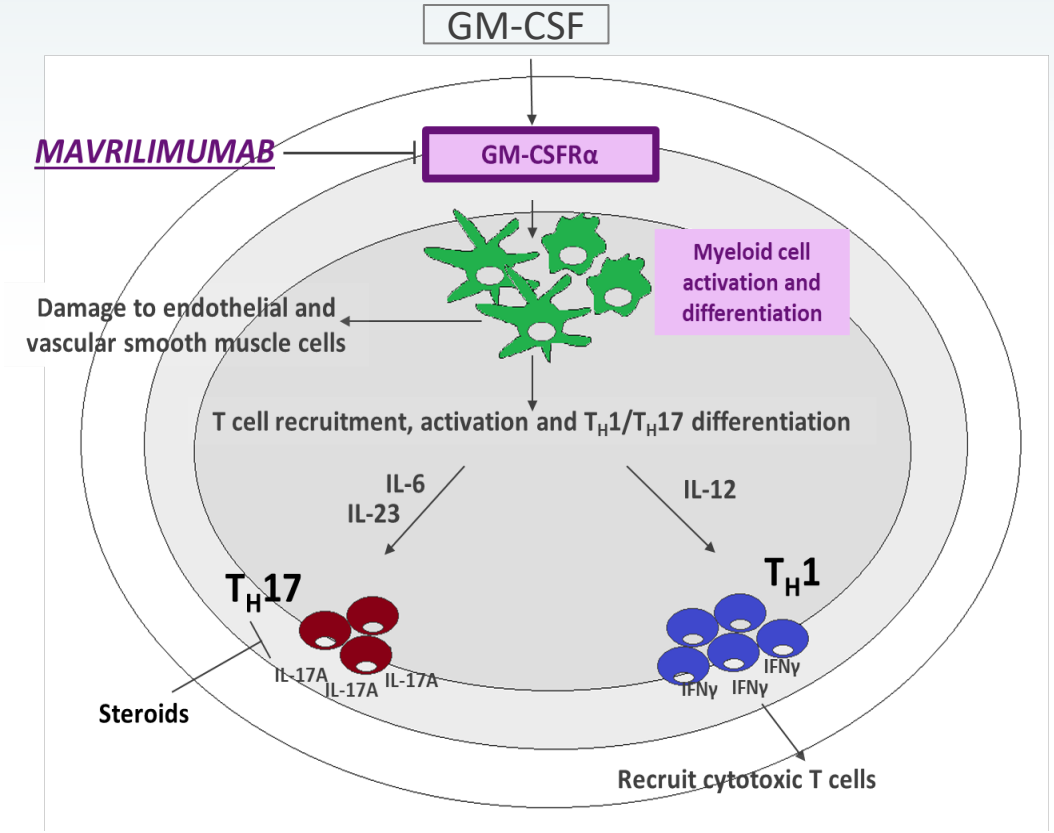
Central Role of GM-CSF in Pathophysiology of Giant Cell Arteritis



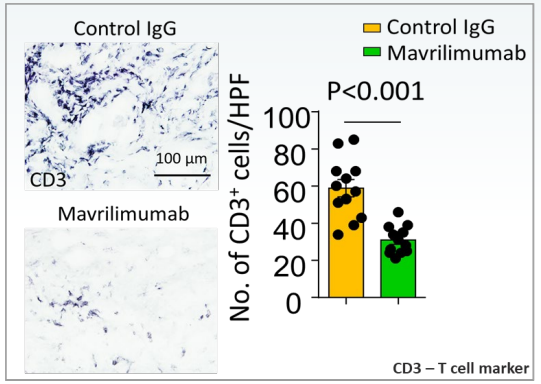
1. Al-Mousawi AZ, et al. Ophthalmol Ther 2019;8:177-193. 2. Boura P, et al. Updates in the Diagnosis and Treatment of Vasculitis. Chapter 4 2013; http://dx.doi.org/10.5772/55222. 3. Cho HJ, et al. Disease-a-Month 2017;63:88-91. 4. Ly KH, et al. Autoimm Review 2010;9:635-645. 5. Lazarewicz K, et al. BMJ 2019;365l1964 doi: 10.1136/bmj.l1964. 6. O'Neill L, et al. Rheumatol 2016;55:1921-1931. 7. Planas-Rigol E, et al. J Vasc 2016;1:2:DOI: 10.4172/2471-9544.100103. 8. Samson M, et al. Autoimmun Rev 2017;16:833-844. 9. Cid MC, et al. GM-CSF Pathway Signature Identified in Temporal Artery Biopsies of Patients With Giant Cell Arteritis. 2019 EULAR;12-15 June. Madrid, Spain. 10. Cid M, et al. Ann Rheumatol 2019; DOI: 10.1136/annrheumdis-2019-eular.2694. 11. Pupim L, et al. Rheumatology 2019;58:https://doi.org/10.1093/rheumatology/kez063.060. 12. Herndler-Brandstetter D, et al. Cell Research 2014;24:1379-1380. 13. Becher B, et al. Immunity 2016;45:963-973.

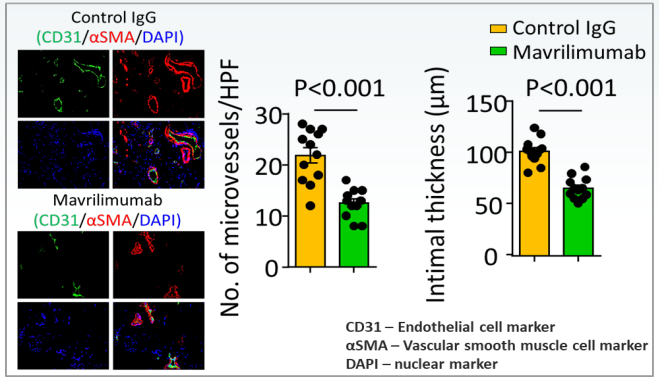
Preclinical Data Support the Mechanistic Rationale of Targeting GM-CSF in GCA

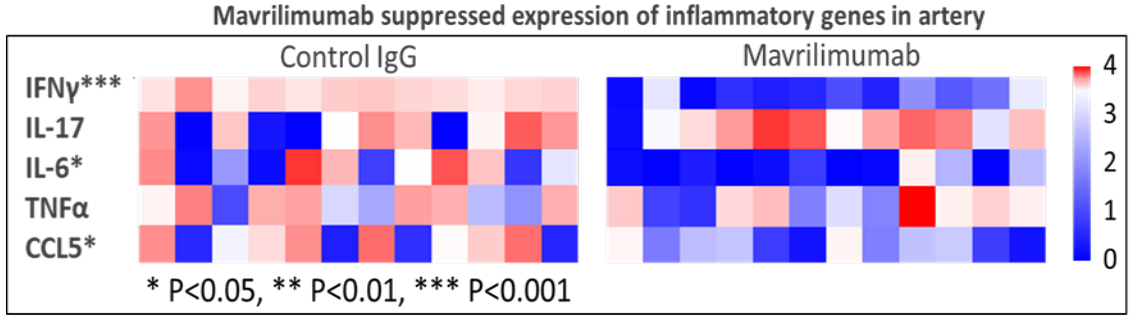
GM-CSF and its receptor, GM-CSFRα, shown to be elevated in GCA biopsies compared to control[1]



Mavrilimumab reduced arterial inflammation compared to control in an *in vivo* model of vasculitis[2]





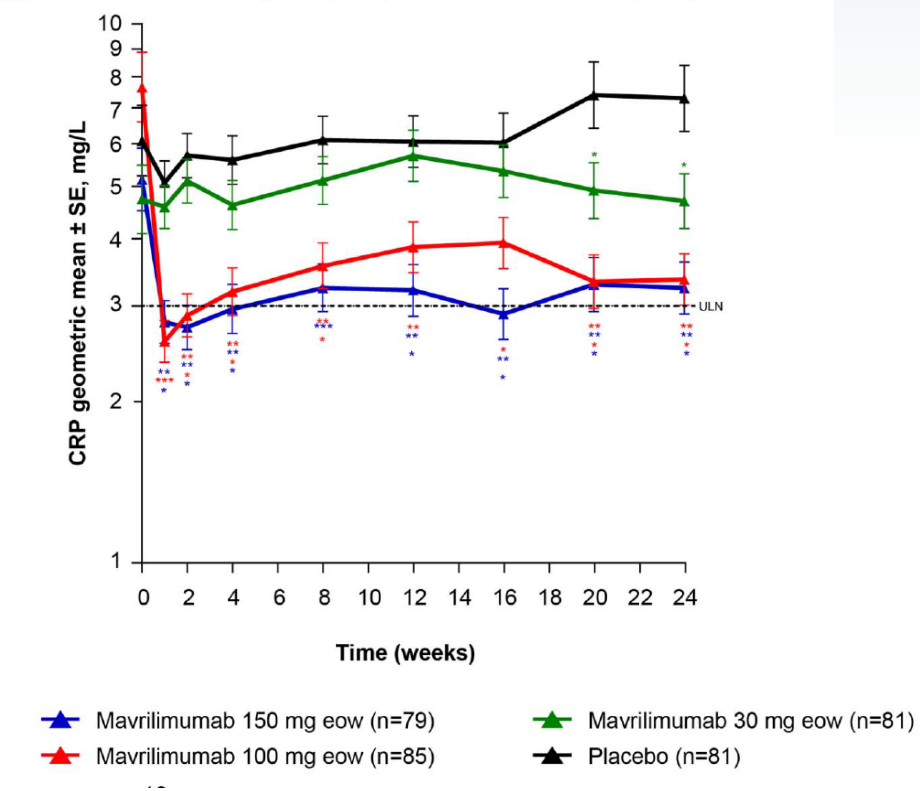


1) Poster presentation at European Congress of Rheumatology 2019 (EULAR): GM-CSF Pathway Signature Identified in Temporal Artery Biopsies of Patients With Giant Cell Arteritis Maria C. Cid, Rohan Gandhi, Marc Corbera-Bellalta, Nekane Terrades-Garcia, Sujatha Muralidharan, John F. Paolini; 2) Presentation at 2019 American College of Rheumatology (ACR): GM-CSF is a Pro-Inflammatory Cytokine in Experimental Vasculitis of Medium and Large Arteries Ryu Watanabe, Hui Zhang, Toshihisa Maeda, Mitsuhiro Akiyama, Rohan Gandhi, John F. Paolini, Gerald J. Berry, Cornelia M. Weyand

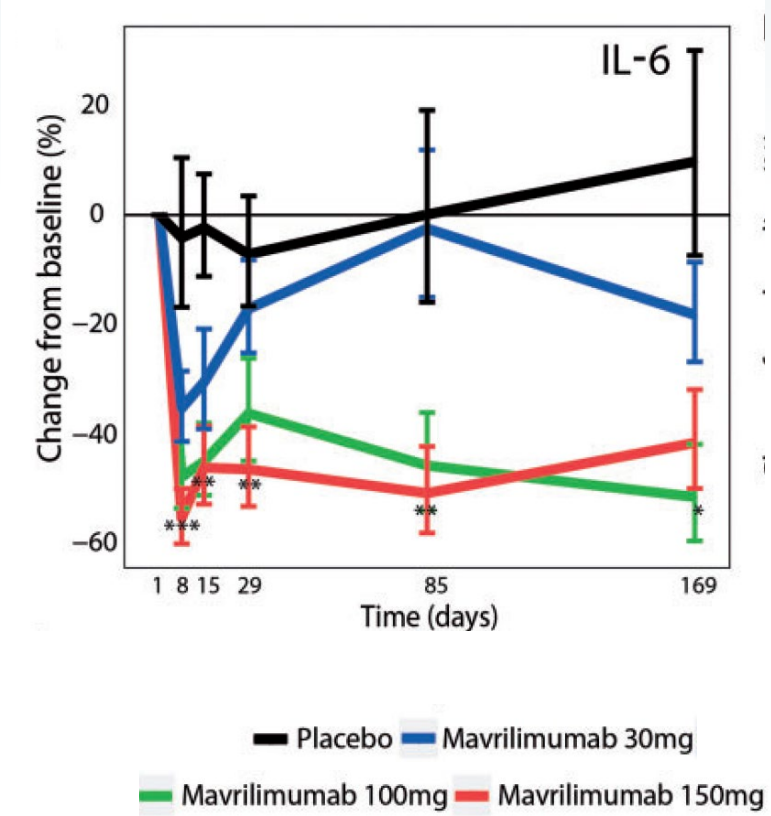
In Phase 2b Rheumatoid Arthritis Study Mavrilimumab Reduced CRP and IL-6, Key Markers of Disease Activity for Giant Cell Arteritis

Indicative of potential broad utility across spectrum of indications with similar biomarker profiles

C-reactive Protein (CRP)[1]



Interleukin-6 (IL-6)[2]



1) Burmester GR, McInnes IB, Kremer, J et al. Ann Rheum Dis 2017; 76, 1020-1030; 2) Xiang Guo et al. Rheumatology, 2017

Phase 2 Data from the Phase 2/3 trial of Mavrilimumab in COVID-19-Related ARDS

The Phase 2/3 trial is a global, randomized, double-blind, placebo-controlled study designed to evaluate the efficacy and safety of mavrilimumab treatment in adults hospitalized with severe COVID-19 pneumonia and hyperinflammation.

- In the non-mechanically ventilated cohort (Cohort 1), 116 patients with hypoxia and severe COVID-19 pneumonia/hyperinflammation were enrolled across sites in the United States, Brazil, Chile, Peru, and South Africa. Patients were randomized in a 1:1:1 ratio to receive a single intravenous (IV) dose of mavrilimumab 10 mg/kg, 6 mg/kg, or placebo.
- Baseline demographics were balanced across treatment arms: the population was ethnically/racially diverse (43% non-white), 49% were obese (body mass index ≥ 30), and 29% were older than 65 years.
- Local standard of care therapy: 96% received corticosteroids/dexamethasone and 29% received antivirals/remdesivir.

Primary Efficacy Endpoint: The proportion of patients alive and free of mechanical ventilation at Day 29.

Key Secondary Efficacy Endpoints: Time to two-point clinical improvement on the NIAID[1] scale, time to return to room air, and mortality at Day 29.

The prespecified evidentiary standard for Phase 2 endpoints was a 2-sided alpha value of 0.2, without adjustment for multiplicity.

Non-mechanically ventilated patients (Cohort 1) treated with mavrilimumab demonstrated a reduction in mechanical ventilation and death at Day 29 pooled across dose levels:

- The proportion of patients alive and free of mechanical ventilation at Day 29 was 12.3 percentage points higher in mavrilimumab recipients (86.7%) compared to placebo recipients (74.4%) (Primary efficacy endpoint; p=0.1224).
  - Mavrilimumab recipients experienced a 65% reduction in the risk of mechanical ventilation or death (Hazard Ratio (HR) = 0.35; p=0.0175).
- Day 29 mortality was 12.5 percentage points lower in mavrilimumab recipients (8%) compared to placebo recipients (20.5%) (p=0.0718).
  - Mavrilimumab recipients experienced a 61% reduction in the risk of death (HR= 0.39; p=0.0726).
- No apparent differences were observed between the 10 mg/kg and 6mg/kg IV treatment arms.

Follow-up preliminary overall survival data from the cohort of non-mechanically ventilated patients at Day 60 and Day 90 demonstrated persistence of clinical effect of mavrilimumab in these patients and were consistent with the previously-reported Day 29 data.

Mavrilimumab was well-tolerated and exhibited a favorable safety profile:

- One treatment-emergent serious adverse event related to study drug was reported on placebo, and there were no notable dose-related adverse events. Infections were noted in all groups including placebo recipients. All thrombotic events occurred in placebo recipients.

KINIKSA

1) National Institute of Allergy and Infectious Diseases; ARDS = acute respiratory distress syndrome

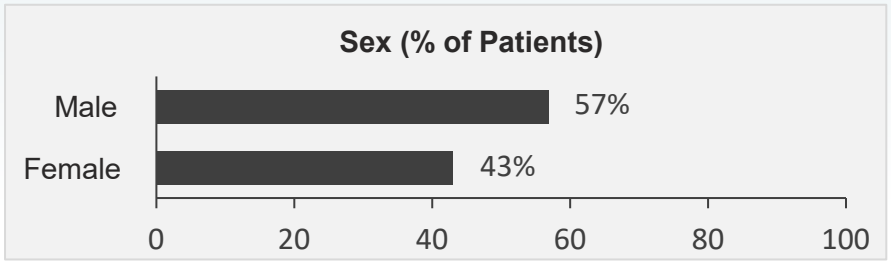
Baseline Demographics and Baseline Characteristics

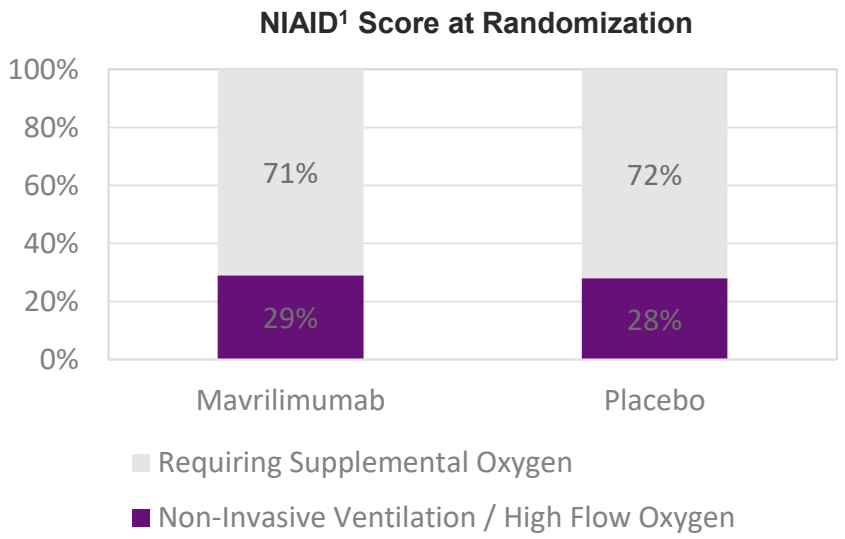
Phase 2 Portion of Phase 2/3 trial of Mavrilimumab in COVID-19-related ARDS

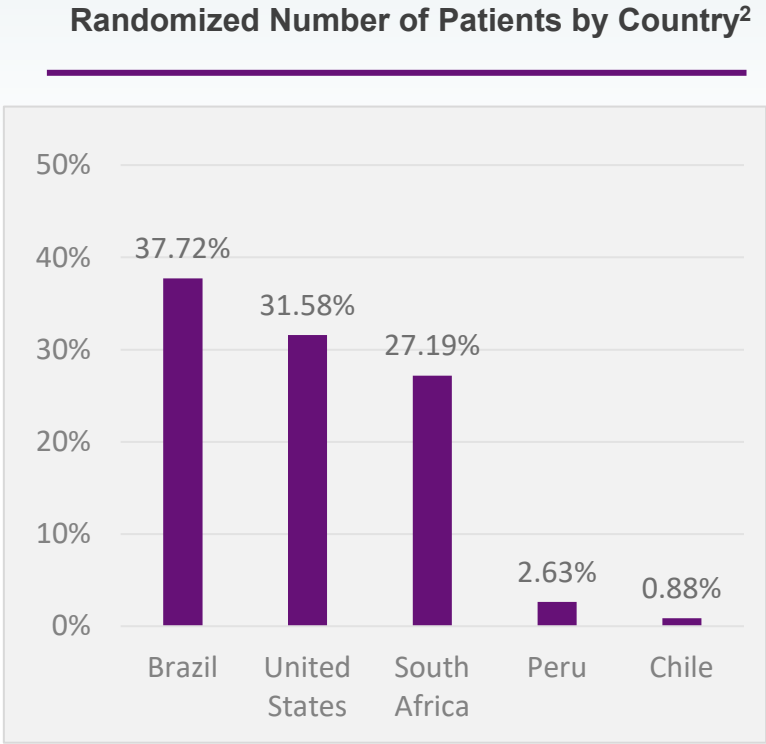
Median time to randomization from diagnosis was 7 days

Baseline Demographics were Balanced Across Treatment Arms	
Mean Age (years)	57.1
Age Range (years)	29-86
> 65 years old	29%
Non-white	43%
Body mass index ≥ 30	49%

Local Standard of Care During 29-Day Treatment Period	
Received Corticosteroids/Dexamethasone	96%
Received Antivirals/Remdesivir	29%







1) National Institute of Allergy and Infectious Diseases; 2) One patient randomized to Cohort 2 but analyzed as part of Cohort 1

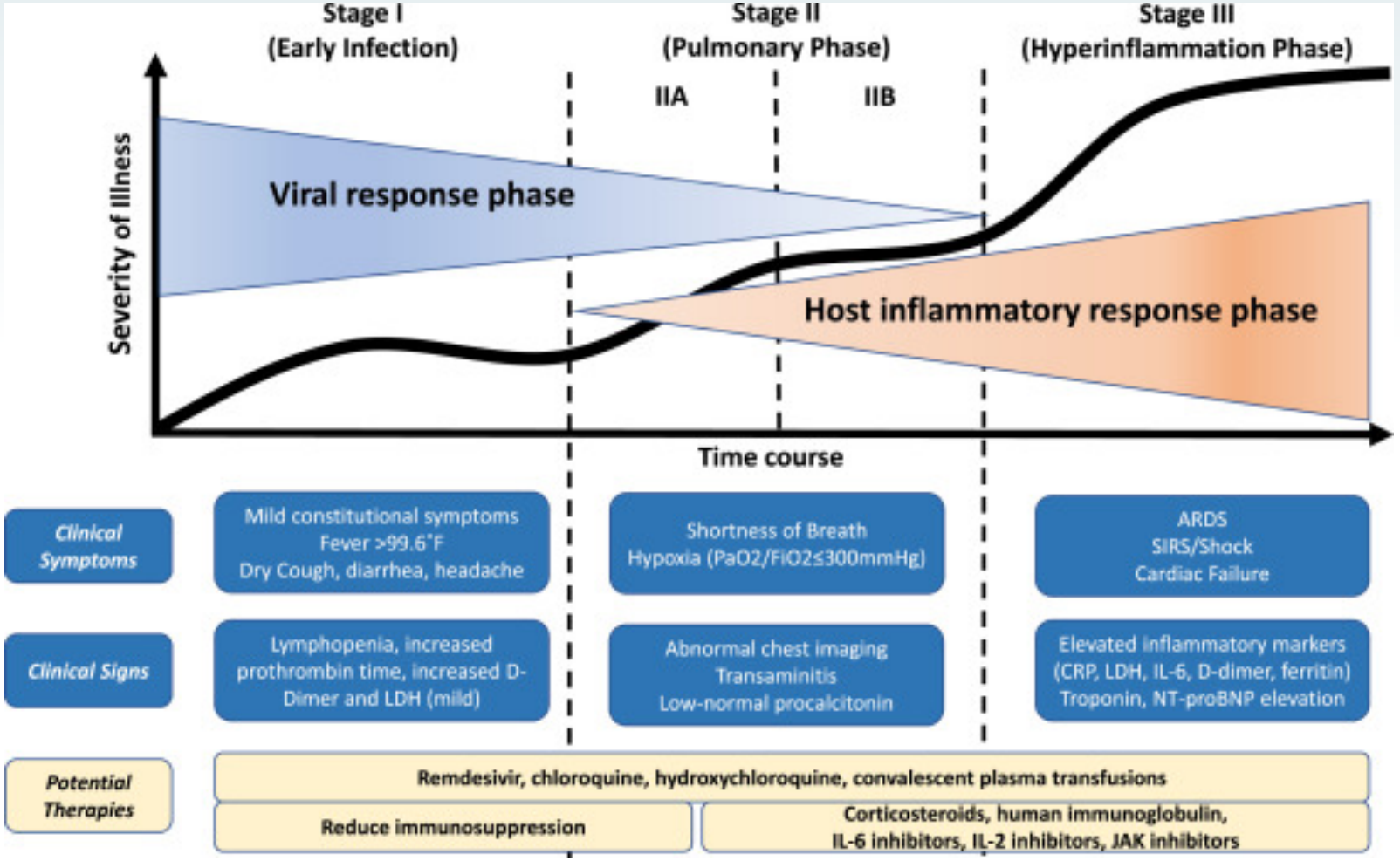
Mavrilimumab was Well-Tolerated and Exhibited a Favorable Safety Profile

Phase 2 Portion of Phase 2/3 trial of Mavrilimumab in COVID-19-Related ARDS

Category	KPL-301 10mg/kg (N=35) n (%)	KPL-301 6mg/kg (N=41) n (%)	Placebo (N=40) n (%)
Treatment Emergent Adverse Events (TEAEs)	19 (54.3)	19 (46.3)	26 (65.0)
TEAEs by Maximum Severity [1]			
Mild	10 (28.6)	8 (19.5)	6 (15.0)
Moderate	5 (14.3)	5 (12.2)	6 (15.0)
Severe	4 (11.4)	6 (14.6)	14 (35.0)
TEAEs related to KPL-301 or Placebo [2]	2 (5.7)	3 (7.3)	4 (10.0)
Serious TEAEs (SAE)	4 (11.4)	5 (12.2)	13 (32.5)
SAEs related to KPL-301 or Placebo [2]	0	0	1 (2.5)
TEAEs Leading to Death	3 (8.6)	4 (9.8)	9 (22.5)
TEAEs Leading to Dose Interruption	0	0	1 (2.5)
TEAEs of Special Interest	3 (8.6)	2 (4.9)	6 (15.0)

1) AESIs include: Hepatic Function Abnormality / induced Liver Injury, Acute and Delayed, Hypersensitivity Reactions, Neutropenia, Serious Infection, Worsening of Cytokine Release Syndrome

Escalating Phases of Disease Progression with COVID-19



Source:
Hasan K. Siddiqi MD, MSCR , Mandeep R. Mehra MD, MSc , COVID-19 Illness in Native and Immunosuppressed States: A Clinical-Therapeutic Staging Proposal, Journal of Heart and Lung Transplantation (2020), doi: https://doi.org/10.1016/j.healun.2020.03.012

ARDS = Acute respiratory distress syndrome; CRP = C-reactive protein; IL = Interleukin; JAK = Janus Kinase; LDH=Lactate DeHydrogenase; SIRS = Systemic inflammatory response syndrome

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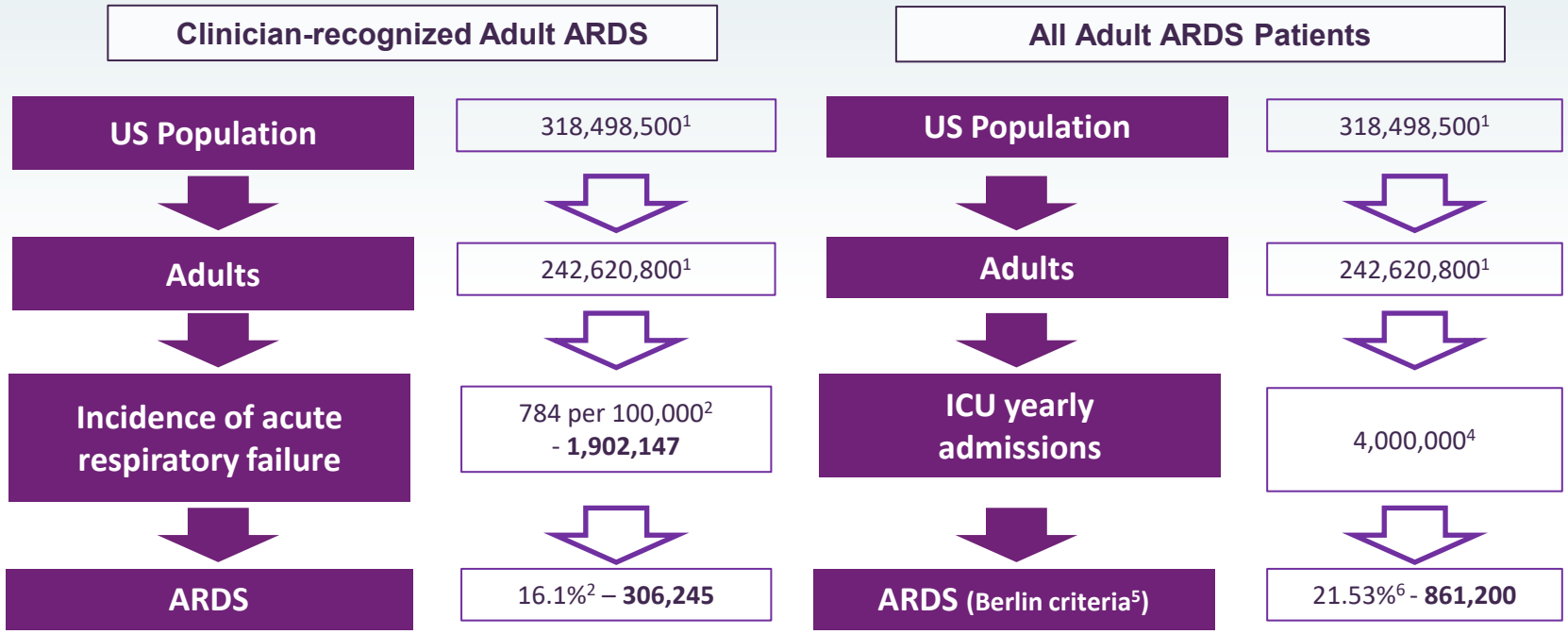
There are between 300k and 860k Cases of Adult ARDS in the U.S. Every Year; Significant Unmet Need Remains in These Populations



- Excludes ARDS associated with COVID-19
- Pediatric ARDS occurs less often
- Most common causes of ARDS are pneumonia (59%) and sepsis (16%)[3]
- 84.5% of ARDS cases require mechanical ventilation[7]
- Considerable mortality (~40%[8]) with no effective treatments outside mechanical ventilation

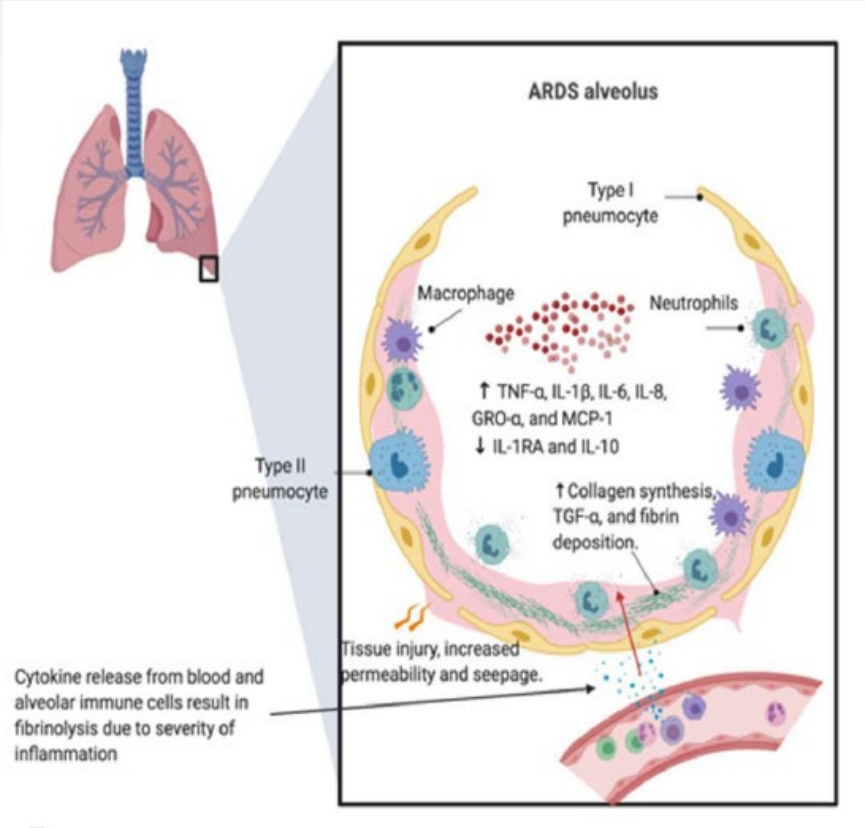
~300,000 – 860,000 ARDS Cases Annually in US*

1) KFF's State Health Facts. Population Distribution by Age [Kaiser Family Foundation estimates based on the Census Bureau's American Community Survey, 2008-2018].
2) Stefan MS, Shieh MS, Pekow PS, et al. J Hosp Med. 2013;8(2):76–82. doi:10.1002/jhm.2004
3) Bellani G, Laffey JG, Pham T, et al JAMA. 2016;315(8):788–800. doi:10.1001/jama.2016.0291
4) Mullins PM, Goyal M, Pines JM. Acad Emerg Med. 2013;20(5):479–486. doi:10.1111/acem.12134
5) ARDS Definition Task Force. JAMA 20112;307(23):2526-2533.
6) Laffey JG, Madotto F, Bellani G, et al. Lancet Resp Med. 2017;5(8):627-638
7) Bellani G, Laffey JG, Pham T, et al Am J Respir Crit Care Med 2017:195(1):67–77
8) Calfee CS, Delucchi KL, Sinha P, et al. Lancet Respir Med. 2018;6(9):691–698. doi:10.1016/S2213-2600(18)30177-2

*There may be different ARDS phenotypes – some of which may not be ideal for GM-CSF inhibition. Further research is needed to understand which patient sub-types would best benefit from treatment with mavrilimumab

Viral Infections Causing ARDS (i.e., influenza, H1N1, RSV, COVID-19, etc.) Have an Inflammatory Pathophysiology, Primarily Precipitated by Cytokine Storm

- Uncontrolled pro-inflammatory response, originating from the focal infected area, spreading through circulation and manifests as a **multiorgan failure** and **ARDS**
- Inflammation of the alveolar epithelial cells drives development of severe disease, destroying gas exchange and allowing **further viral exposure**
- Approach to treatment is **addressing host response** directly by targeting innate immune pathways that amplify inflammatory signals and contribute to epithelial damage



McGonagle, et al., Autoimmunity Reviews (2020), https://doi.org/10.1016/j.autrev.2020.102537

Under-diagnosis of viral infections causing ARDS

- Viral infection is sufficient to cause severe pneumonia and ARDS, but it can also act in conjunction with or be followed by bacterial agents, (most commonly by S. aureus and S. pneumoniae)
- Clinicians fail to clinically diagnose influenza in **up to two-thirds** of patients with confirmed influenza

1) Kalil A.C and Thomas P.G. Critical Care (2019) 23:258
2) Guo XZ, Thomas PG,. Semin Immunopathol. 2017 July ; 39(5): 541–550. doi:10.1007/s00281-017-0636-y.
3) Zhang, et al. Clinical Immunology 214 (2020) 108393

GCA is a Serious Condition Characterized by Inflammation of Medium-to-Large Arteries

1

Chronic inflammation of medium-to-large arteries

- GCA is characterized by inflammation of medium-to-large arteries with predisposition for the cranial branches of the carotid artery and is typically found in patients over 50 years old
- Due to the impact on the carotid arteries, GCA is often characterized by temporal-specific symptoms like headaches, jaw claudication, and scalp tenderness

2

If left untreated, GCA can cause serious complications

- While the onset of symptoms tends to be subacute, patients can experience acute events, including permanent vision loss (~10-20% of patients) and/or aneurysms/dissections (~1-6% of patients)
- Due to the threat of these more serious complications, giant cell arteritis is considered a medical emergency

3

GCA variants associated with unique presentations

- LV-GCA, characterized by the involvement of the aorta and its major proximal branches, is estimated to be involved in anywhere from ~30-80% of patients
- ~40-50% of GCA patients suffer from polymyalgia rheumatica, a rheumatic disease characterized by widespread aching and stiffness; symptoms are relieved immediately upon starting on low-dose steroids

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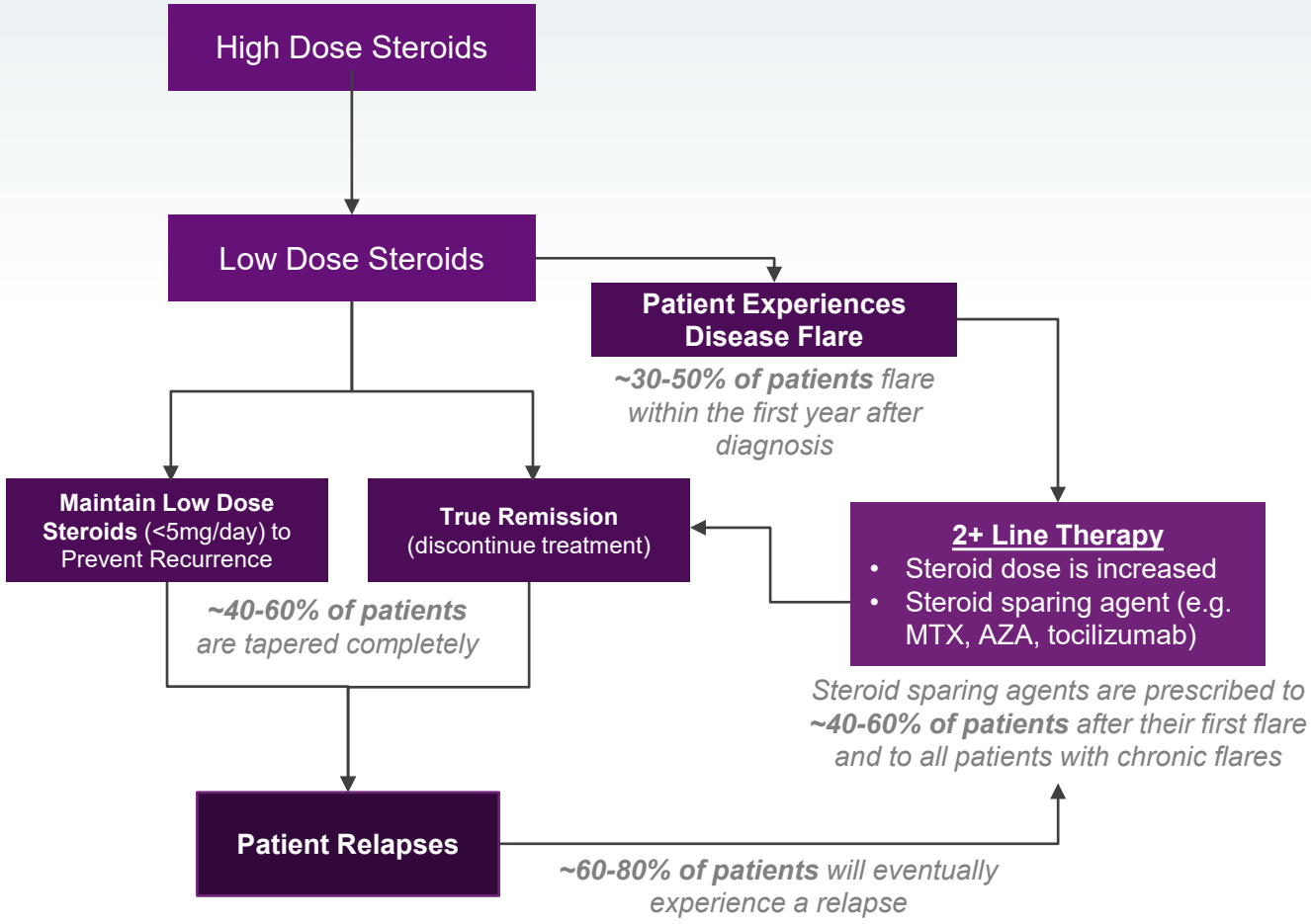
Current Treatment Paradigm for GCA Involves High-Dose Steroids Upon Clinical Suspicion

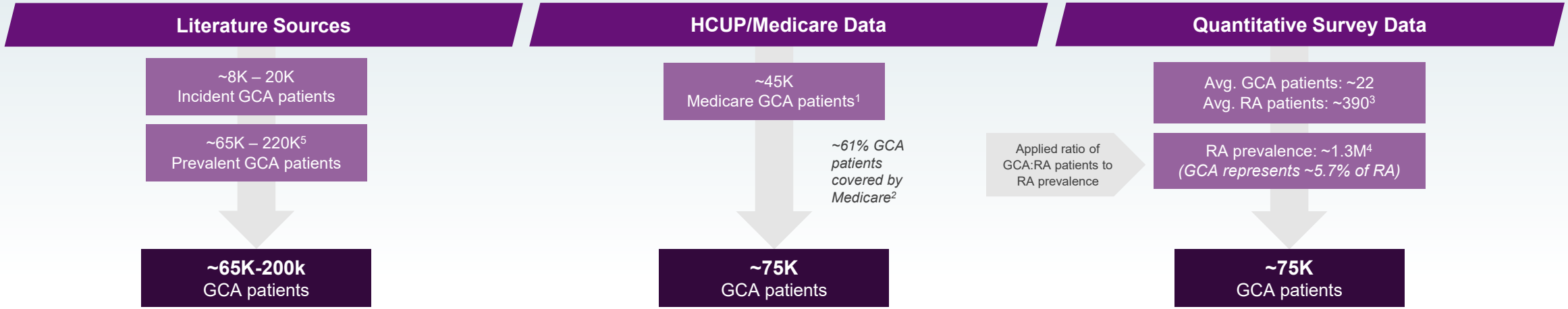


TREATMENT APPROACH:

- All treated patients receive high-dose steroids, which are effective at preventing disease related complications; however, they may lead to life altering side-effects like osteoporosis and diabetes
- A few treaters initiate steroid sparing agents early in the treatment paradigm, relying on them more for the chronic treatment of GCA
- Others treat GCA in more of a stepwise fashion, adding new agents on top of steroids only following disease flares/relapse

Source: Trinity Partners Primary Market Research (n=10 Rheumatologists)

GCA U.S. Prevalence Estimated to be ~75-150k Patients



Key Considerations to Market Sizing Approach

Wide Range

High geographic variation
GCA prevalence estimates vary across geographies with Northern European populations showing the highest rates and Asian populations the lowest

Weighted by US demographics
Given the demographic breakdown of the US, prevalence of GCA is likely ~75-150k (less than that of purely Northern Europeans, but more than estimates from Asian countries)

Under-Representation

Represents Actively Managed Patients
Medicare analysis does not capture GCA patients who were not actively managed within a given year; thus, the estimate from this analysis will exclude some remission patients or patients likely to relapse

Under-Representation

Represents patients actively seen by a Rheum
Rheumatologists reported the number of GCA patients they manage. Patients who are not actively managed would likely be excluded from these estimates

Sources: 1.) Medicare analysis conducted 1/2018 2.) Trinity Partner's Quantitative Primary Market Research (n=74) 3.) Trinity Partner's Quantitative Primary Market Research (n=196) (includes data from screener portion of survey) 4.)Prevalence of rheumatoid arthritis in the United States adult population in healthcare claims databases, 2004-2014, Hunter et al. 2017, 5.) Crowson et. al, 2017

Mavrilimumab Phase 2 Study in Giant Cell Arteritis

Primary and Secondary Endpoints Statistically Significant

The randomized, double-blind, placebo-controlled, global Phase 2 trial consists of a 6-week screening period, a 26-week double-blind placebo-controlled treatment period, and a 12-week washout safety follow-up period.

- Patients age 50 to 85 years with active GCA, confirmed by temporal artery biopsy and/or imaging, with erythrocyte sedimentation rate (ESR) ≥ 30 mm/hour or C-reactive protein (CRP) ≥ 1 mg/dL, and symptoms of GCA within 6 weeks from randomization, were included
- All patients were required to have achieved corticosteroid-induced remission (resolution of symptoms, ESR < 20 mm/hour, CRP < 1 mg/dL) prior to randomization.
- Seventy (70) patients were randomized 3:2 to mavrilimumab 150 mg or placebo biweekly injected subcutaneously, co-administered with a protocol-defined 26-week oral corticosteroid taper
- Patients were stratified by new onset (n=35) or relapsing/refractory (n=35) disease

Primary Efficacy Endpoint: Time-to-first adjudicated GCA flare by Week 26 in all treated patients

Secondary Efficacy Endpoint: Sustained remission at Week 26 in all treated patients

Observations:

- The primary efficacy endpoint of time-to-first adjudicated GCA flare by Week 26 in all treated patients was statistically significant (Hazard Ratio = 0.38, p=0.0263)
  - Median time-to-flare by Week 26 could not be estimated in mavrilimumab recipients due to the low number of flares in the mavrilimumab treatment arm. The median time-to-flare for placebo recipients was 25.1 weeks
  - There was a 62% lower risk of flare in mavrilimumab recipients compared to placebo recipients
- The secondary efficacy endpoint of sustained remission at Week 26 in all treated patients was also statistically significant
  - The sustained remission rate at Week 26 was 33.3 percentage points higher in mavrilimumab recipients (83.2%) compared to placebo recipients (49.9%) (p=0.0038)
- While the study was not powered for disease cohorts, there was a consistent trend of efficacy across the new onset and relapsing/refractory cohorts
- **New Onset Cohort**
  - There was a 71% lower risk of flare in mavrilimumab recipients compared to placebo recipients (Hazard Ratio = 0.29, p=0.0873)
  - The sustained remission rate at Week 26 was 28.9 percentage points higher in mavrilimumab recipients (91.3%) compared to placebo recipients (62.3%) (p=0.0727)
- **Relapsing/Refractory Cohort**
  - There was a 57% lower risk of flare in mavrilimumab recipients compared to placebo recipients (Hazard Ratio = 0.43, p=0.1231)
  - The sustained remission rate at Week 26 was 30.6 percentage points higher in mavrilimumab recipients (72.2%) compared to placebo recipients (41.7%) (p=0.0668)
- Mavrilimumab was well-tolerated; there were no drug-related serious adverse events, and the rates of drug-related treatment-emergent adverse events between mavrilimumab recipients and placebo recipients were similar
- The 12-week washout safety follow-up period is ongoing, and additional analyses of this Phase 2 trial are planned. Next steps for the development program in GCA will be further informed by anticipated discussions with the U.S. Food and Drug Administration (FDA)

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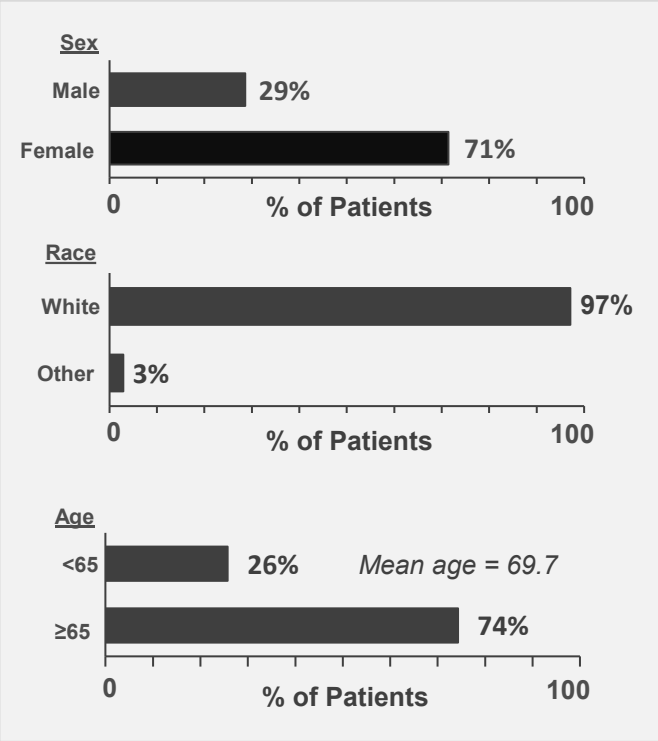
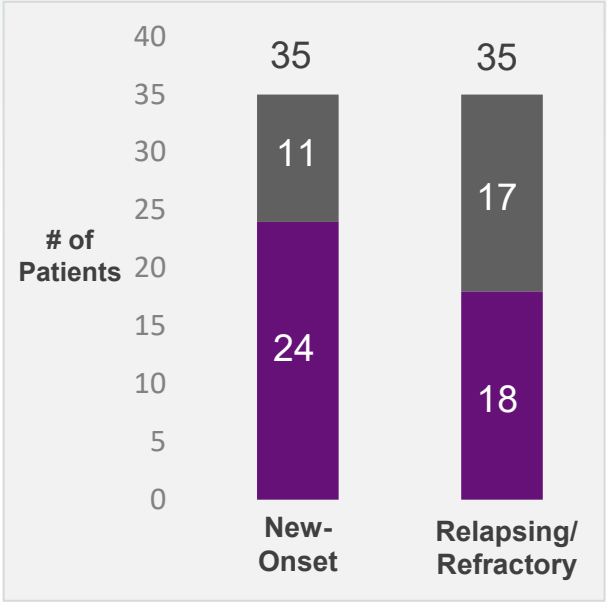
Baseline Demographics and Clinical Characteristics

Mavrilimumab Phase 2 Giant Cell Arteritis Data

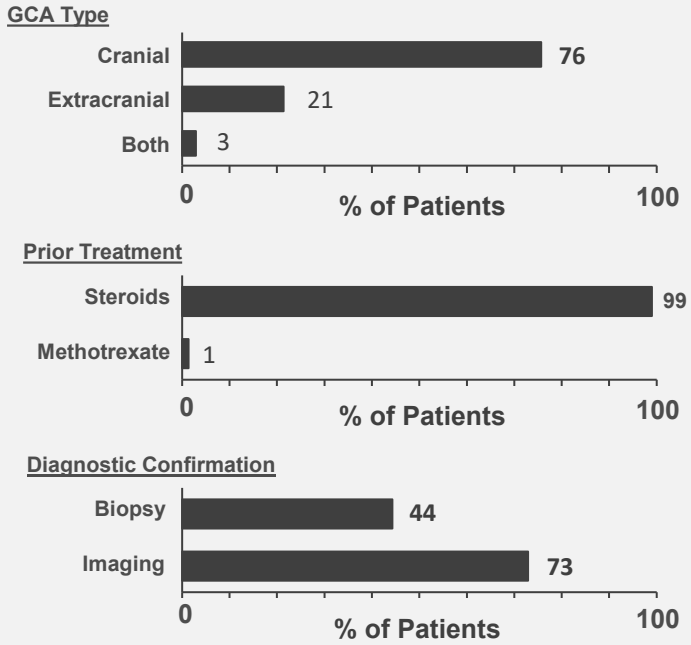
Baseline Demographics (n=70)



Randomization Strata



Baseline Disease Characteristics (n=70)



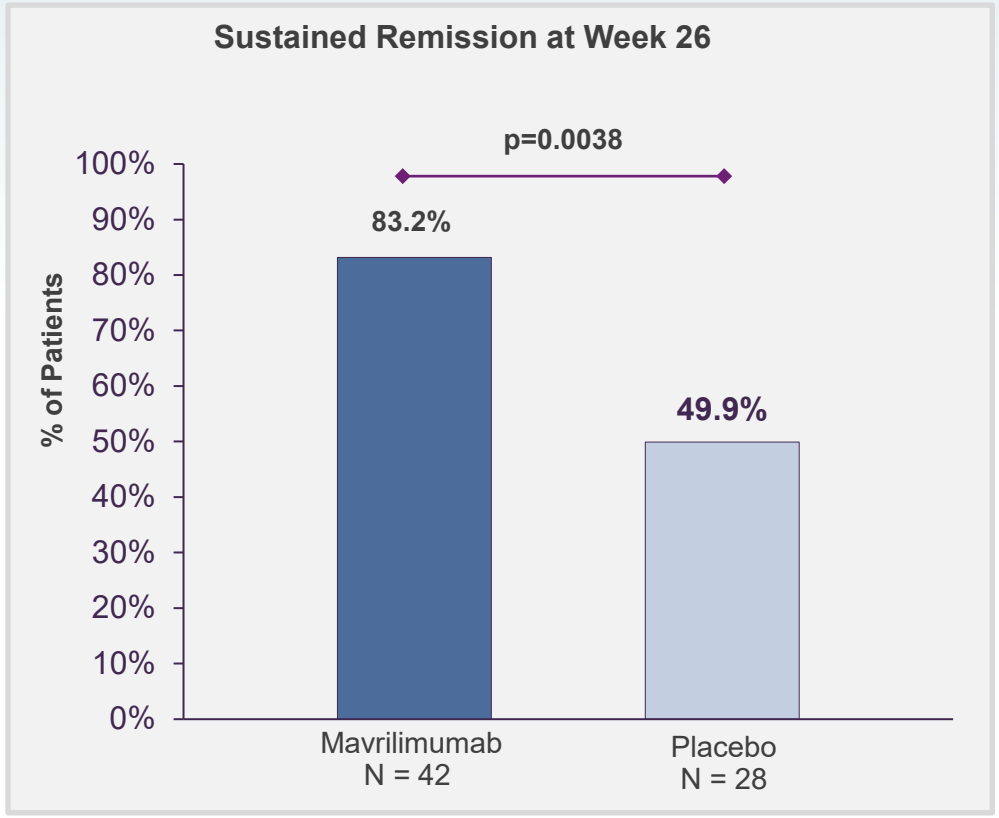
Mean time since diagnosis = 1.1 months (new-onset)
Mean time since diagnosis = 16.2 months (relapsing/refractory)

Mean eligibility ESR = 56.2 mm/hr

Mean eligibility CRP = 4.27 mg/dL

Secondary Efficacy Endpoint: Sustained Remission at Week 26

Mavrilimumab Phase 2 Giant Cell Arteritis Data



The sustained remission rate at Week 26 was 33.3 percentage points higher in mavrilimumab recipients (83.2%) compared to placebo recipients (49.9%) (p=0.0038).

Time to Flare and Sustained Remission at Week 26

Mavrilimumab Phase 2 Giant Cell Arteritis Data

Time to Flare by Week 26 and Sustained Remission at Week 26 - Total mITT Population	Mavrilimumab 150 mg (N=42)	Placebo (N=28)
Number of Subjects with Flare, n (%)	8 (19.0)	13 (46.4)
Primary Efficacy Endpoint: Time to Flare (weeks) by Week 26 [1]		
Median, 95% CI	NE (NE, NE)	25.1 (16.0, NE)
Hazard Ratio (Mavrilimumab vs Placebo), 95% CI [2]	0.38 (0.15, 0.92)	
P-value [3]	0.0263	
Secondary Efficacy Endpoint: Sustained Remission at Week 26 (%), 95% CI [4]	83.2 (67.9, 91.6)	49.9 (29.6, 67.3)
Difference in Proportions (95% CI) [5]	33.3 (10.7, 55.8)	
P-value [5]	0.0038	

Time to Flare by Week 26 and Sustained Remission at Week 26 by Randomization Strata	New-onset		Relapsing/Refractory	
	Mavrilimumab 150 mg (N=24)	Placebo (N=11)	Mavrilimumab 150 mg (N=18)	Placebo (N=17)
Number of Subjects with Flare, n (%)	3 (12.5)	4 (36.4)	5 (27.8)	9 (52.9)
Primary Endpoint: Time to Flare (weeks) by Week 26 [1]				
Median, 95% CI	NE (NE, NE)	NE (11.7, NE)	NE (16.4, NE)	22.6 (16.0, NE)
Hazard Ratio (Mavrilimumab vs Placebo), 95% CI [6]	0.29 (0.06, 1.31)		0.43 (0.14, 1.30)	
P-value [7] [8]	0.0873		0.1231	
Secondary Endpoint: Sustained Remission at Week 26 (%) , 95% CI [4]	91.3 (69.3, 97.7)	62.3 (27.7, 84.0)	72.2 (45.6, 87.4)	41.7 (17.4, 64.5)
Difference in Proportions (95% CI) [5]	28.9 (-2.7, 60.5)		30.6 (-2.1, 63.2)	
P-value [5][8]	0.0727		0.0668	

NE = Not estimable.

[1] Kaplan-Meier method used to estimate the survival functions for each treatment arm.

[2] Calculated based on a Cox proportional-hazards model with treatment as covariate and stratified by randomization strata.

[3] Comparison of KPL-301 and placebo with respect to time to flare calculated by using a log-rank test and stratified by randomization strata.

[4] Kaplan-Meier Survival Estimates with standard error and 95% CI for each arm.

[5] Two-sided p-value and 95% CI for the difference in sustained remission between two arms using normal approximation. Placebo arm is the reference.

[6] Calculated based on a Cox proportional-hazards model with treatment as covariate.

[7] Comparison of KPL-301 and placebo with respect to time to flare calculated by using a log-rank test.

[8] Subgroup analyses were not powered for significance; nominal p values reported.

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Number of Subjects with Flare, n (%)	3 (12.5)	4 (36.4)	5 (27.8)	9 (52.9)
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Median, 95% CI	NE (NE, NE)	NE (11.7, NE)	NE (16.4, NE)	22.6 (16.0, NE)
Hazard Ratio (Mavrilimumab vs Placebo), 95% CI [6]	0.29 (0.06, 1.31)		0.43 (0.14, 1.30)	
P-value [7] [8]	0.0873		0.1231	
Secondary Endpoint: Sustained Remission at Week 26 (%) , 95% CI [4]	91.3 (69.3, 97.7)	62.3 (27.7, 84.0)	72.2 (45.6, 87.4)	41.7 (17.4, 64.5)
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[8] Subgroup analyses were not powered for significance; nominal p values reported.

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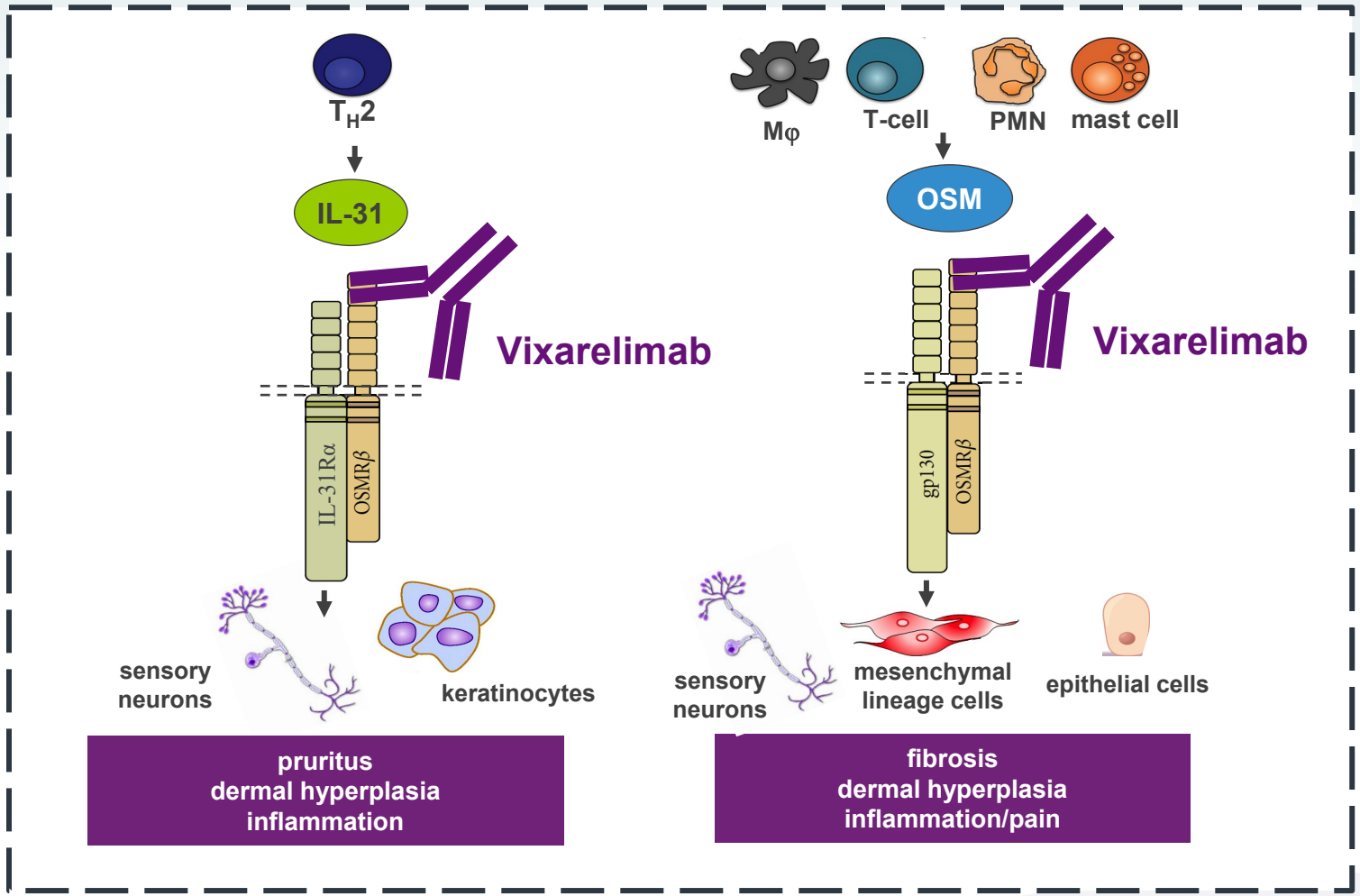
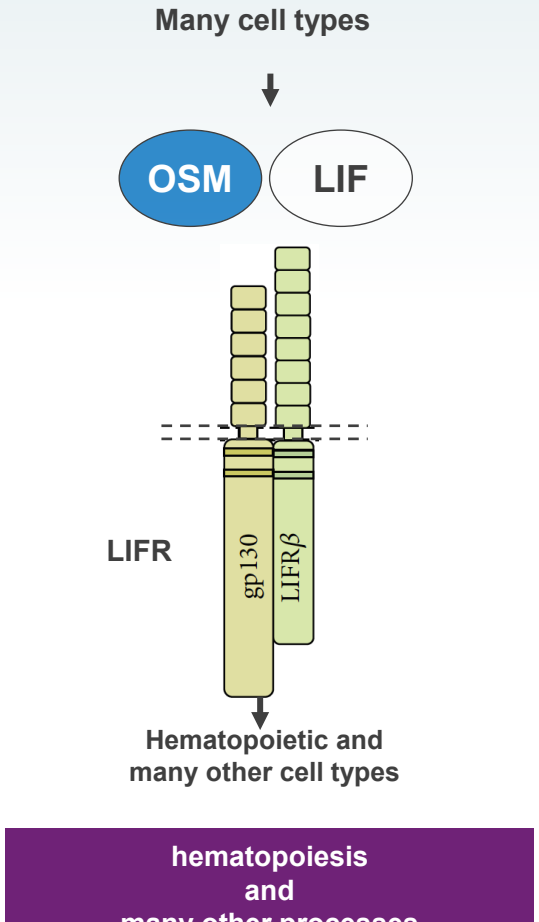
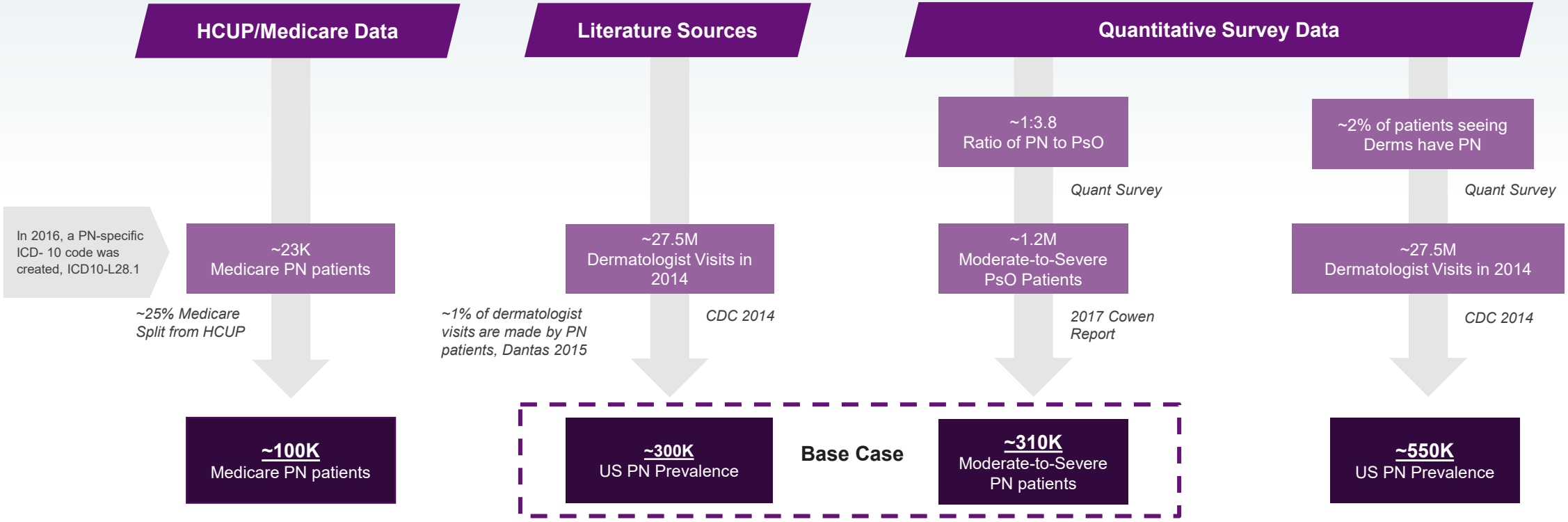
Appendix
VIXARELIMAB

Vixarelimab Inhibits IL-31 & OSM Signaling Through OSMRβ but Avoids Inhibiting Signaling Critical to Hematopoiesis Through OSM/LIFR in vitro Studies



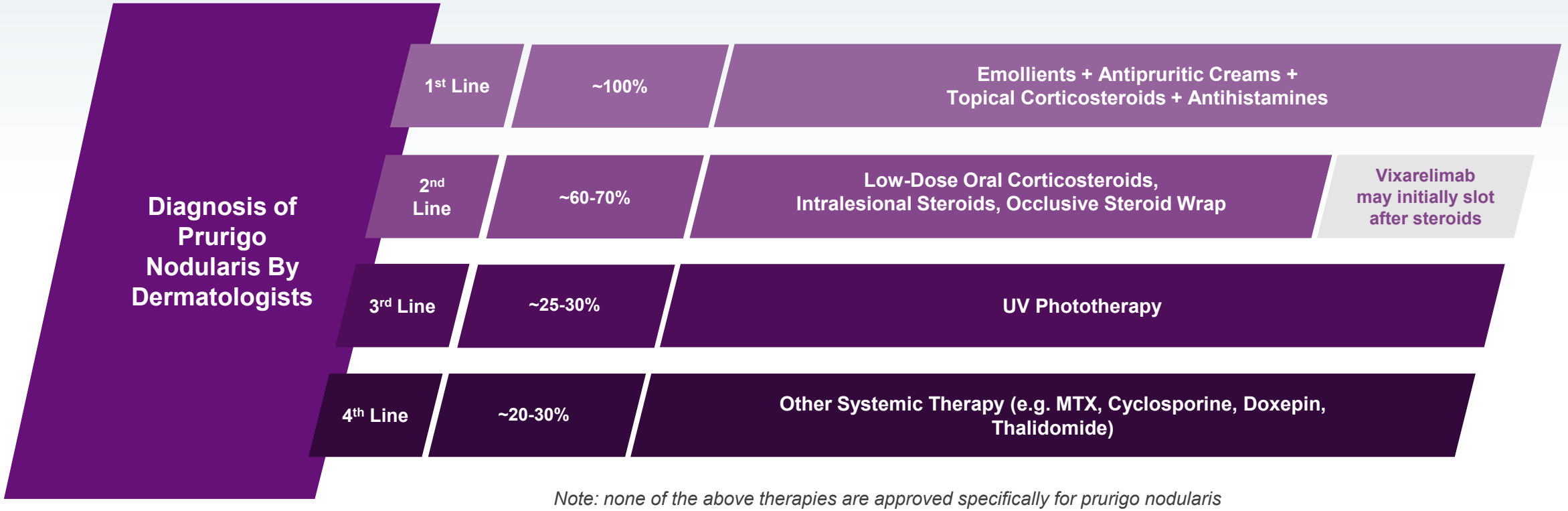


Prurigo Nodularis U.S. Prevalence Estimated to be ~300K Patients



Sources: CDC 2014: National Ambulatory Medical Care Survey: 2014 State and National Summary Tables <https://www.cdc.gov/nchs/data/ahcd/namcs_summary/2014_namcs_web_tables.pdf>; Cowen and Company, Therapeutic Categories Outlook: Comprehensive Study September 2017; Primary Market Research; 3. Dantas, 2015, "Prevalence of dermatoses in dermatologic evaluation requests from patients admitted to a tertiary hospital for 10 years"

Prurigo Nodularis is Typically Treated by Dermatologists Through a Combination of Medications and Behavioral Therapies; Treatment is Usually Unsuccessful



Note: none of the above therapies are approved specifically for prurigo nodularis

Sources: 1. Medscape, 2. Trinity Qualitative Research

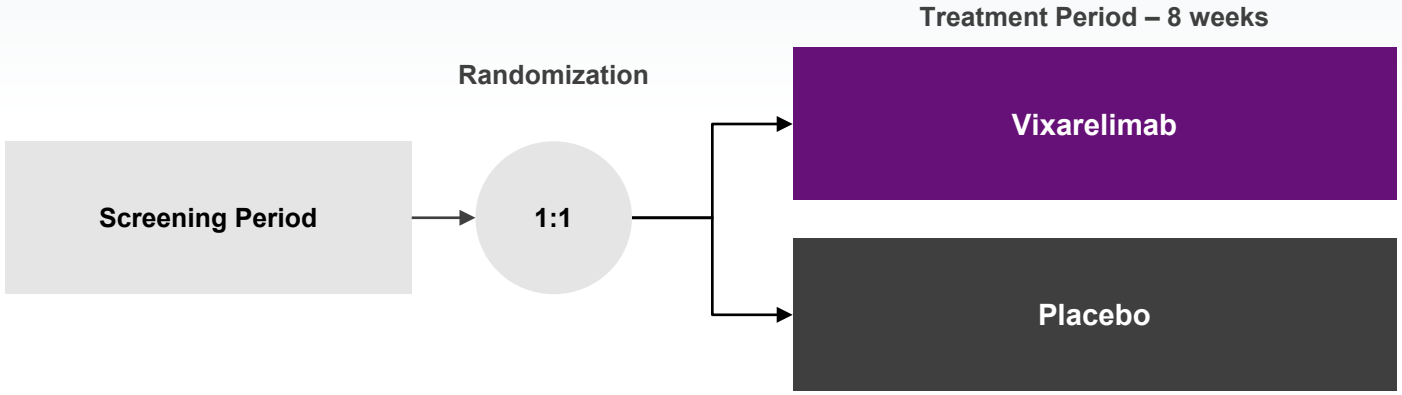
Vixarelimab Phase 2a Study in Prurigo Nodularis

Phase 2a Proof-of-Concept

Objective: Assess pruritus reduction

Dose: 720 mg SC loading dose --> 360 mg single SC QW thereafter

Primary Efficacy Endpoint : % change from baseline in weekly average Worst Itch-Numeric Rating Scale (WI-NRS)



Inclusion Criteria

- Male or female aged 18 to 75 years, inclusive, at the time of consent
- Have a physician-documented diagnosis of prurigo nodularis that is confirmed by review of medical photography during the Screening Period. Duration of prurigo nodularis (since the time of first PN nodule) must be at least 6 months from the time of first PN nodule to Day 1, as affirmed by the subject
- Have at least 10 nodules of approximately 0.5 to 2 cm at the Screening Visit and Day 1. The nodules must be pruritic and present on at least 2 different anatomical locations (not be localized), involve the extremities, with extensor extremity involvement greater than the flexor extremity involvement. Nodules on the head (face and scalp) are not counted as an anatomical location for eligibility criteria. There must be normal appearing skin present in between nodules with the exception of atopic dermatitis. Each arm, each leg, and trunk are considered different anatomical locations
- Subject has moderate to severe pruritus, defined as WI-NRS ≥ 7 at the Screening Visit and a mean weekly WI-NRS ≥ 5 for each of the 2 consecutive weeks immediately prior to randomization
- Patients were required to stop antihistamines and topical treatments, including corticosteroids, for at least two weeks prior to dosing
- Prurigo nodularis treatments, other than study drug, were not allowed except for rescue

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Vixarelimab Phase 2a Study in Prurigo Nodularis

Statistically significant primary efficacy endpoint of reduction in weekly-average WI-NRS at Week 8

Enrolled and treated 49 patients with moderate-to-severe prurigo nodularis (mean PN- IGA of 3.4) experiencing moderate-to-severe pruritus (mean WI-NRS score of 8.3)

- Randomized 1:1 to receive a loading dose of vixarelimab 720 mg (n=23) or placebo (n=26) subcutaneous (SC) followed by vixarelimab 360 mg or placebo SC weekly
- Data includes 49 subjects through the 8-week treatment period

Primary Efficacy Endpoint: percent change versus baseline in weekly-average WI-NRS at Week 8 (using the last observation carried forward analysis)

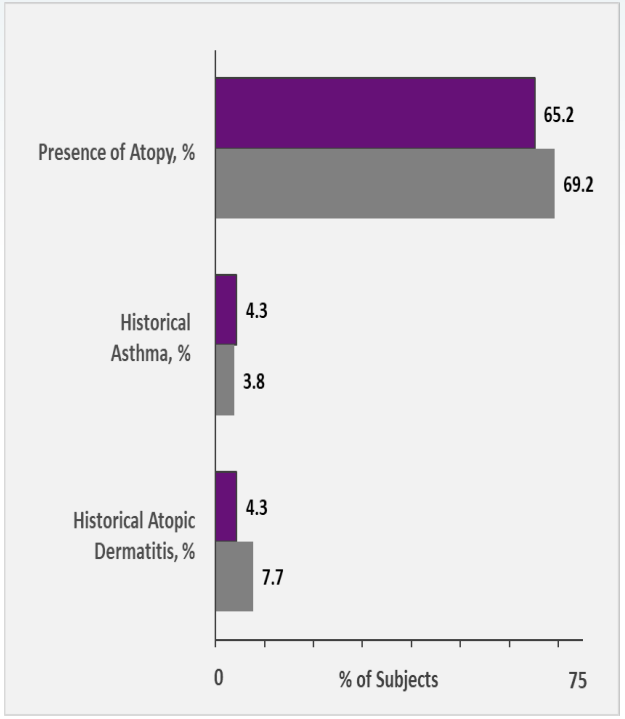
Topline Observations:

- Least squares-mean change from baseline in weekly-average WI-NRS at Week 8 was -50.6% in vixarelimab recipients compared to -29.4% in placebo recipients (mean difference 21.1%; p=0.035)
- Median change from baseline in weekly-average WI-NRS at Week 8 was -69.8% in vixarelimab recipients compared to -36.1% in placebo recipients
- 30.4% of vixarelimab recipients achieved a PN-IGA score of 0/1 at Week 8 compared to 7.7% of placebo recipients (p=0.032)
- 52.2% of vixarelimab recipients demonstrated a ≥ 4-point reduction in weekly-average WI-NRS at Week 8 compared to 30.8% of placebo recipients (p=0.109)
- In this Phase 2a trial, vixarelimab was well-tolerated by all subjects and no dose-limiting adverse experiences were observed. There were no serious adverse events or atopic dermatitis flares

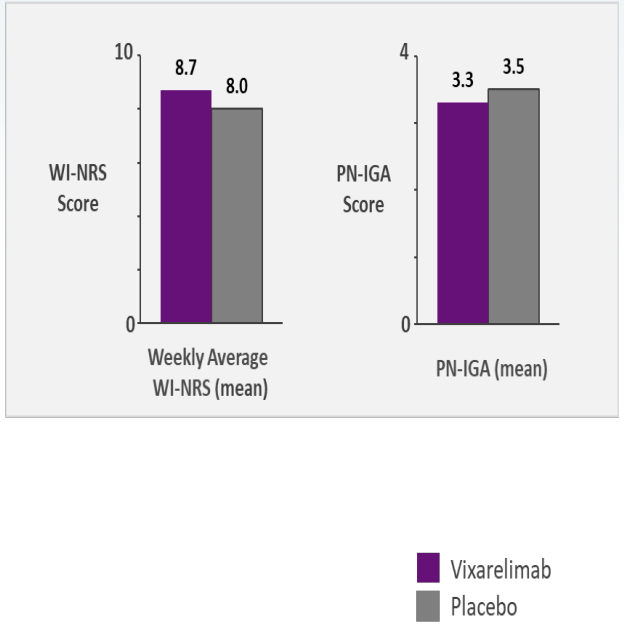
Vixarelimab Phase 2a Study in Prurigo Nodularis: Baseline Characteristics

General Characteristics*	Vixarelimab (n=23)	Placebo (n=26)	Total (n=49)
Age (Mean Years)	52	64	58
Sex (Male/Female)	10/13	10/16	20/29
Race			
White (n)	65.2% (15)	80.8% (21)	73.5% (36)
Black or African American (n)	21.7% (5)	11.5% (3)	16.3% (8)
Asian (n)	8.7% (2)	0	4.1% (2)
American Indian or Alaska Native (n)	0	3.8% (1)	2.0% (1)
Multiple (n)	4.3% (1)	0	2.0% (1)
Other (n)	0	3.8% (1)	2.0% (1)

Clinical Findings at Baseline: History of Atopy



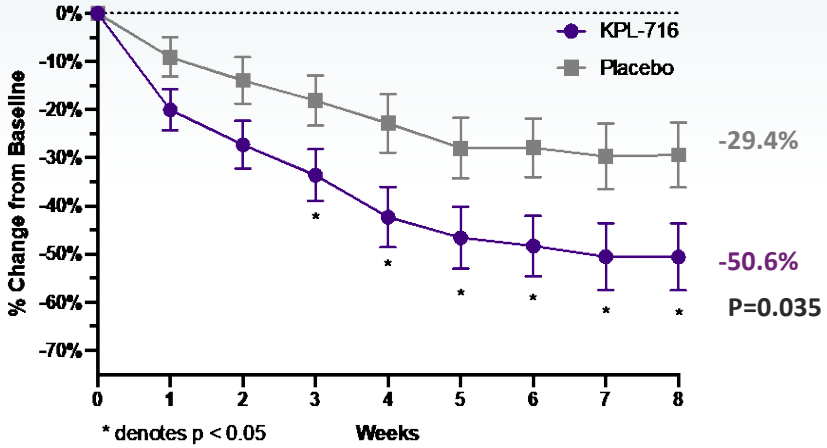
Clinical Findings at Baseline: WI-NRS & PN-IGA



*mITT Analysis Set

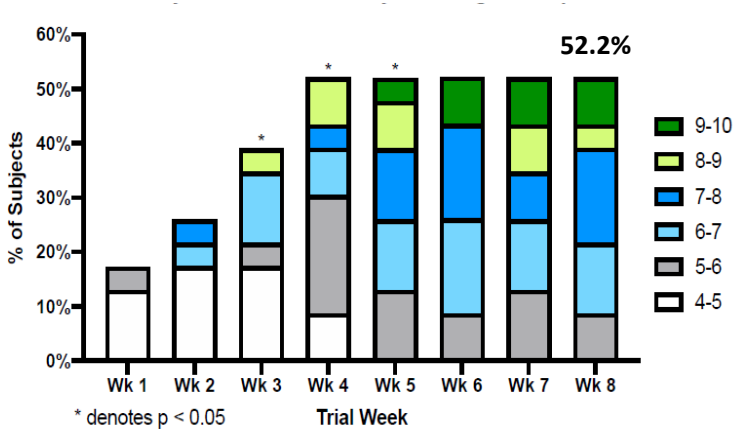
Vixarelimab Phase 2a Data in Prurigo Nodularis

LS-Mean % Change in Weekly Average WI-NRS



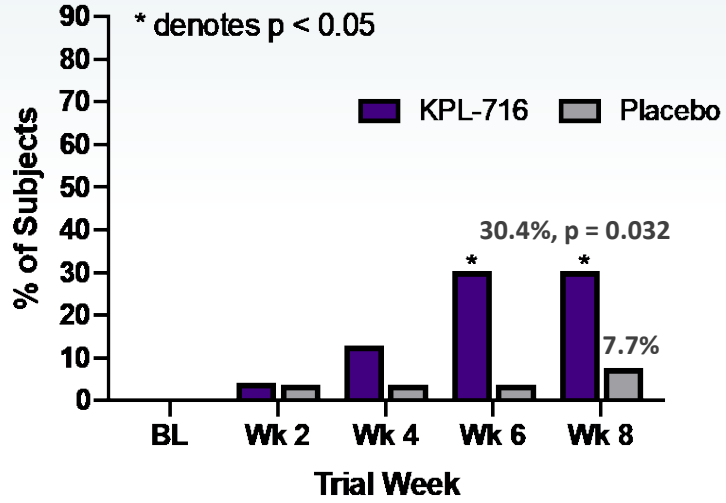
Statistically Significant Primary Efficacy Endpoint of Reduction in Weekly-Average WI-NRS at Week 8

% of Vixarelimab Subjects with a Clinically Meaningful Response in WI-NRS



Majority of Vixarelimab Recipients Showed a Clinically Meaningful ≥4-Point Weekly-Average WI-NRS Reduction at Week 8

PN-IGA Score of 0 or 1

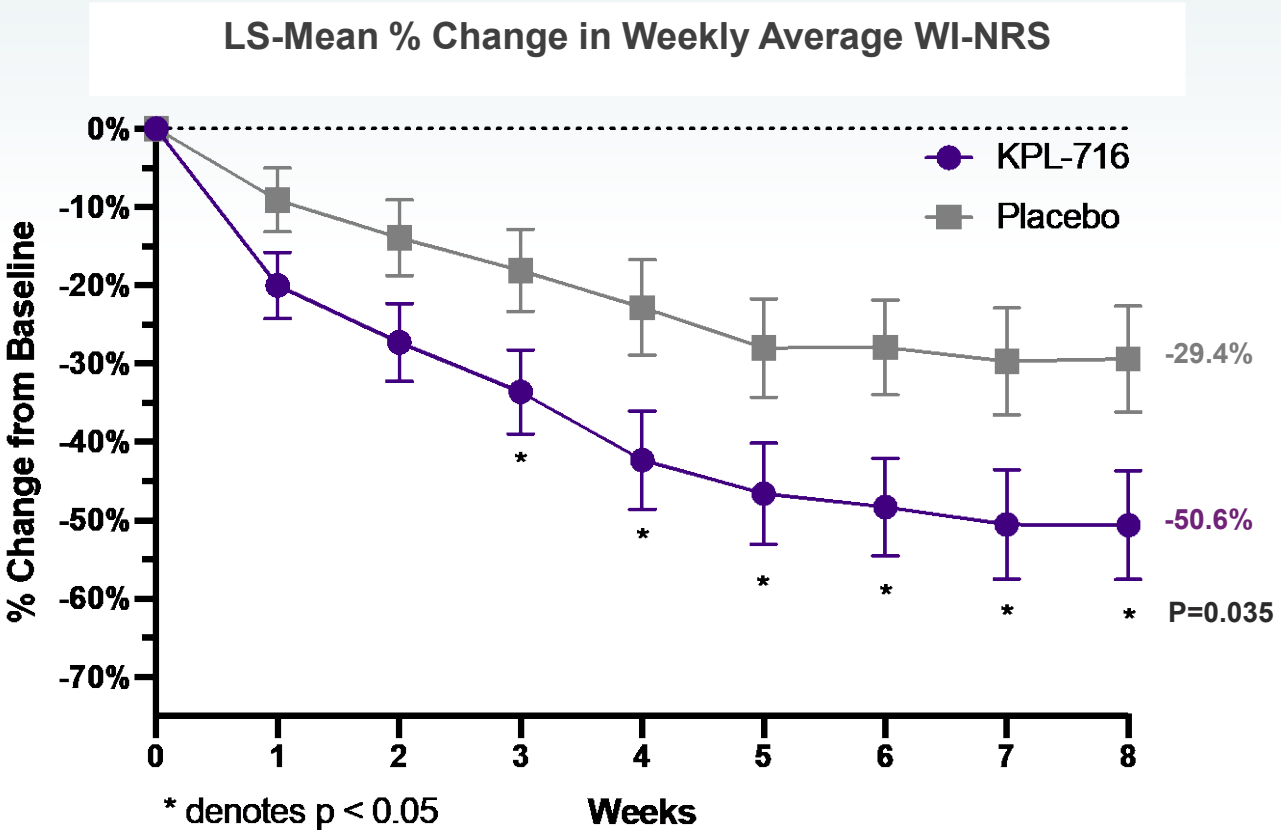


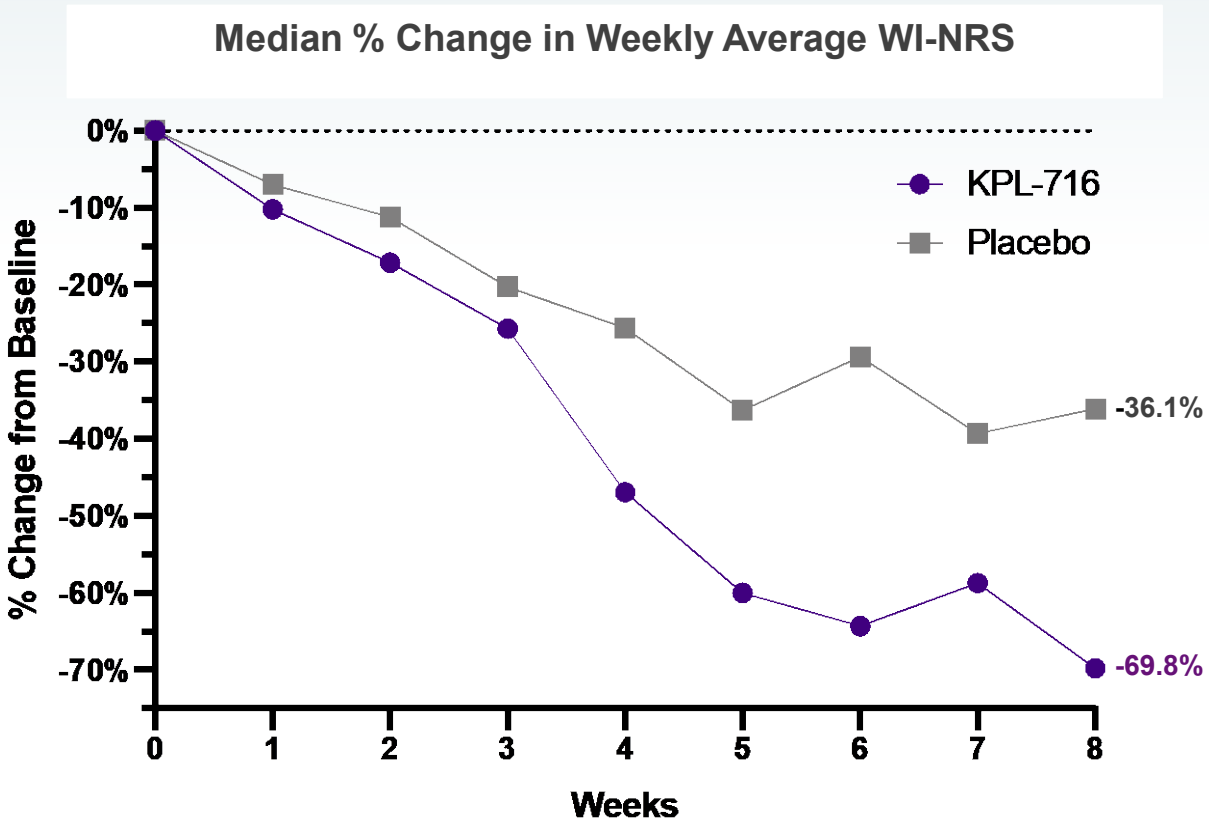
Significantly More Vixarelimab Recipients Attained A Clear/Almost Clear Lesion Score by Week 8

Vixarelimab = KPL-716
WI-NRS = Worst-Itch Numeric Rating Scale
LS = least squares

Vixarelimab Phase 2a Study in Prurigo Nodularis: Statistically Significant Primary Efficacy Endpoint of Reduction in Weekly-Average WI-NRS at Week 8

Median change from baseline in weekly-average WI-NRS at Week 8 was -69.8%





Vixarelimab = KPL-716
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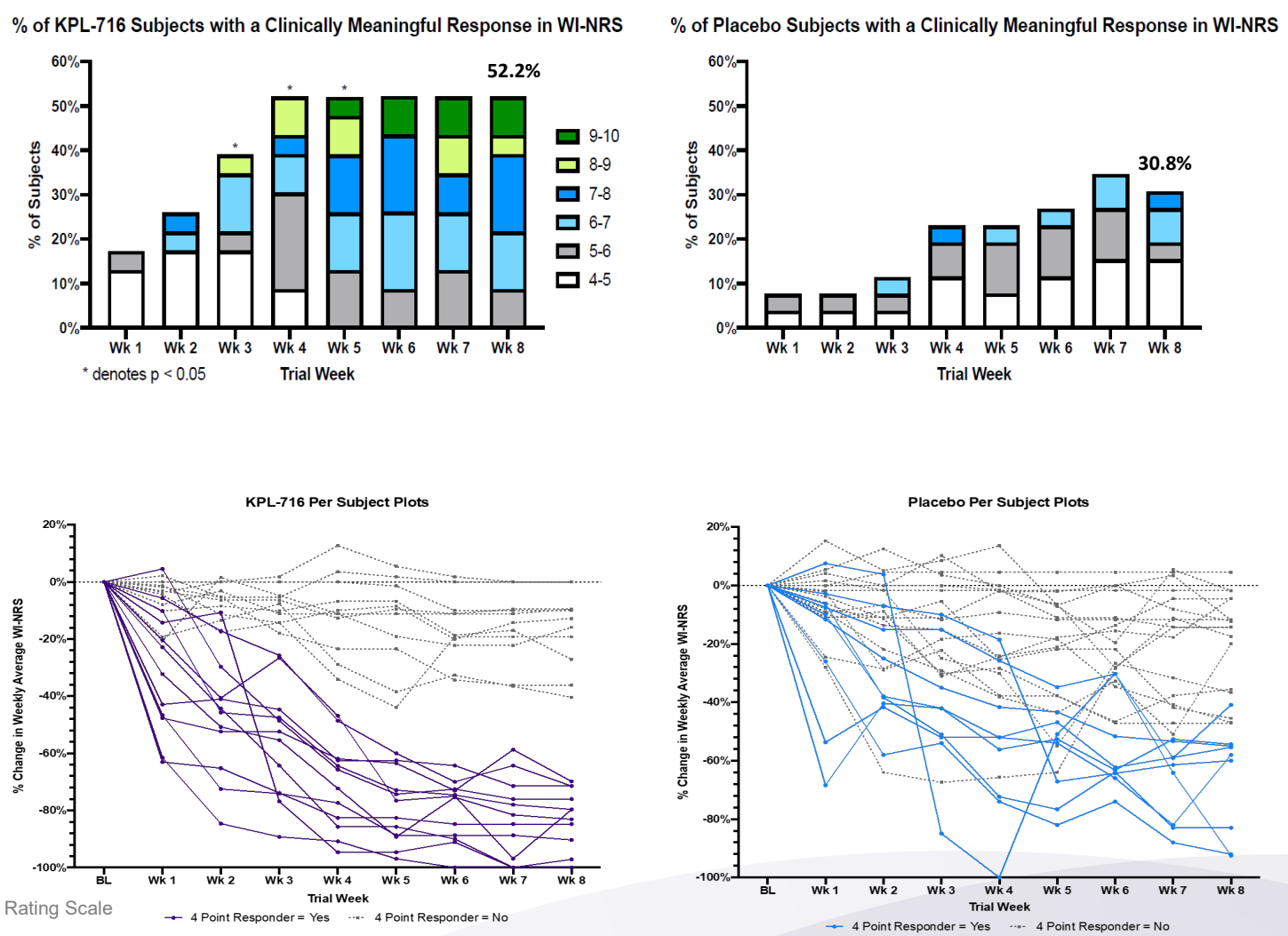
Vixarelimab Phase 2a Study in Prurigo Nodularis: Majority of Vixarelimab Recipients Showed a Clinically Meaningful ≥4-Point Weekly-Average WI-NRS Reduction at Week 8



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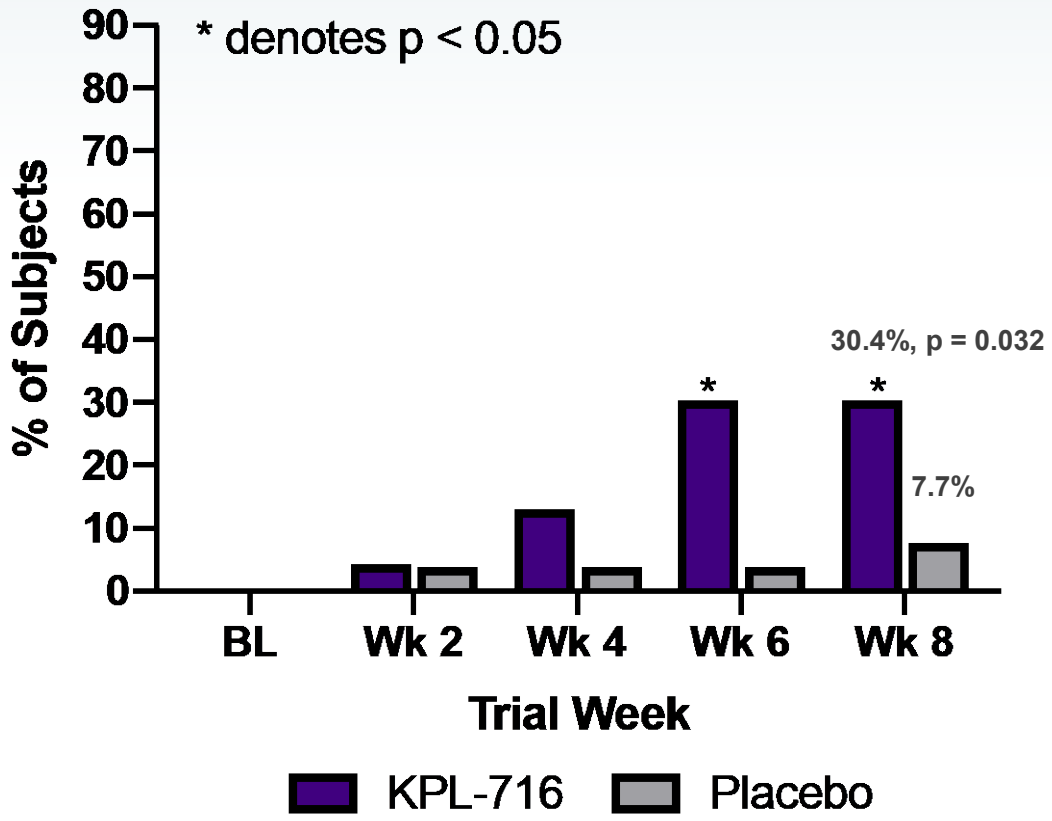
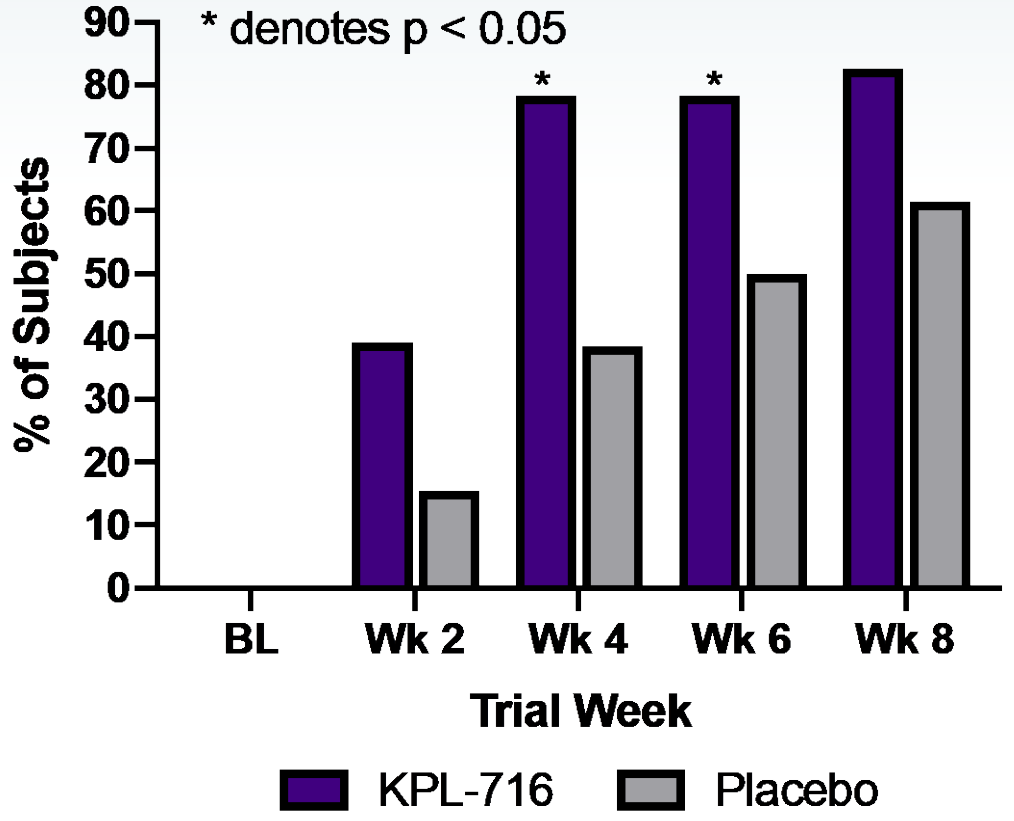
Vixarelimab Phase 2a Study in Prurigo Nodularis: Significantly More Vixarelimab Recipients Attained A Clear/Almost Clear Lesion Score by Week 8

PN-IGA Score of 0 or 1



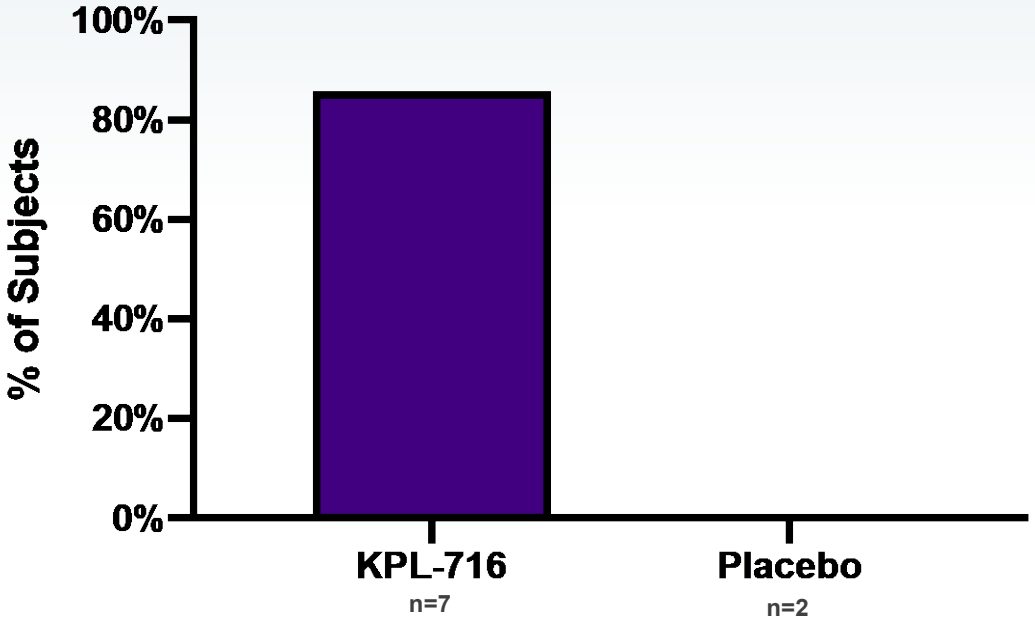
≥1 Point Change in PN-IGA



Vixarelimab = KPL-716
WI-NRS = Worst-Itch Numeric Rating Scale
LS = least squares

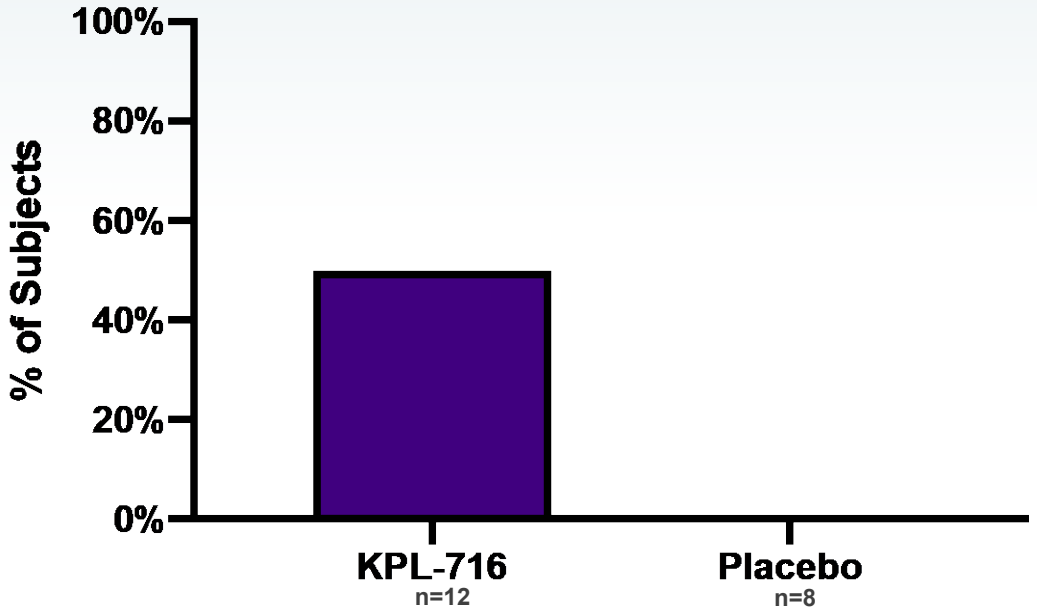
Vixarelimab Phase 2a Study in Prurigo Nodularis: Concordant Activity of Vixarelimab on PN-IGA and Pruritus

% of IGA 0-1 Subjects with ≥4 Point Change in WI-NRS



85.7% of the subjects who achieved 0-1 on the PN-IGA scale were also 4-point responders on WI-NRS vs. none for placebo

% of Subjects with ≥4 Point Change in WI-NRS and an IGA of 0-1



50% of the subjects who had a clinically meaningful reduction in itch by week 8 also had an PN-IGA score of 0-1 vs. none for placebo

Vixarelimab = KPL-716
WI-NRS = Worst-Itch Numeric Rating Scale
LS = least squares

Vixarelimab was Well-Tolerated in Prurigo Nodularis Phase 2a Study

Summary of Adverse Events	Vixarelimab (n=23)	Placebo (n=26)
Any AE (n)	82.6% (19)	65.4% (17)
TEAE (n)	82.6% (19)	65.4% (17)
Drug-Related TEAE (n)	39.1% (9)	30.8% (8)
Serious TEAE	0	0
Drug-Related Serious TEAE	0	0
TEAE Leading to Treatment Discontinuation	0	0
Drug-Related TEAE Leading to Treatment Discontinuation	0	0
Serious TEAE Leading to Treatment Discontinuation	0	0
Drug-Related Serious TEAE Leading to Treatment Discontinuation	0	0
TEAE Leading to Death	0	0

AE = adverse event
TEAE = treatment emergent adverse event

Vixarelimab was Well-Tolerated in Prurigo Nodularis Phase 2a Study

System Organ Class Preferred Term	Vixarelimab (n=23)	Placebo (n=26)
Infections and Infestations (n)	30.4% (7)	46.2% (12)
Upper Respiratory Tract Infection (n)	17.4% (4)	3.8% (1)
Nasopharyngitis (n)	4.3% (1)	7.7% (2)
Gastroenteritis Viral (n)	4.3% (1)	0
Influenza (n)	4.3% (1)	0
Postoperative Wound Infection (n)	4.3% (1)	0
Subcutaneous Abscess (n)	4.3% (1)	0
Urinary Tract Infection (n)	0	11.5% (3)
Bronchitis (n)	0	3.8% (1)
Cellulitis (n)	0	3.8% (1)
Eczema Impetiginous (n)	0	3.8% (1)
Herpes Simplex (n)	0	3.8% (1)
Otis Media (n)	0	3.8% (1)
Skin Infection (n)	0	3.8% (1)
Tooth Abscess (n)	0	3.8% (1)

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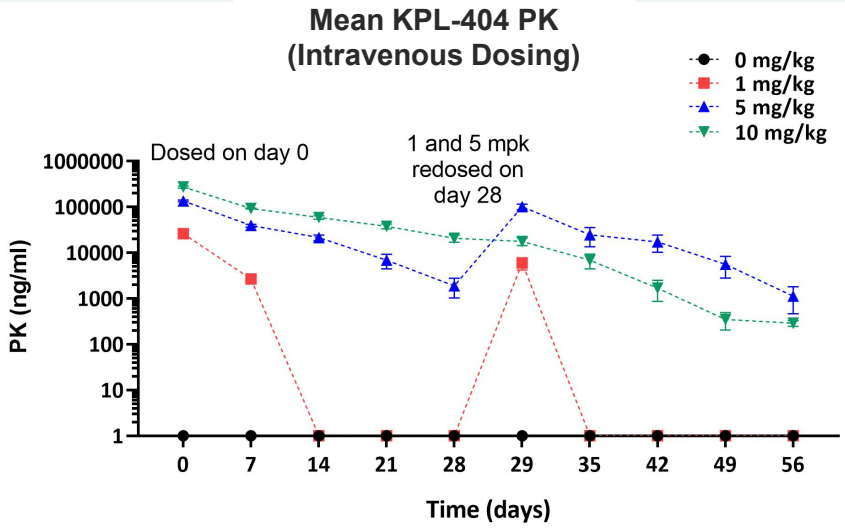
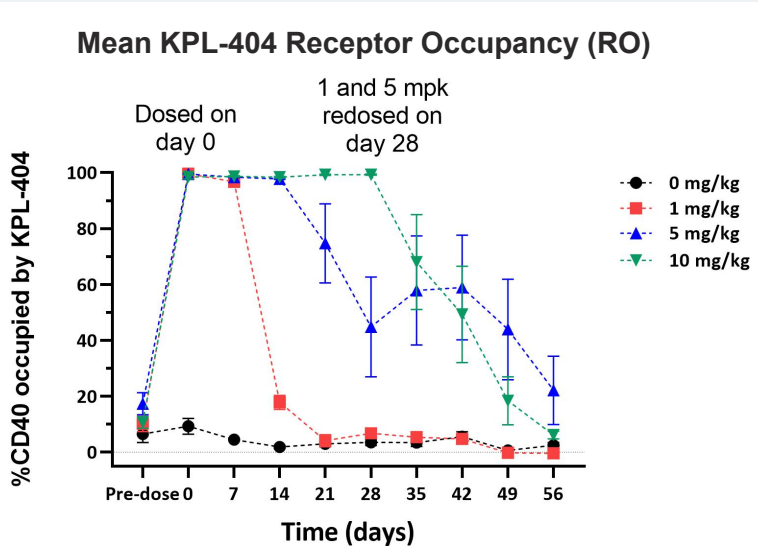
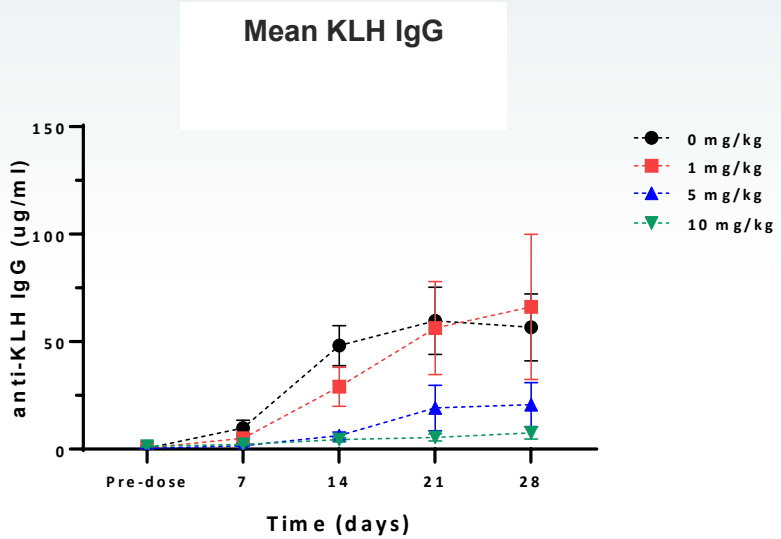
Appendix KPL-404

KPL-404 Showed Encouraging Results in a Non-Human Primate Model of TDAR







Showed linear pharmacokinetic profile with low variability between non-human primate subjects (n=7)

KPL-404 achieved 100% receptor occupancy for 2 weeks in all animals at 5mg/kg and 4 weeks in all animals at 10mg/kg

Complete suppression of primary T-cell dependent antigen response correlated with 100% receptor occupancy

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Source = 1) Poster presentation at the Keystone Symposia: Antibodies as Drugs: New Horizons in the Therapeutic Use of Engineered Antibodies: KPL-404, a CD40 antagonist, blocked antigen-specific antibody responses in an in vivo NHP model and demonstrated strong PK/PD correlation; TDAR = T-cell dependent antibody response; KLH = keyhole limpet hemocyanin

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Corporate Presentation

AUGUST 2021