Corporate Presentation

MAY 2023

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 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; financial guidance; third-party collaborations and licensing; 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 realize value from our licensing and collaboration arrangements; 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 any of our product candidates or to require additional data or trials to support any such approval or authorization; delays, difficulty or inability to successfully execute on our commercial strategy for ARCALYST; potential changes in our strategy, clinical trial priority, operating plan, business development strategy or funding requirements; raw materials, important ancillary product and drug substance and/or drug product shortages; substantial new or existing competition; risks related to the ongoing war in Ukraine; risks arising from political and economic instability; 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.

Portfolio of Immune-Modulating Assets

Program	Target	Preclinical	Phase 1	Phase 2	Phase 3	Commercial
CARDIOVASCULAR FRANCHISE						
ARCALYST® (rilonacept)[1,2] IL-1α & IL-1β	*Recurrent Pericarditis*					
Mavrilimumab[3] GM-CSFRα	*Evaluating Development in Rare Cardiovascular Diseases*					
AUTOIMMUNE FRANCHISE						
KPL-404 CD40/CD154	*Rheumatoid Arthritis*					

Program	Licensee	Exclusive Licensed Territory
OUT-LICENSING AGREEMENTS		
ARCALYST® (rilonacept)[1,2] IL-1α & IL-1β	*Huadong Medicine*	*Asia Pacific Region, Excluding Japan*
Mavrilimumab[3] GM-CSFRα	*Huadong Medicine*	*Asia Pacific Region, Excluding Japan*
Vixarelimab OSMRβ	*Roche and Genentech*	*Worldwide*

1. Approved in the U.S.; ARCALYST is also approved for cryopyrin-associated periodic syndromes (CAPS) and deficiency of the interleukin-1 receptor antagonist (DIRA); 2. The FDA granted Breakthrough Therapy designation to ARCALYST for recurrent pericarditis in 2019; the FDA granted Orphan Drug exclusivity to ARCALYST in March 2021 for the treatment of recurrent pericarditis and reduction in risk of recurrence in adults and pediatric patients 12 years and older. The European Commission granted Orphan Drug designation to ARCALYST for the treatment of idiopathic pericarditis in 2021; 3. Phase 2 clinical trials of mavrilimumab in rheumatoid arthritis and giant cell arteritis achieved their primary and secondary endpoints with statistical significance;
IL-1α = interleukin-1α; IL-1β = interleukin-1β; GM-CSFRα = granulocyte macrophage colony stimulating factor receptor alpha; OSMRβ = oncostatin M receptor beta

KINIKSA

Building Blocks for Value Creation in 2023 and Beyond

Kiniksa is an Emerging Leader in the Development of **Immune-Modulating Therapies**

Cardiovascular Franchise
(ARCALYST/ Mavrilimumab)
+
Autoimmune Franchise
(KPL-404)

Commercial Asset Delivering Strong Growth Today

- Expected ARCALYST net product revenue of **$200-$215M** in 2023, representing ~69% growth at the midpoint
- **Significant upside** remains with only 5% penetration of target recurrent pericarditis population as of YE22

Pipeline Delivering for the Future

- **KPL-404** is a potentially best-in-class asset; now in Phase 2 proof-of-concept study
- Pursuing collaborative study agreements for **mavrilimumab** in rare cardiovascular diseases

Strong Financial Position to Support Growth

- **$187.5M Q123 cash position**
- **Cash runway into at least 2026** supported by profitable ARCALYST collaboration, collaboration revenue from our out-license agreements, and financial discipline

Innovative Business Development Execution to Optimize Portfolio

- Established track record of executing strategic transactions
- Targeting differentiated science to **maximize portfolio value**

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Track Record of Execution Positions Kiniksa for Continued Success

Kiniksa Continues to Utilize Business Development Expertise to Create Value

- **Acquired four clinical programs with differentiated mechanisms** through **innovative transactions** and **advanced** to mid-/late-stage clinical trials
- Executed **strategic partnership** with Huadong Medicine to bring in **non-dilutive capital** and help accelerate development and commercialization efforts of ARCALYST and mavrilimumab
- Entered **license agreement** with Genentech for vixarelimab to bring in significant non-dilutive capital

Kiniksa is Building a Cardiovascular Franchise

- **ARCALYST:** Within 3.5 years conducted Phase 2 and Phase 3 studies, received breakthrough therapy designation and orphan drug designation, and received FDA approval in March 2021 for **first and only** approved therapy for recurrent pericarditis
- **Mavrilimumab**: Generated substantial clinical data on role of GM-CSF mechanism across **three clinical trials and** now pursuing collaborative study agreements in **rare cardiovascular diseases**

Kiniksa is Building an Autoimmune Franchise

- **KPL-404**: Took pre-clinical asset into Phase 1; data support testing of longer-term subcutaneous administration in patients with autoimmune disease; now in multiple-ascending-dose Phase 2 study

Kiniksa is in a Strong Financial Position to Support Growth

- **Well-capitalized with $187.5M** of cash[1]
- Profitable ARCALYST collaboration, non-dilutive capital from strategic out-licensing transactions, and continued financial discipline provide **cash runway into at least 2026**

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1) As of March 31, 2023

Partnership with Huadong Medicine Gives Kiniksa Opportunity to Expand Footprint into Asia Pacific Region (Excluding Japan)

In February 2022, Kiniksa announced a strategic collaboration with Huadong to develop and commercialize ARCALYST and mavrilimumab in Greater China, South Korea, Australia and 18 other countries, excluding Japan

Kiniksa received a $22M upfront payment and is eligible to receive up to approximately $640M in specified development, regulatory and sales-based milestone along with tiered royalty payments

Collaboration provided non-dilutive capital, cost-sharing, and additional resources to help accelerate development and commercialization efforts

License Agreement with Roche Genentech for Global Rights to Develop and Commercialize Vixarelimab

Kiniksa has received $100 million in upfront and near-term payments:

- $80 million, which was received following the transaction's closing in Q3 2023
- $20 million, which was received following Kiniksa's last delivery of certain drug supplies to Genentech in Q1 2023

Kiniksa is eligible to receive up to approximately $600 million in certain clinical, regulatory, and sales-based milestones, before fulfilling upstream financial obligations

Kiniksa is also eligible to receive royalties on annual net sales ranging from low-double digits to mid-teens, before fulfilling upstream financial obligations

$100 million in non-dilutive proceeds from the transaction to help grow cardiovascular franchise and build autoimmune franchise

KINIKSA

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 exclusivity for treatment of and reduction in risk of recurrence of recurrent pericarditis; European Commission Orphan Drug designation in idiopathic pericarditis

STATUS: FDA-Approved

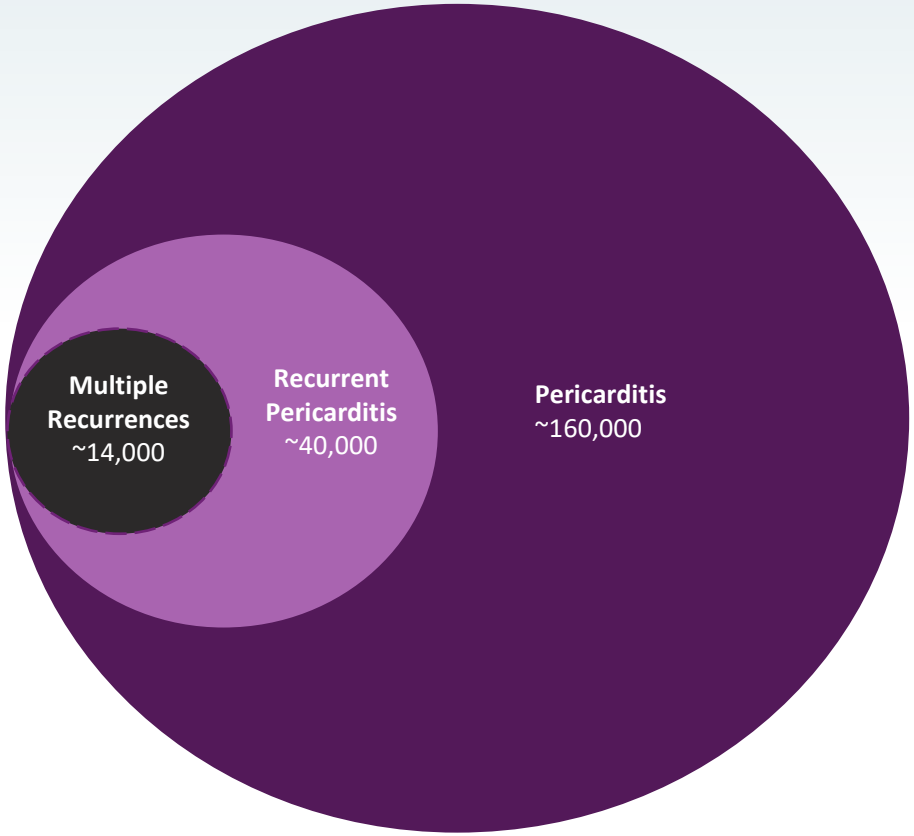
ECONOMICS: 50/50 split on profit and third-party proceeds

RIGHTS: Kiniksa has worldwide rights[3] (excluding MENA) for all indications outside those in oncology and local administration to the eye or ear

KINIKSA

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; 3) Kiniksa granted Huadong Medicine exclusive rights in the Asia Pacific Region, excluding Japan;
IL-1α = interleukin-1α ; IL-1β = interleukin-1β; MENA = Middle East North Africa

Pericarditis Epidemiology



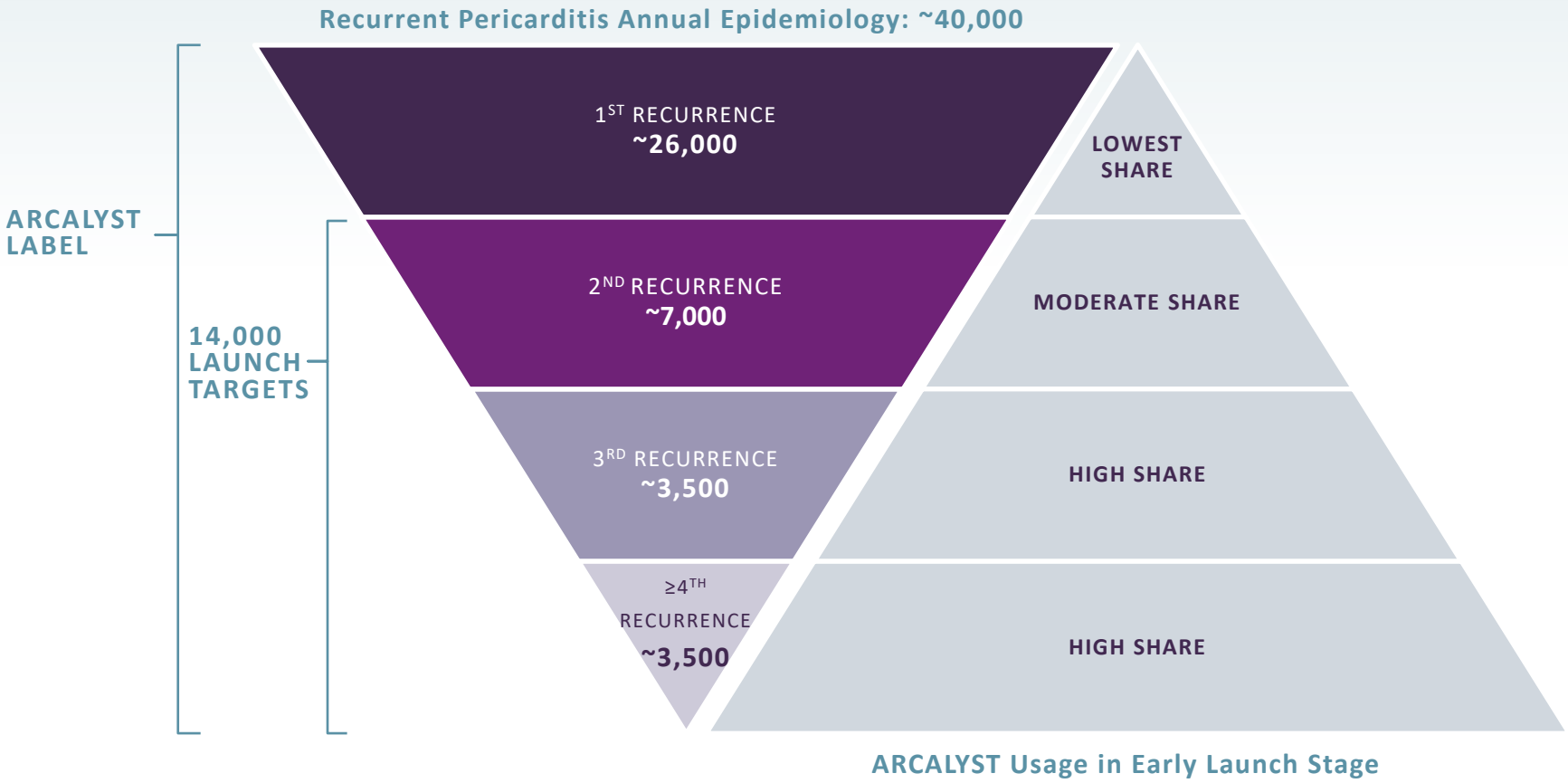
All figures annual period prevalence

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

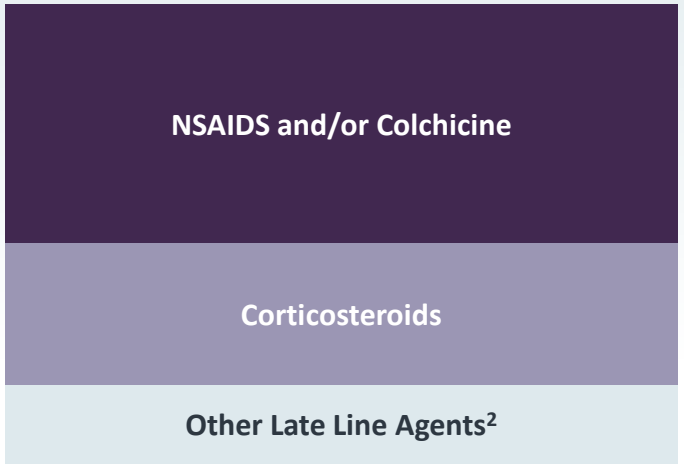
- **~ 160,000:** Epidemiological analysis using large national surveillance databases to calculate the pooled annualized prevalence of pericarditis ***(Basis for Orphan Drug Designation approval)[2]***
- **~40,000:** Up to 30% experience at least one recurrence; some recur over multiple years[6,7]
- **~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) Kiniksa Pharmaceuticals data on file.

Early Treated Patients Are Closely Associated to the Launch Target Population, While Prescribers Can Utilize ARCALYST Earlier in the Disease



ARCALYST PATIENTS BY PRIOR PRODUCT[1]



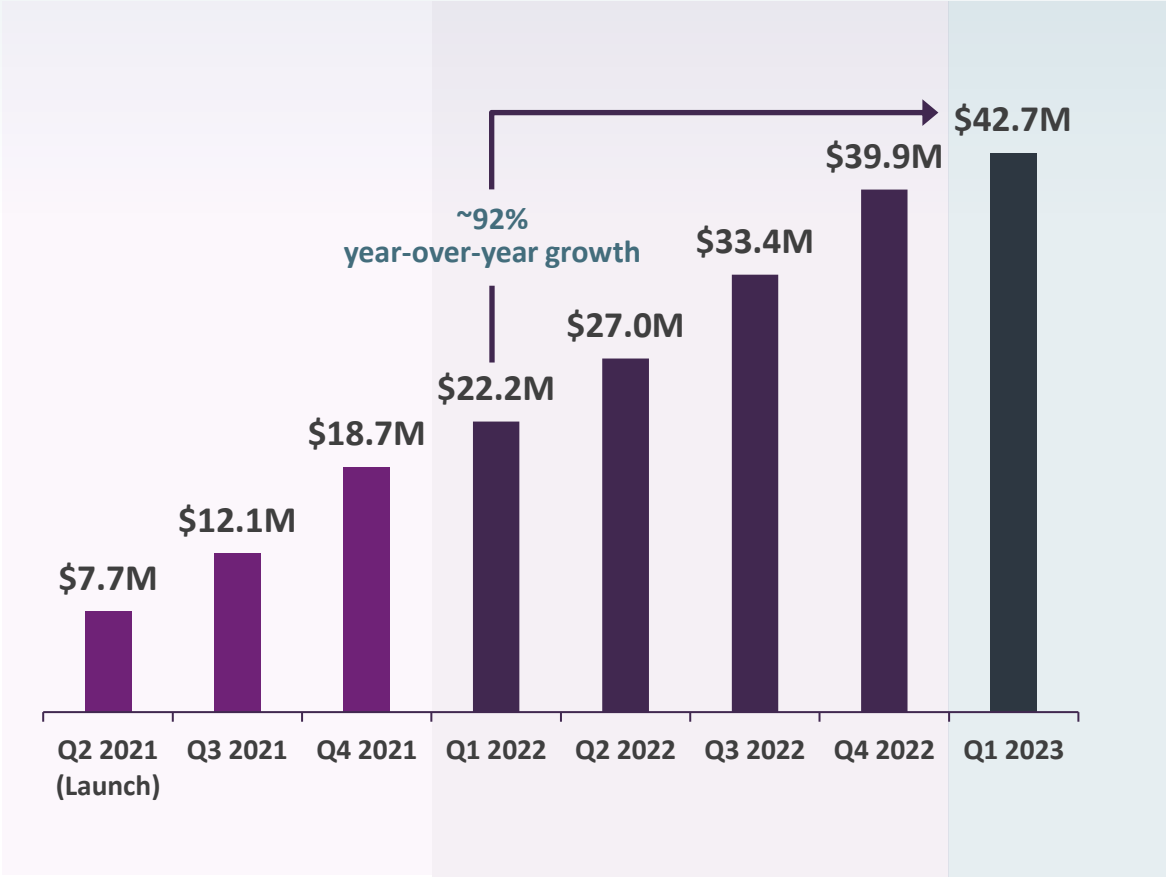
ARCALYST PATIENTS BY FLARE STATUS @ INITIATION[1]

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

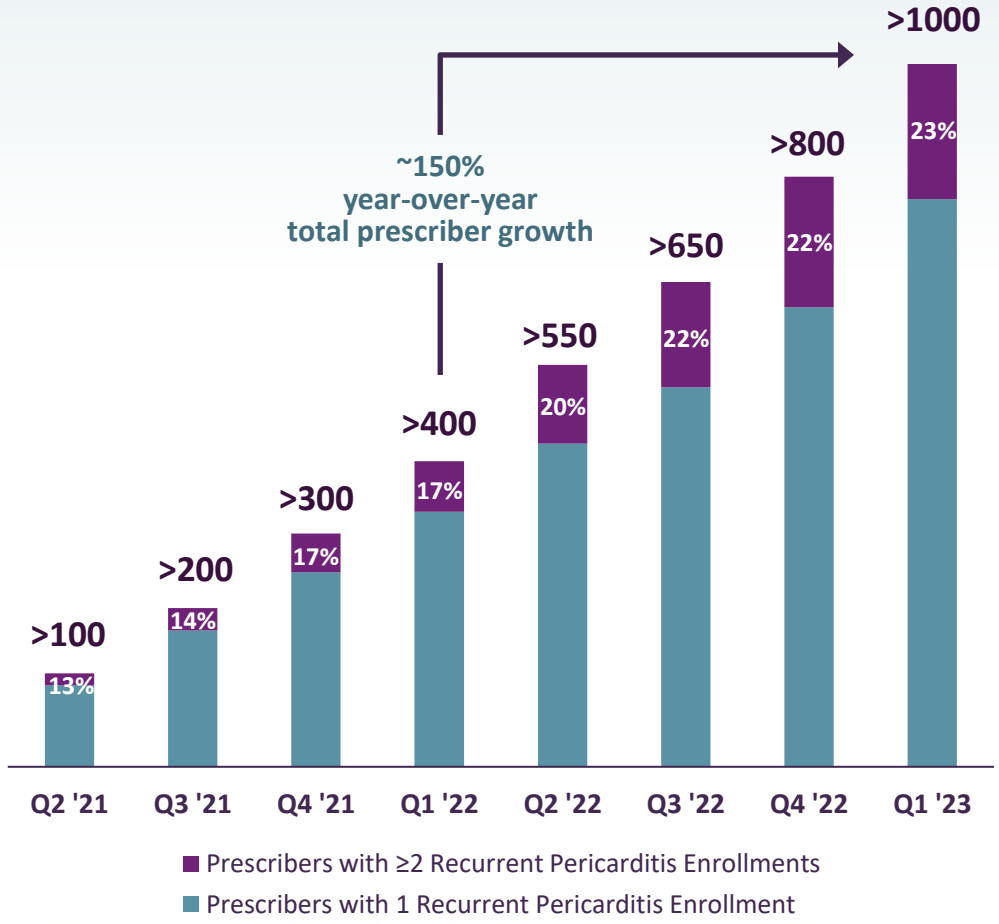
Source: 1) Kiniksa Pharmaceuticals data on file 2023. 2) Other late line agents include anakinra, azathioprine, methotrexate

Strong Q1 2023 Revenue Growth Driven by Robust Commercial Execution

Total Net Revenue Growth per Quarter



Total and Repeat Prescriber Growth per Quarter



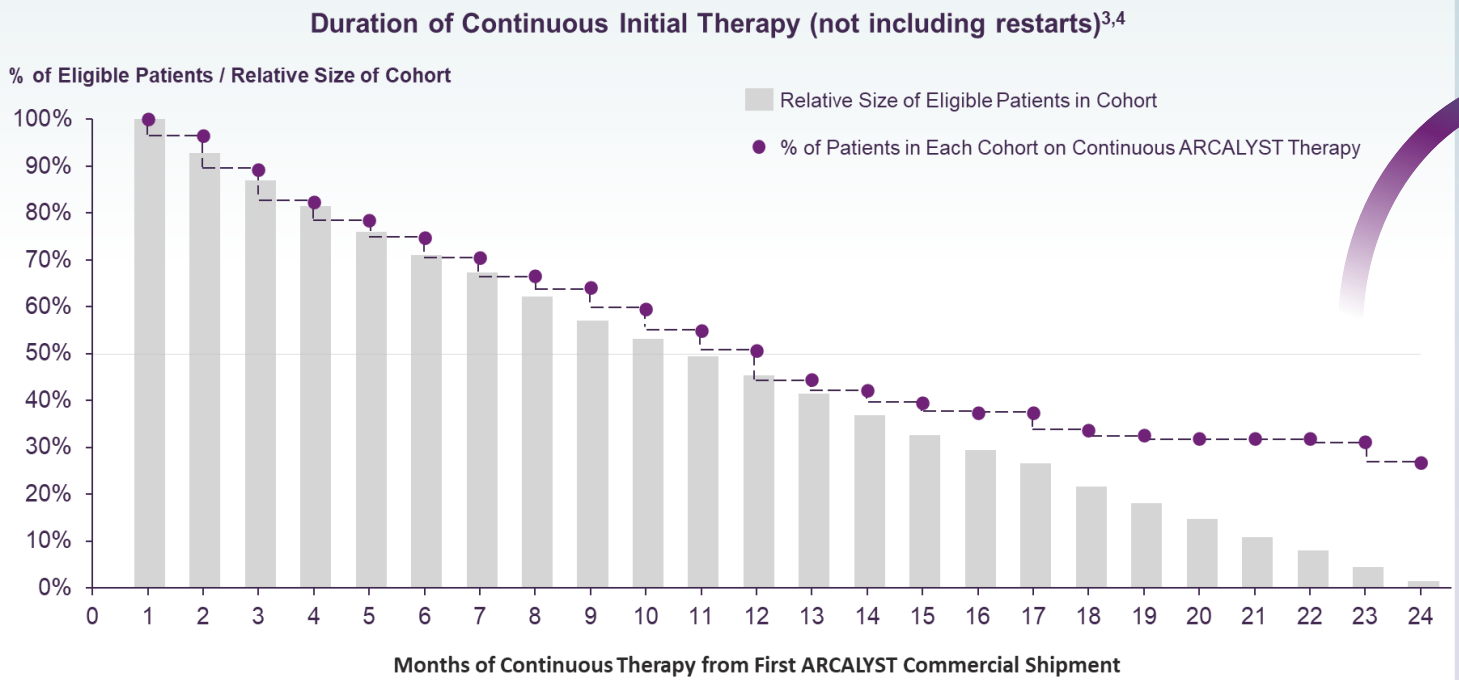
Average Total Duration of ARCALYST Therapy Increased to ~20 Months[1]

Advancing the treatment paradigm to treat continuously throughout disease duration (median 3 years[2])

Average ***Initial*** Duration of Therapy

~14 Months[1]

(Increased from ~12 months)



~45%

Of Patients Restart Therapy Following Initial Discontinuation

(Typically, within ~8 weeks)

~20 Months Average ***Total*** Duration of Therapy After Accounting for Patient Restarts

1) As of Q1 2023; 2) Lin D, Laliberté F, Majeski C, et al. Disease and economic burden associated with recurrent pericarditis in a privately insured United States population. Adv Ther. 2021;38(10):5127-5143. doi:10.1007/s12325-021-01868-7; 3) Initial continuous therapy is determined to have ended if greater than 28 days elapses beyond the exhaustion date of a patient's most recent days supplied without an observed refill of ARCALYST; 4) Patients restarting after an initial therapy lapse as of 3/31/2023 (patient restarts are not included in the chart)

Field Evolution to Create Greater Reach and Frequency with Top Tier Doctors as well as Reach a Broader Set of Physicians

Field Launch Strategy

LEAN TEAM WITH FOCUSED & TARGETED EXECUTION

~30 Specialty Cardiology Reps

Initial launch focus on top tier accounts:

~3,300 individual prescribers

Strategy Evolution

EXPANDED TEAM CREATING GREATER REACH AND FREQUENCY

~50 Specialty Cardiology Reps

Increased focus within top tier accounts as well as expanded reach at mid tier prescribers, reaching:

~6,000 top and mid tier prescribers

Expanding Breadth & Depth of ARCALYST Use for Recurrent Pericarditis

Expanding Base of New Prescribers

- Salesforce Expansion
- Disease Education
- Pericardial Disease Networks
- Brand Awareness
- Evidence Generation
- Kiniksa OneConnect™ Program

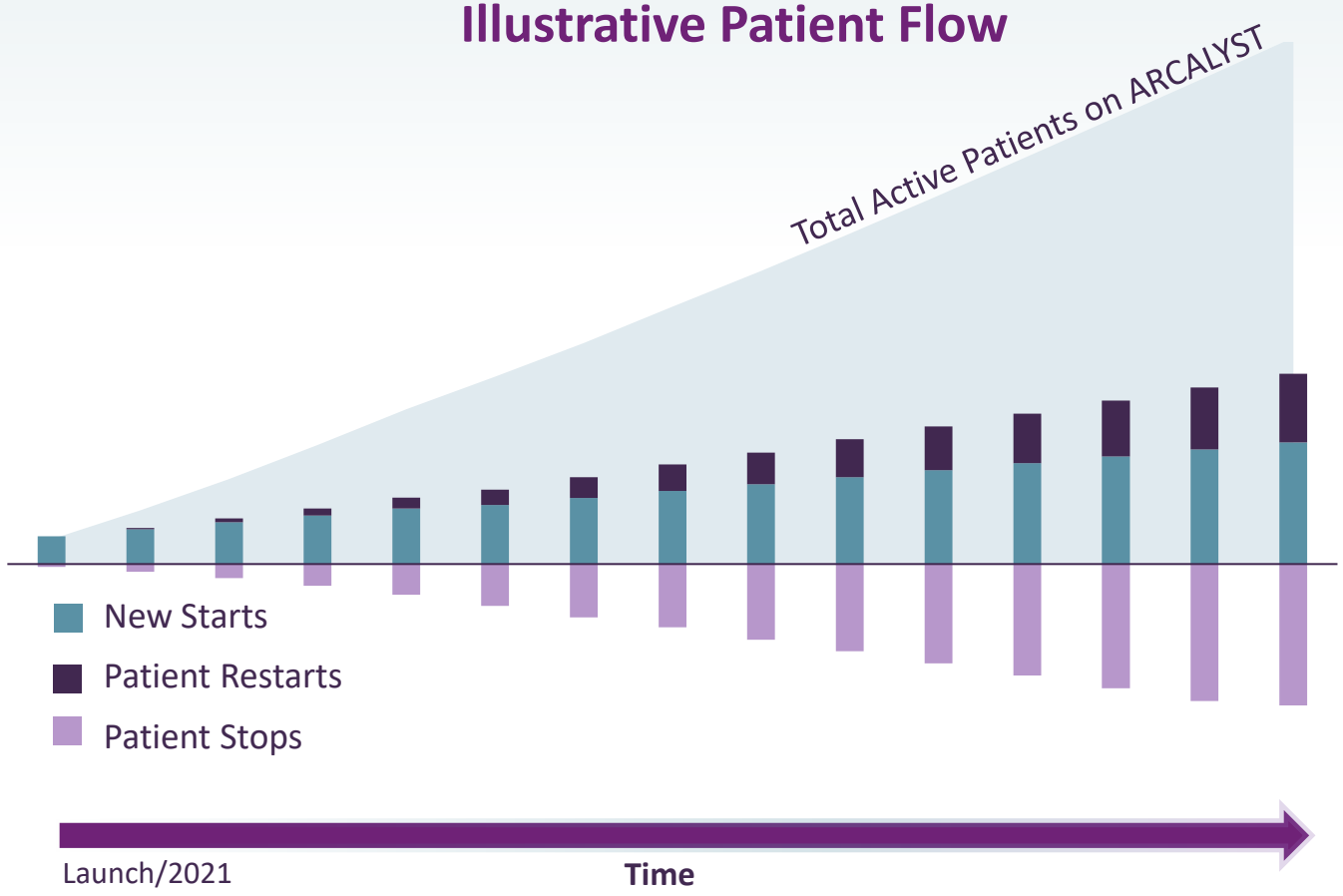
Driving Growth with Existing Prescribers

Growth in Total Patients on Therapy Driven by Continued Acceleration in New to Brand and Restart Patients, Accounting for Increasing Patient Stops Over Time

ARCALYST Patient Flow

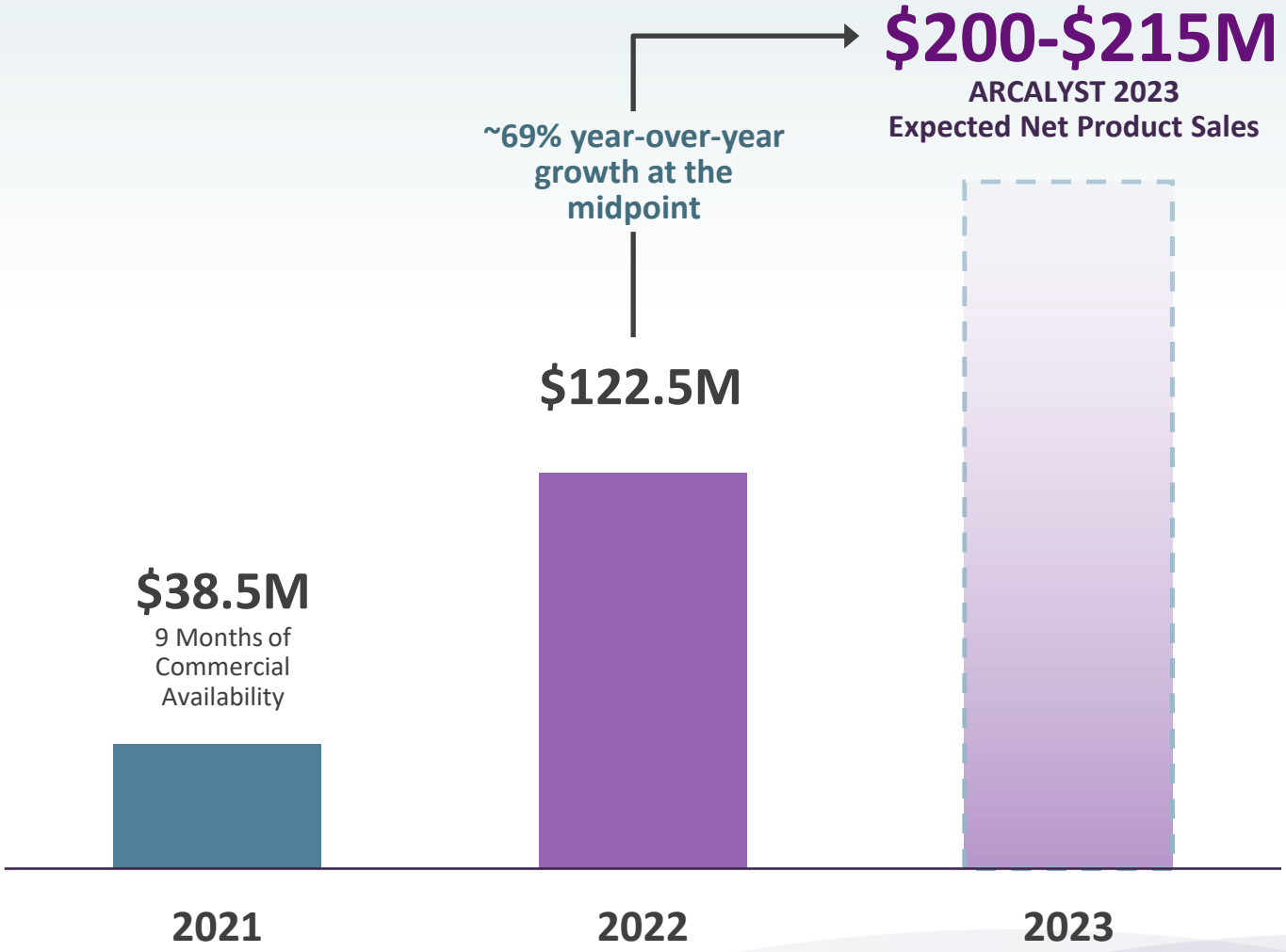
New to Brand Patients	Strong sequential growth: >1000 unique prescribers; ~23% of which are repeat prescribers
−	
Patient Stops	Increases over time as base of active ARCALYST patients grows with Initial Starts and Restarts
+	
Patient Restarts	Increases over time as patient stops increase; currently ~45% after ~8 weeks
=	
Active Patients	Increases over time driven by new-to-brand and restart growth; as of Q4 2022, 5% of 14K multiple recurrence target patient population

Illustrative Patient Flow



2023 ARCALYST Net Product Sales Guidance Increased

Higher expectation driven by increased prescriber adoption, patient enrollment, and duration of therapy



Pricing, Access and Distribution Considerations

Pricing

- ARCALYST list price of $21,425 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; eligible patients are able to get ARCALYST for a copay of $10

Access

- Kiniksa's goal is to maintain rapid and broad access to ARCALYST for patients with Recurrent Pericarditis, CAPS, and DIRA
- Payer mix for ARCALYST is largely **commercial (~70%), Medicare (~20%), Medicaid (~10%)**
- Payer engagement has increased awareness of recurrent pericarditis and the differentiated value of ARCALYST
- The **Kiniksa OneConnect™** program is a personalized treatment support program for patients prescribed ARCALYST

Distribution

- ARCALYST is distributed **through a closed network of designated 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

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

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 MENA, 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.
- Kiniksa evenly splits profits on ARCALYST sales and licensing proceeds with Regeneron

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) Cost of goods sold related to product sales and relevant overhead; amortization of ARCALYST commercial milestone excluded
*Kiniksa exclusively licensed rights for the development and commercialization of ARCALYST in APAC (ex-Japan) to Huadong Medicine
CAPS = Cryopyrin-Associated Periodic Syndromes; DIRA = Deficiency of the Interleukin-1 Receptor Antagonist; MENA =Middle East and North Africa; APAC = Asia Pacific Region

KPL-404

MONOCLONAL ANTIBODY INHIBITOR INTERACTION BETWEEN CD40 AND CD154

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 2 proof-of-concept study of chronic subcutaneous administration ongoing; data expected in 1H24

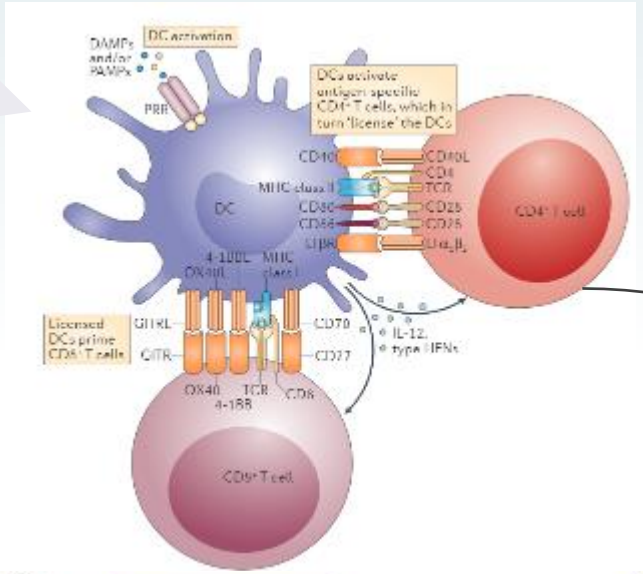
ECONOMICS: Negligible clinical and regulatory milestones and royalty on annual net sales

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; RO = receptor occupancy; TDAR = T-cell Dependent Antibody Response

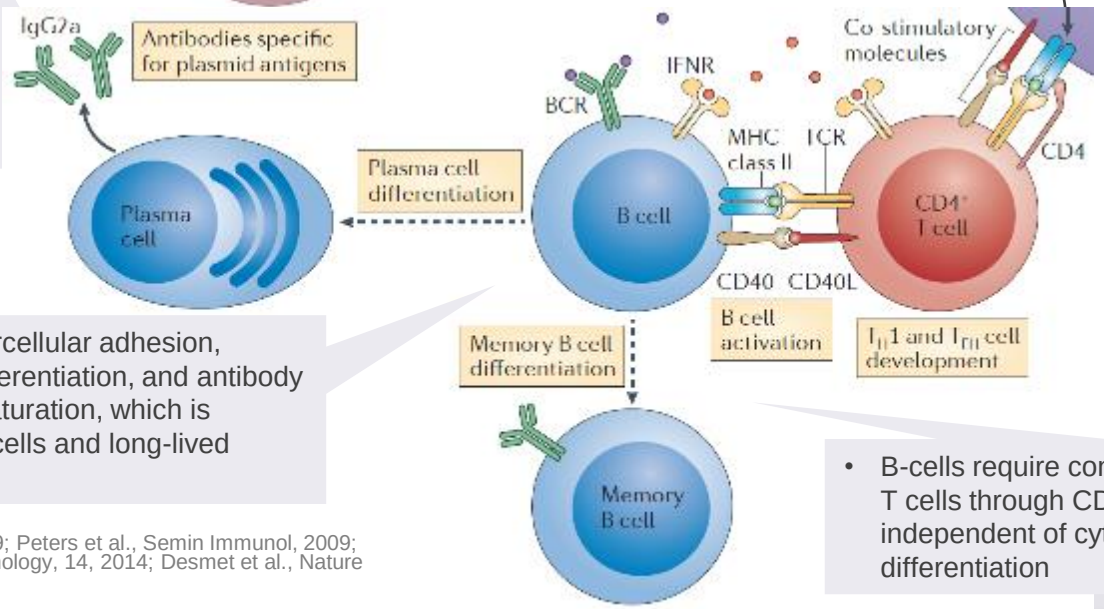
CD40/CD154 is an Essential Immune Pathway for T-Cell Priming and T-Cell Dependent B-Cell Responses

- 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

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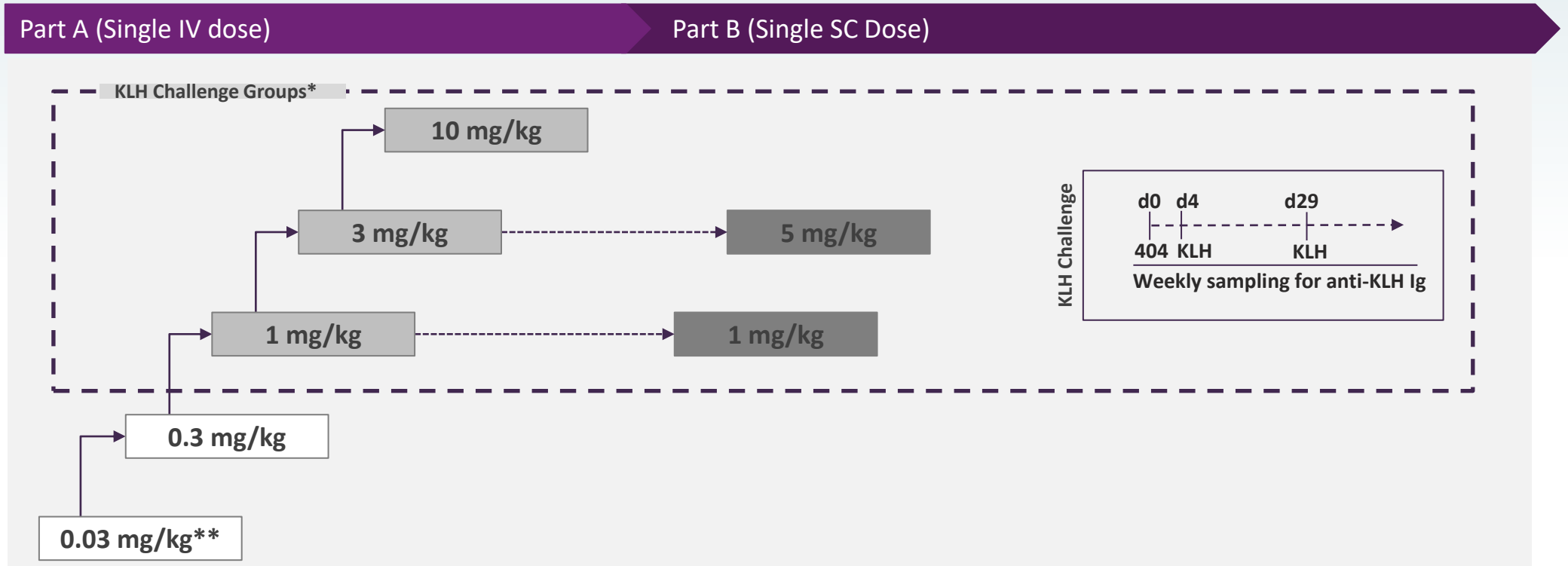
Sources: Elgueta et al., Immunol Rev, 2009; Peters et al., Semin Immunol, 2009; Kambayashi et al., Nature Reviews: Immunology, 14, 2014; Desmet et al., Nature Reviews: Immunology, 12, 2012

KPL-404 Single-Ascending-Dose Phase 1 Study



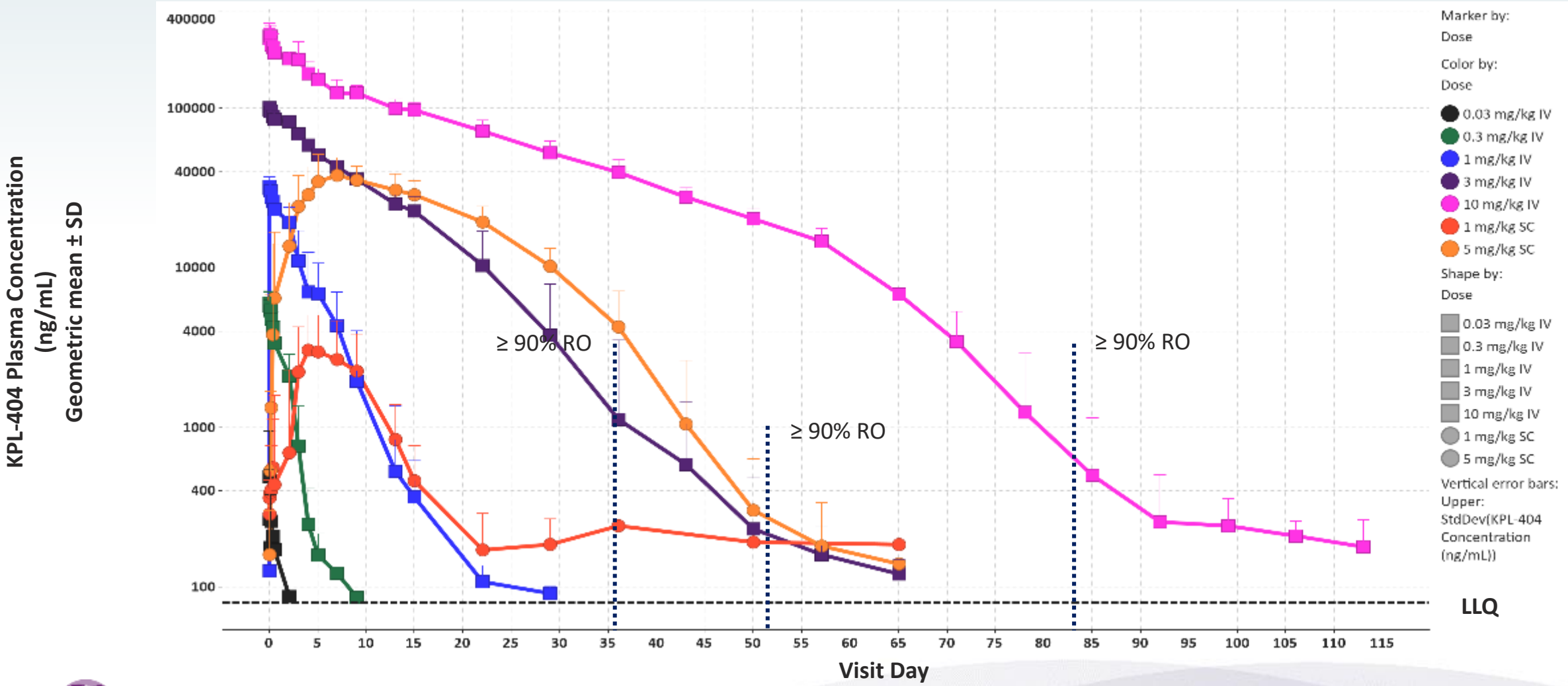
- **Primary endpoints:** Safety and Tolerability
- **Secondary endpoints:** PK and ADA / CD40 RO in blood / Serum anti-KLH Ig levels
- **Exploratory endpoints:** Serum CXCL13 levels

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

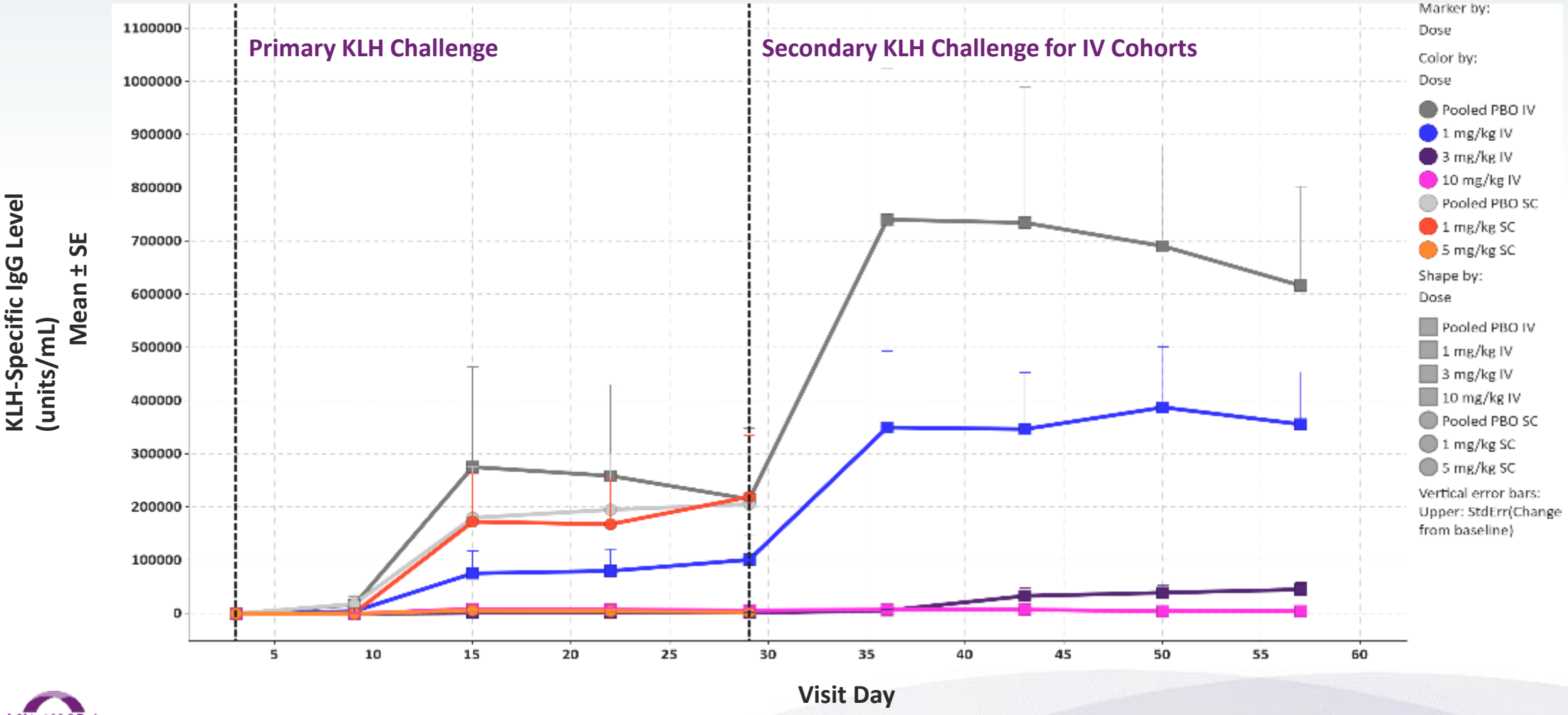
Final Data from KPL-404 Single-Ascending-Dose Phase 1 Study

Pharmacokinetic profiles for KPL-404



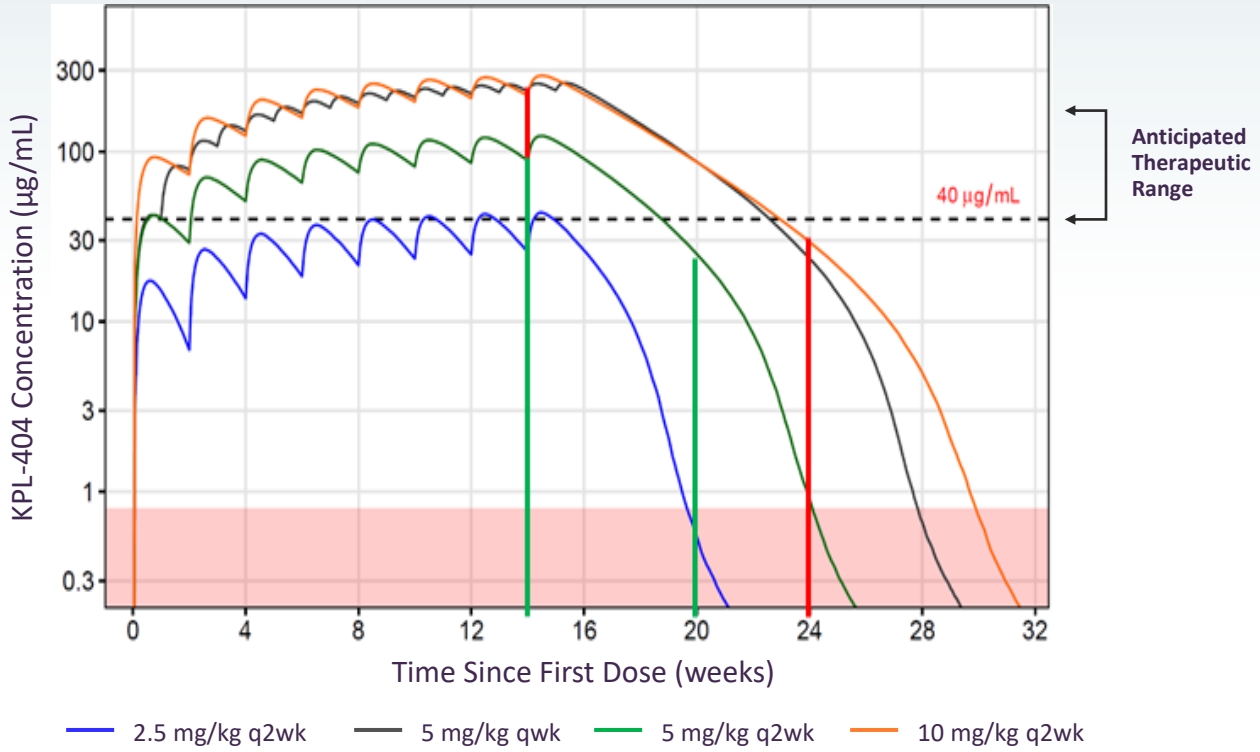
Final Data from KPL-404 Single-Ascending-Dose Phase 1 Study

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



KLH = keyhole limpet hemocyanin

KPL-404 is a Potentially Best-in-Class, Subcutaneously Delivered Monoclonal Antibody Inhibitor of the CD40/CD154 Interaction



- KPL-404 drug product is formulated in a high concentration liquid formulation that enables **subcutaneous-administration**
- KPL-404 non-clinical and clinical data generated to date suggest it is **well positioned against competitors**
- **Kiniksa owns the vast majority of the economics** for KPL-404

PK-modeling and dose simulations for KPL-404 dosing in Phase 2: Data show potential to reach plasma concentrations we believe necessary to see efficacy in the clinic

KPL-404 Phase 2 Trial in Rheumatoid Arthritis

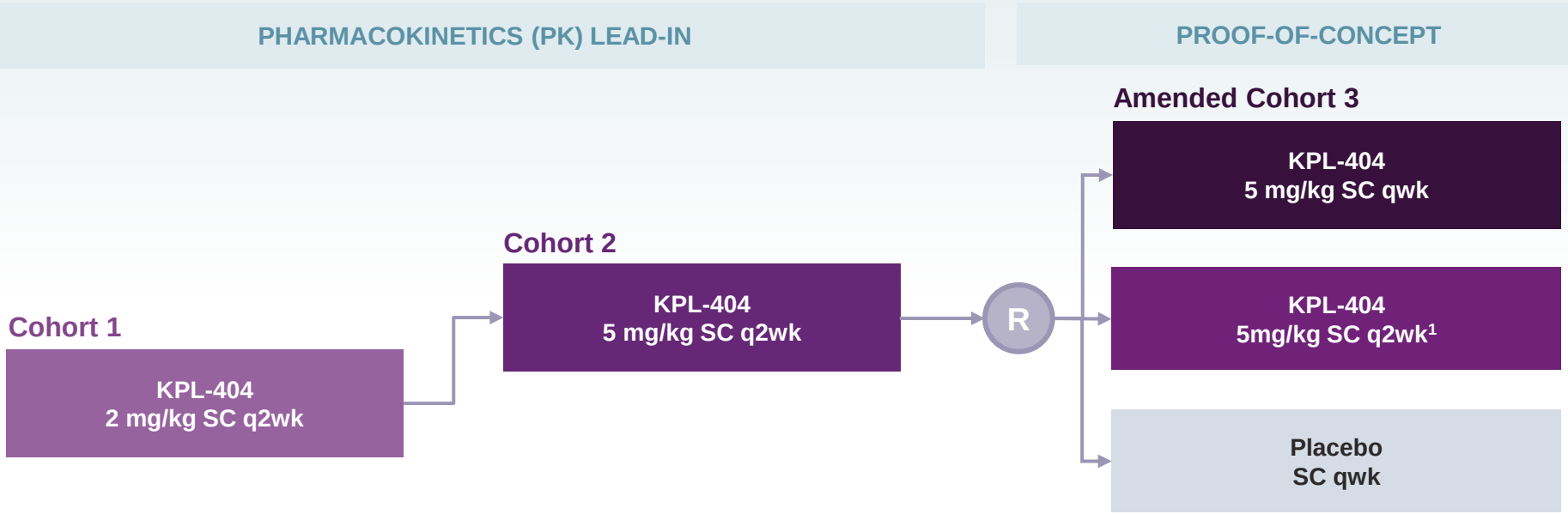
Multiple-ascending-dose study that evaluates PK and safety and then transitions into a parallel dose efficacy portion

PATIENT POPULATION:

- Active RA who have an inadequate response to or are intolerant to a Janus kinase inhibitor (JAKi) or at least one biologic disease-modifying anti-rheumatic drug (bDMARD). Subjects who have failed both bDMARD and JAKi are excluded from the study.

DISEASE CRITERIA:

- Six or more swollen joints and ≥ 6 tender joints at screening and baseline line visits; levels of high sensitivity C-reactive protein ≥ 5 mg/L; seropositivity for serum RF and/or ACPA at screening.



COHORTS 1-2 (PK Lead-In)

- Each cohort will sequentially randomize 8 patients
- Primary Endpoints:
  - Incidence of treatment-emergent adverse events (TEAEs)
  - Pharmacokinetics (C_{max}, $AUC_{(0-t)}$)
- Secondary Endpoint:
  - Change from baseline in DAS28-CRP at Week 12

AMENDED COHORT 3 (Proof of Concept)

- Cohort 3 will randomize up to 75 patients
- Primary Endpoint:
  - Change from baseline in DAS28-CRP at Week 12
- Secondary Endpoints :
  - Incidence of treatment-emergent adverse events (TEAEs)
  - Pharmacokinetics (C_{max}, $AUC_{(0-t)}$)

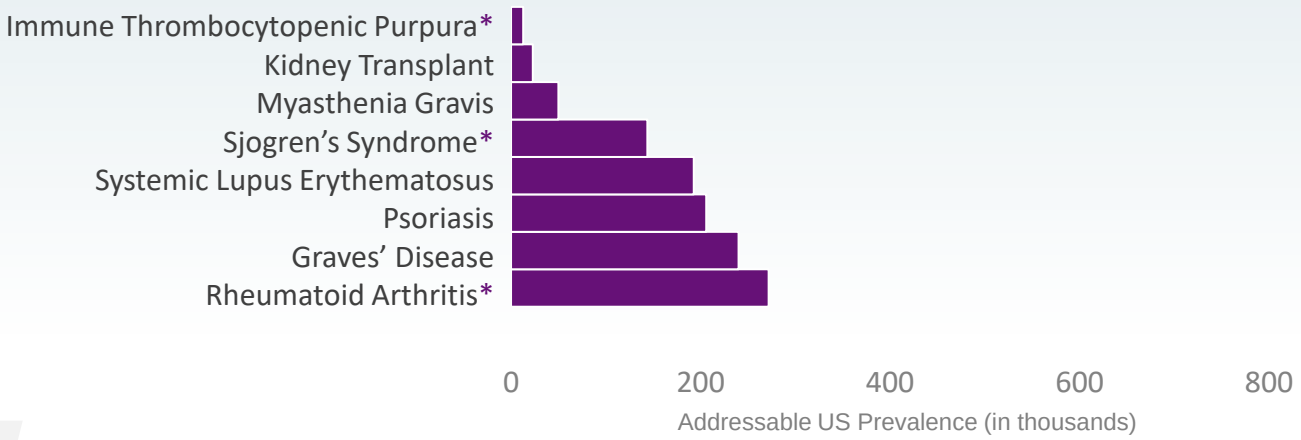
Objectives: Evaluate safety, efficacy, and PD compared with placebo across the estimated therapeutic range and to characterize PK across varying dose levels of KPL-404

1) The 5 mg/kg SC q2wk group will receive weekly administrations of alternating active investigational product and matching blinded placebo
SC = subcutaneous; q2wk = every other week; AUC = Area Under the Curve; RF = Rheumatoid Factor; ACPA = anti-citrullinated protein antibodies, PD = Pharmacodynamics; PK = Pharmacokinetics; R = Randomization

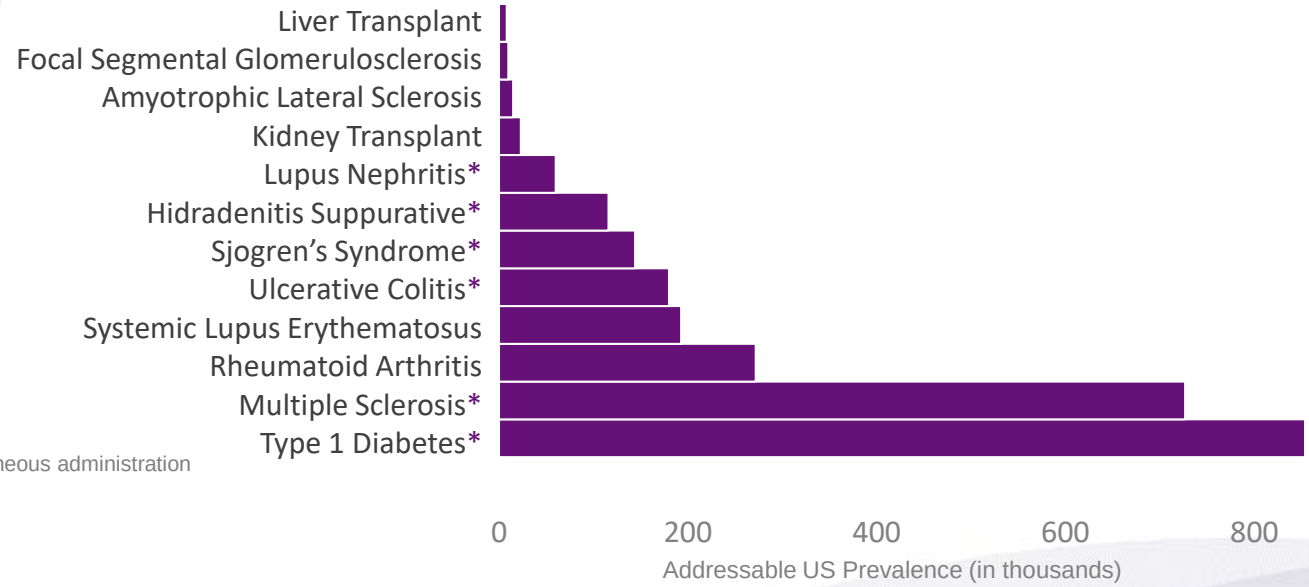
Potential for Evaluation of KPL-404 in a Broad Range of Autoimmune Diseases

CD40/CD154 interaction has been implicated in a number of devastating diseases

Indications with Published Data



Indications with Pending Data & Trials Ongoing



*Indications evaluated with subcutaneous administration

INDICATION SELECTION CRITERIA

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

KINIKSA

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.

Financials
First Quarter 2023

First Quarter 2023 Financial Results

Income Statement	Three Months Ended March 31,	
	2023	2022
Product Revenue	$42.7M	$22.2M
License and Collaboration Revenue	$5.7M	$10.0M
Total Revenue	**$48.3M**	**$32.2M**
Cost of Goods Sold	$7.0M	$4.2M
Collaboration Expenses[1]	$8.3M	$8.3M
Research and Development	$15.2M	$20.8M
Selling, General and Administrative	$29.0M	$22.2M
Total Operating Expenses	**$59.5M**	**$55.5M**
Income Tax Benefit (Provision)	**($2.9M)**	**($1.9M)**
Net Income (Loss)	**($12.3M)**	**($25.2M)**

Collaboration Expenses[1]	Three Months Ended March 31,	
	2023	2022
ARCALYST Net Sales (RP + CAPS + DIRA)	**$42.7M**	**$22.2M**
Cost of Goods Sold Related to Product Sales	($6.8M)	($3.9M)
Commercial, Marketing, Regulatory and Other Expenses	($19.3M)	($13.8M)
ARCALYST Collaboration Operating Profit	**$16.6M**	**$4.5M**
ARCALYST Licensing Proceeds	$0.0M	$12.0M
Collaboration Expenses[1]	**$8.3M**	**$8.3M**

Balance Sheet	March 31, 2023	December 31, 2022
Cash, Cash Equivalents and Short-term Investments	**$187.5M**	**$190.6M**

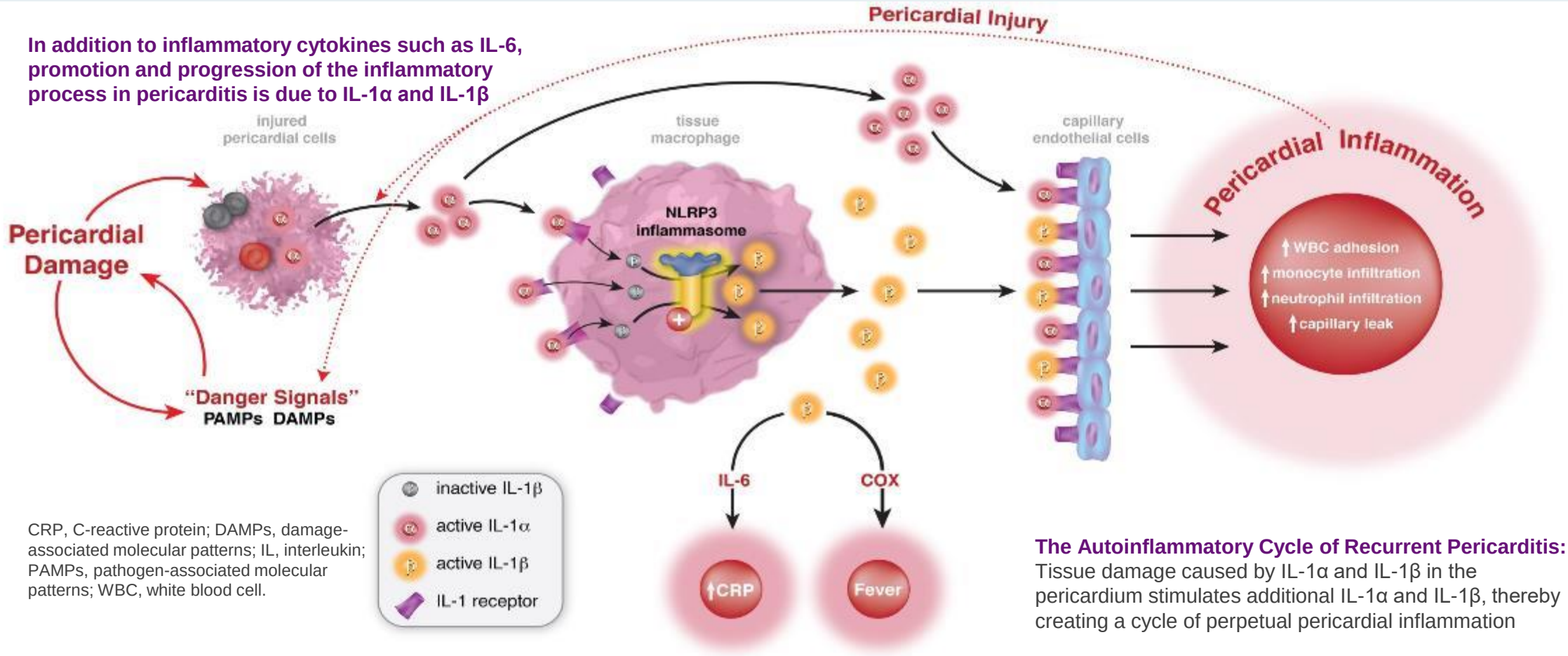
Cash reserves expected to fund current operating plan into at least 2026

1) Subject to the terms of the definitive agreements between Kiniksa and Regeneron; 50% of ARCALYST Collaboration Operating Profit plus 50% of ARCALYST Licensing Proceeds
RP = Recurrent Pericarditis, CAPS = Cryopyrin-Associated Periodic Syndromes, DIRA = Deficiency of Interleukin-1 Receptor Antagonist

Appendix
ARCALYST (rilonacept)

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

In addition to inflammatory cytokines such as IL-6, promotion and progression of the inflammatory process in pericarditis is due to IL-1α and IL-1β



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

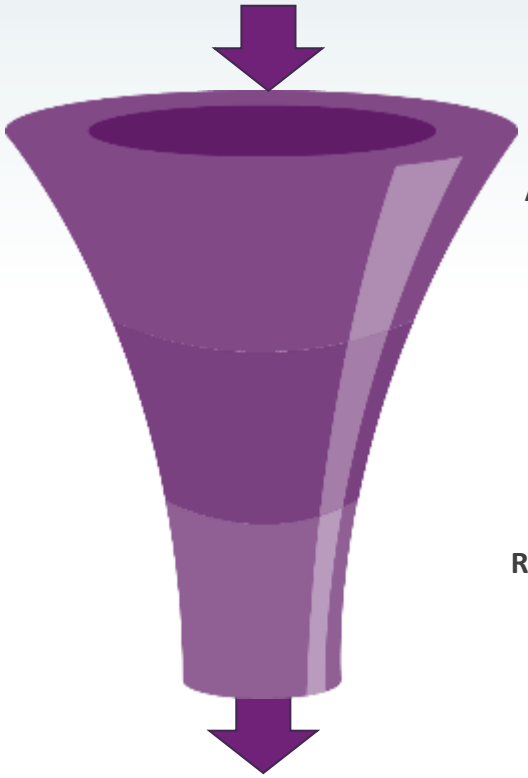
The Autoinflammatory Cycle of Recurrent Pericarditis: Tissue damage caused by IL-1α and IL-1β in the pericardium stimulates additional IL-1α and IL-1β, thereby creating a cycle of perpetual pericardial inflammation

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

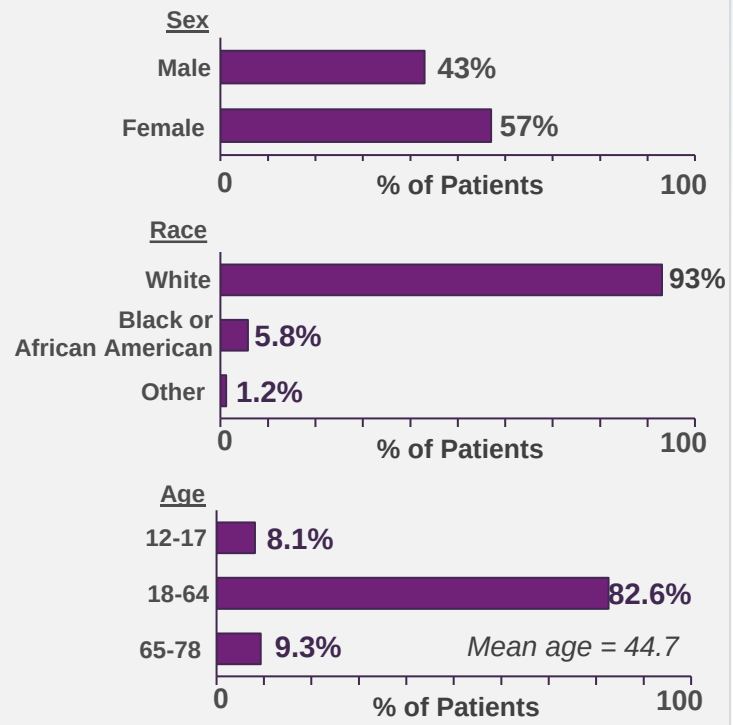
Addressable Opportunity in U.S.

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

Baseline Demographics and Clinical Characteristics

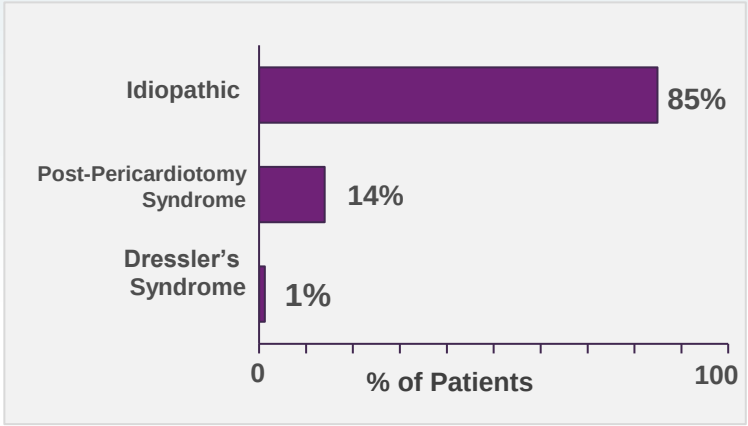
Pivotal Phase 3 Rilonacept Data

Baseline Demographics (n=86)

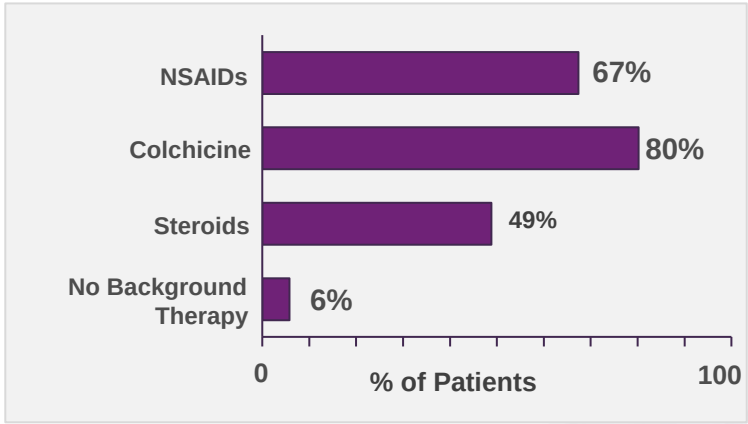


Total Number of Episodes Including Index and Qualifying Episodes	Run-in Period (n=86)
Mean	4.7

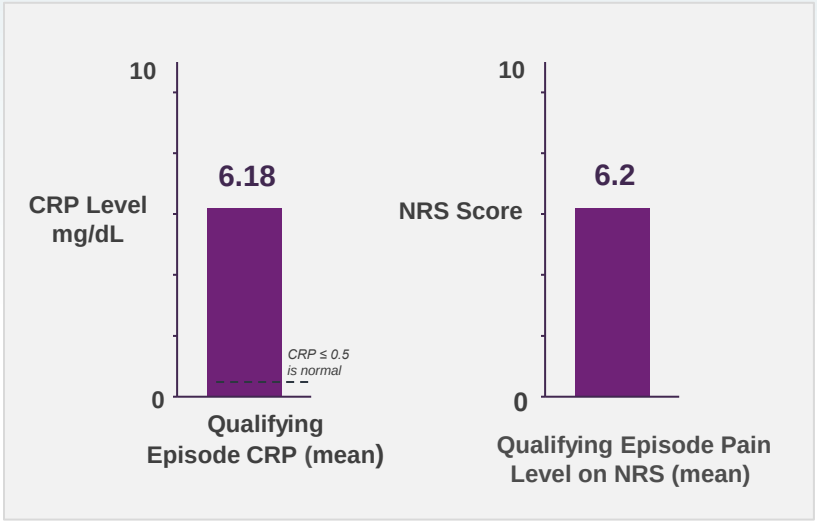
Prior Pericarditis History at Baseline (n=86)



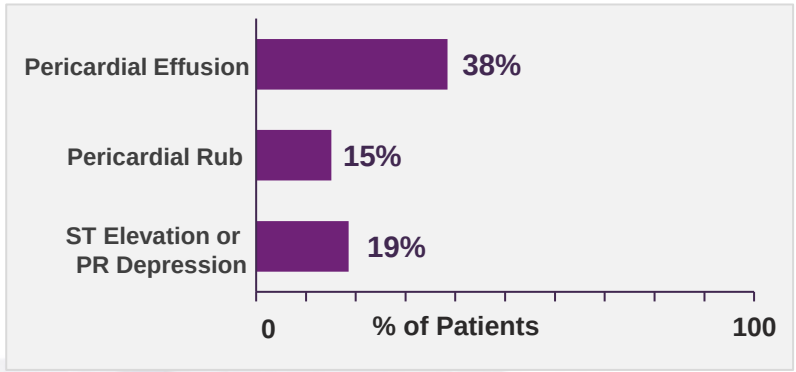
SoC Received at Qualifying Episode (n=86)



Qualifying Episode CRP & NRS (n=86)



Pericarditis Manifestations at Qualifying Episode (n=86)

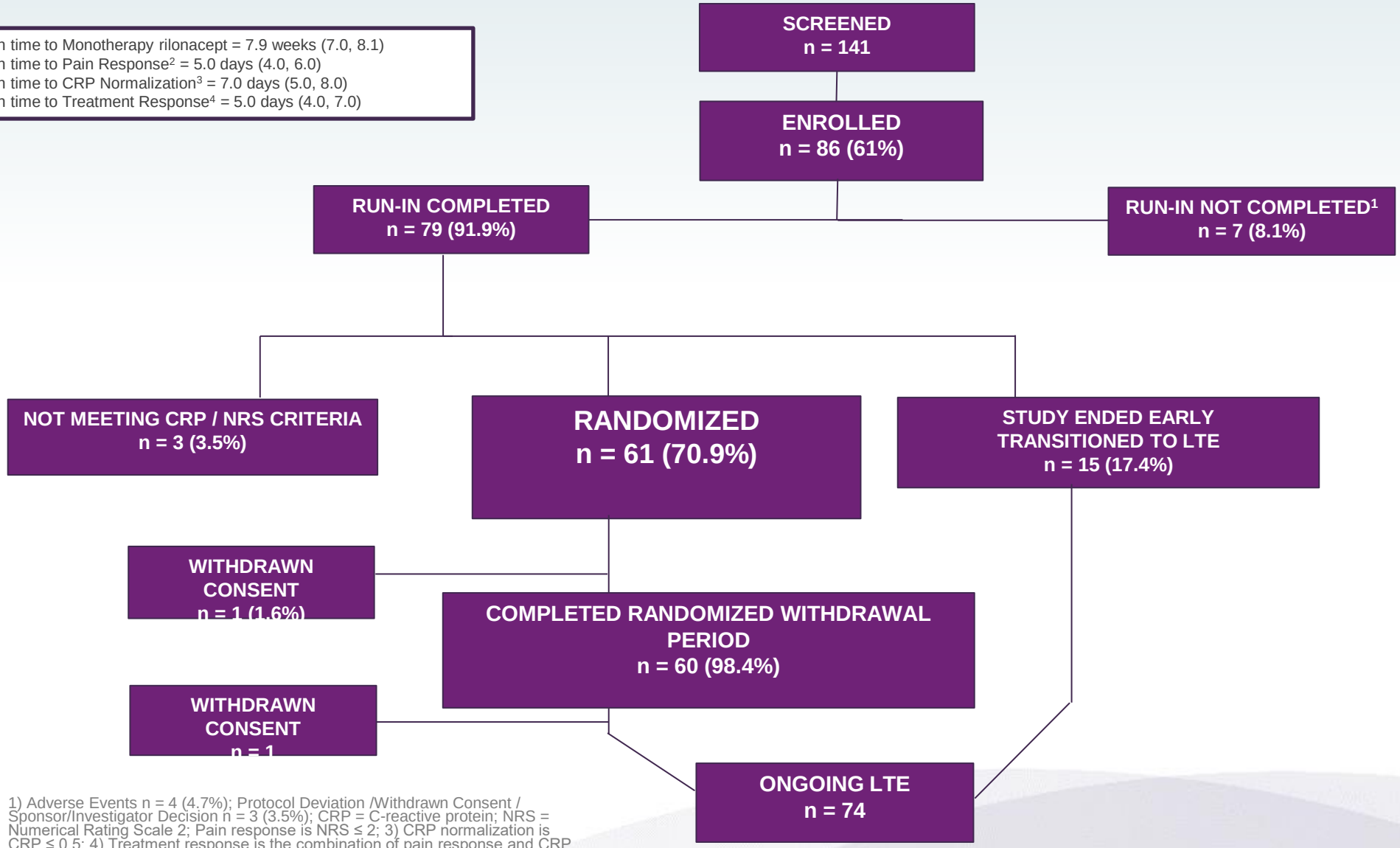


CRP = C-reactive protein; NRS = Numerical Rating Scale; SoC = Standard of Care; NSAIDs = nonsteroidal anti-inflammatory drugs

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

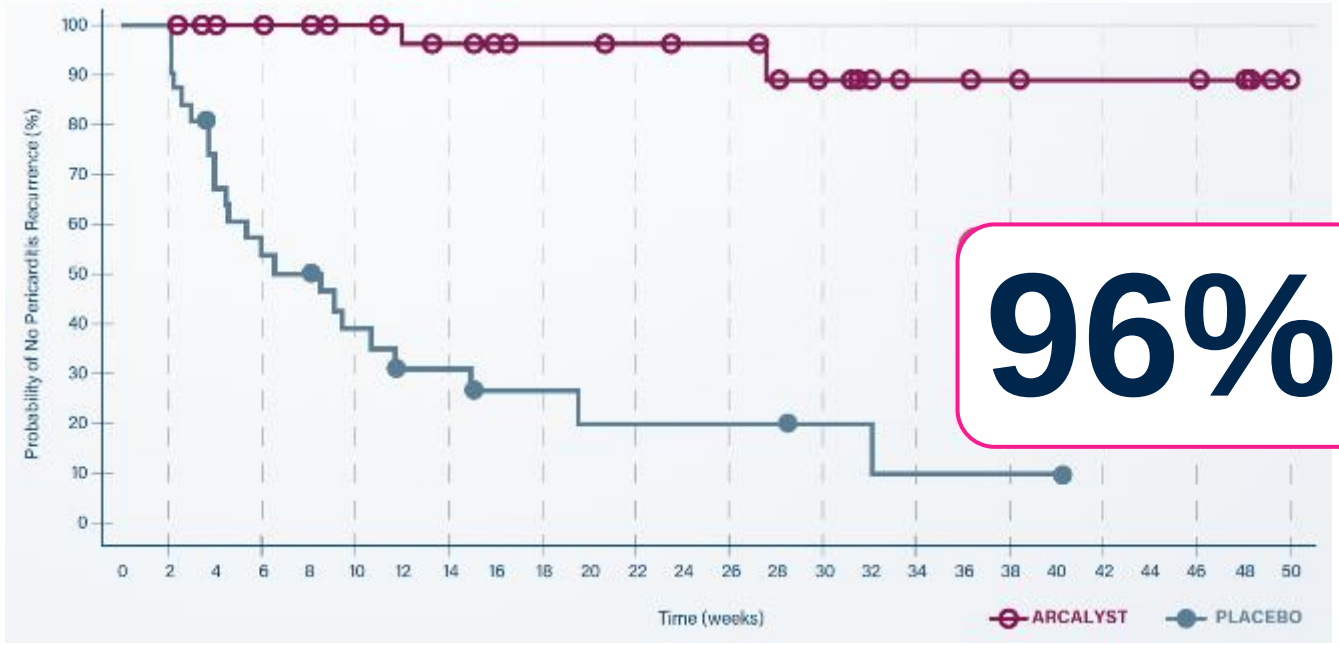
Klein AL, Imazio M, Cremer P, et al. Phase 3 trial of interleukin-1 trap rilonacept in recurrent pericarditis. N Engl J Med. 2021;384(1):31-41.
ARCALYST (rilonacept) prescribing information 2021

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 ($p=0.0002$)

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

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.

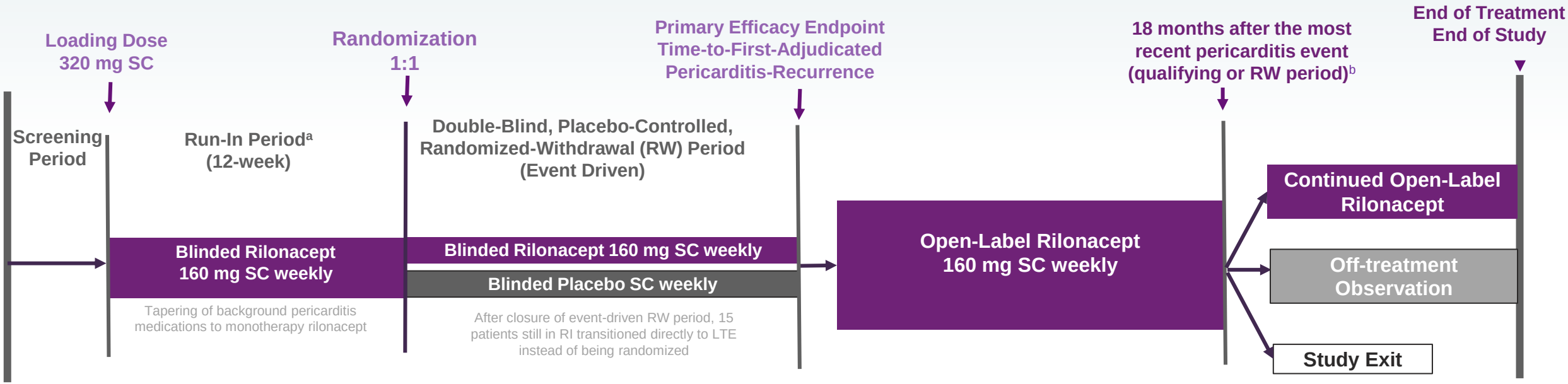
1) Klein AL, Imazio M, Cremer P, et al. Phase 3 trial of interleukin-1 trap rilonacept in recurrent pericarditis. N Engl J Med. 2021;384(1):31-41.

RHAPSODY Design

Event-Driven Pivotal Study

Median rilonacept treatment duration prior to the LTE (RI+RW) was 9 months (range, 3-14)

Long-Term Extension (LTE) (up to 24 months)



[a] The duration of the run-in period was concealed from patients, so that they were blinded to the timing of randomization

[b] For each patient in the LTE**, a decision was made 18 months after the most recent pericarditis recurrence (Qualifying or RW period)** based on clinical status and one of the following actions was taken at the investigator's discretion:

- Continue rilonacept on-study

OR

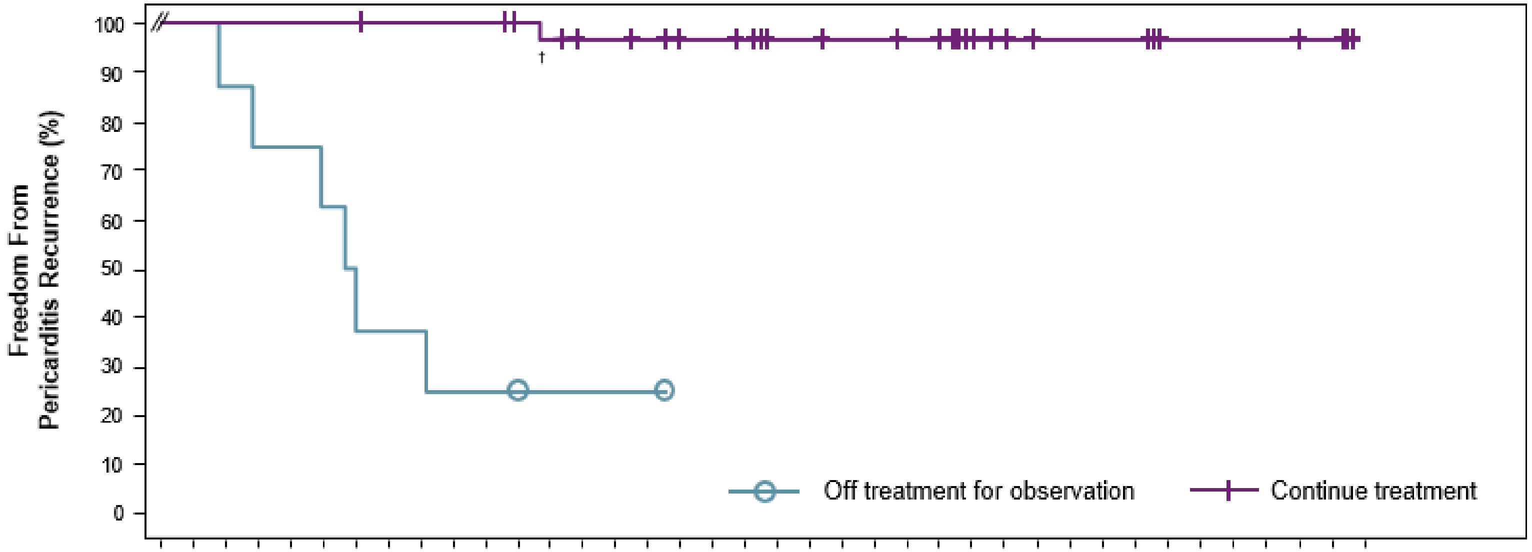
- Suspend rilonacept treatment and remain on-study for observation (rilonacept rescue for recurrence allowed)

OR

- Discontinue the LTE completely (no further observation)

Adapted from: Imazio M, Klein AL, et al. Prolonged Rilonacept Treatment in Rhapsody Long-term Extension Provided Persistent Reduction of Pericarditis Recurrence Risk. Poster 2223 (Presented at AHA Scientific Sessions 2022)

RHAPSODY Long-Term Extension Data Demonstrated Rilonacept Treatment Beyond 18 months Resulted in Continued Treatment Response[1]



Week after 18-Month Decision:	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36
Continued Rilonacept Treatment, Patients at Risk, n	33	33	33	33	33	33	33	32	32	32	32	30	29	27	27	25	24	23	22
Off Treatment for Observation, Patients at Risk, n	8	8	7	6	6	6	4	3	3	2	2	2	1	1	1	1	0		

Week after 18-Month Decision:	38	40	42	44	46	48	50	52	54	56	58	60	62	64	66	68	70	72	74
Continued Rilonacept Treatment, Patients at Risk, n	18	18	17	17	16	16	11	9	7	7	7	7	4	4	4	4	4	3	0
Off Treatment for Observation, Patients at Risk, n																			

†The patient with a recurrence at 23.4 weeks had interrupted rilonacept treatment ~4 weeks prior.

Hazard ratio = 0.02
Log-rank *P*<0.0001
Risk reduction = 98%

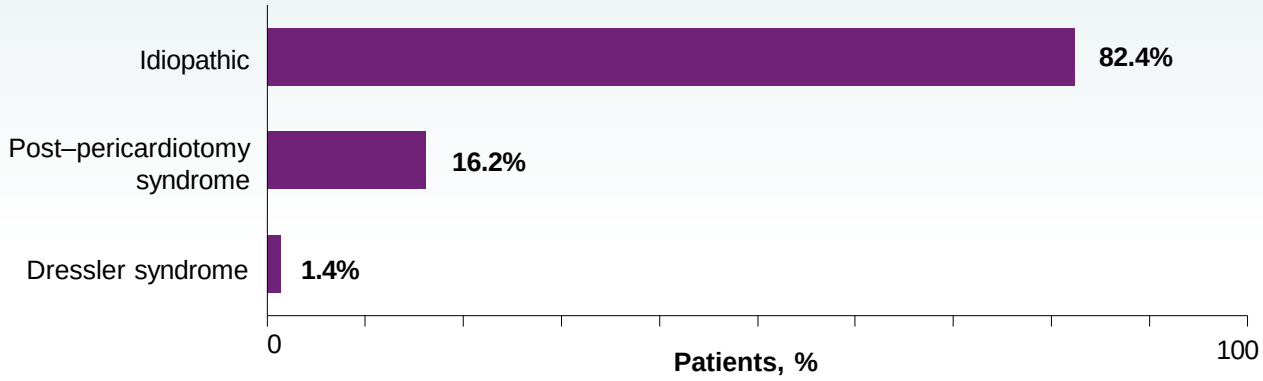
	N	Patients with Recurrence,[a] n (%)	Weeks to Recurrence,[a] Median (95% CI)
Continued rilonacept treatment	33	1 (3)	NE (NE–NE)
Off treatment for observation	8	6 (75)	11.8 (3.7–NE)

[a]After 18-month decision.
CI, confidence interval; NE, not estimable.

1) Imazio M, Klein AL, et al. Prolonged Rilonacept Treatment in Rhapsody Long-term Extension Provided Persistent Reduction of Pericarditis Recurrence Risk. Poster 2223 (Presented at AHA Scientific Sessions 2022)

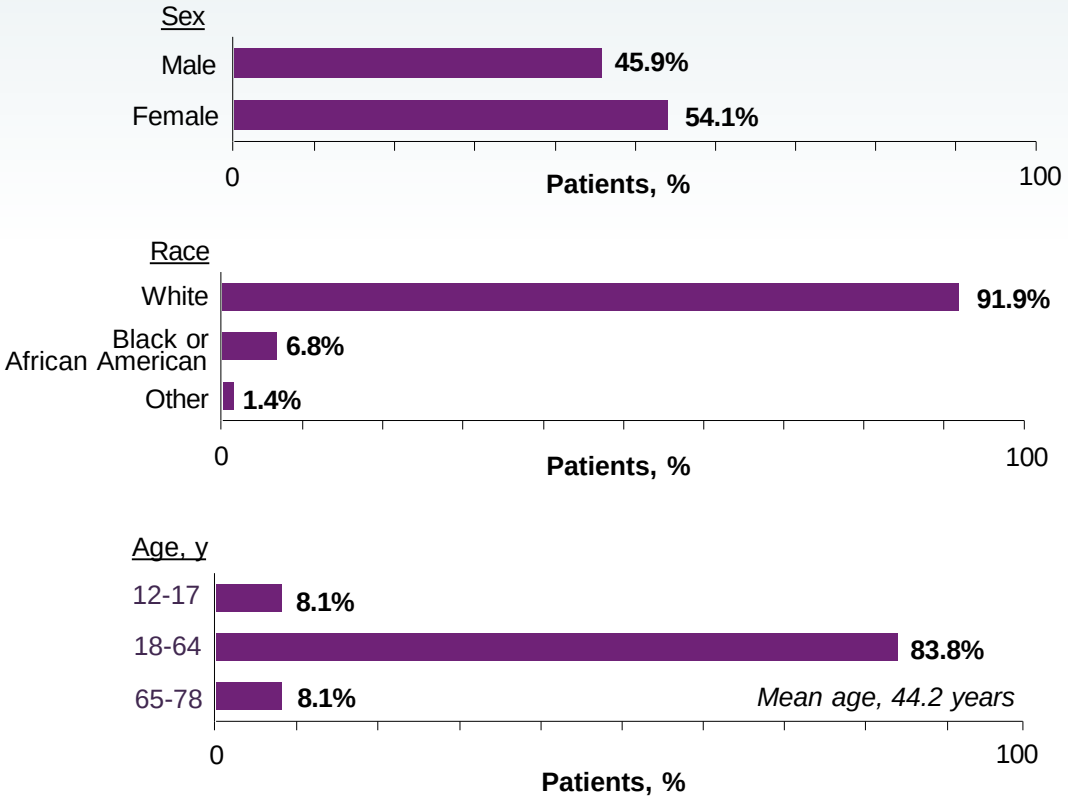
Patient Cohort (n = 74) in RHAPSODY Long-Term Extension

Prior Pericarditis History at Run-In Baseline



Mean Number of Episodes, Including Index and Qualifying Episodes at Run-In Baseline (n = 74)	Mean Disease Duration at Run-In Baseline (n = 74)
4.8	2.5 years

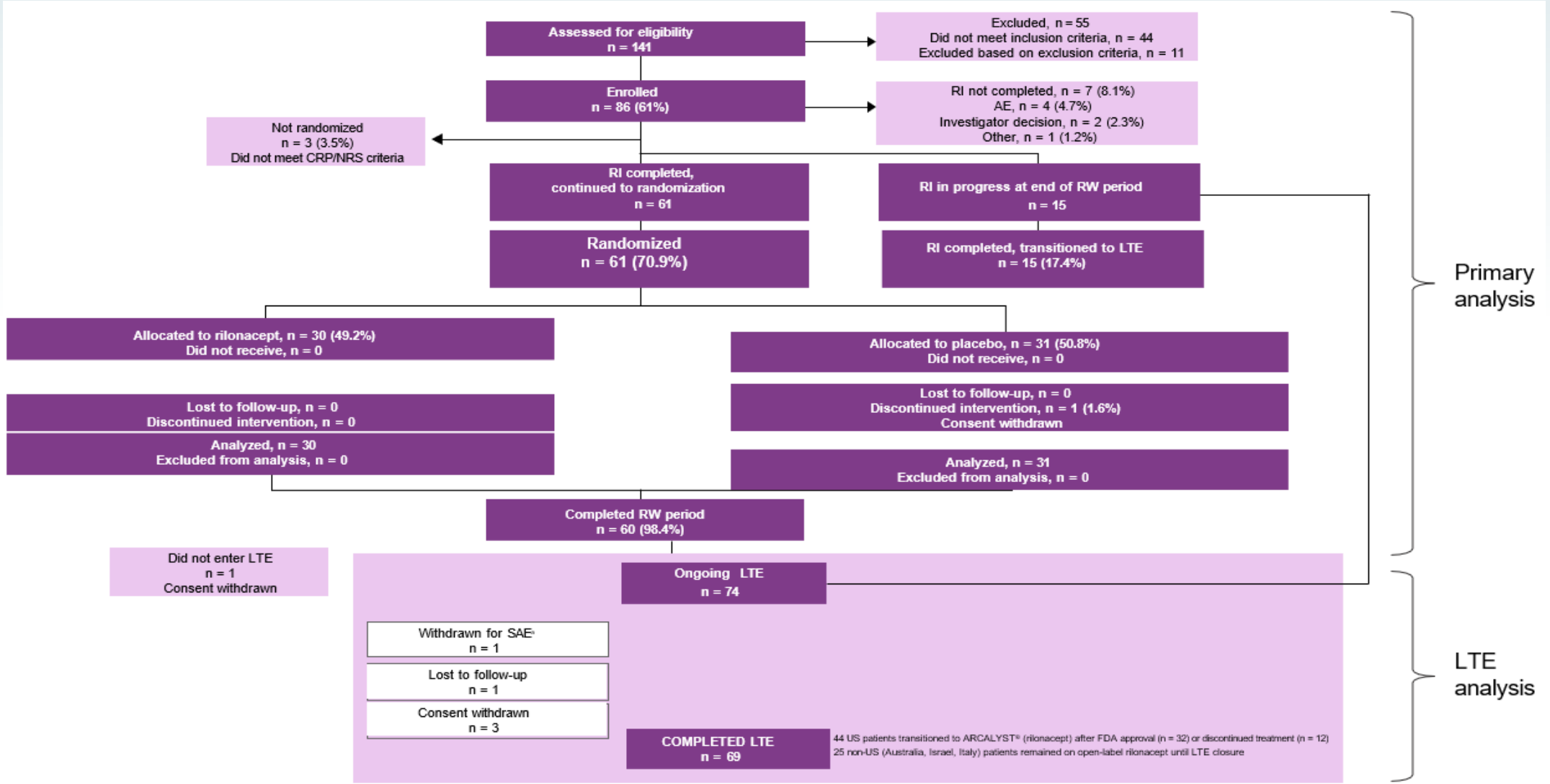
Baseline Demographics



RHAPSODY LTE Patient Disposition

- Patients entering the LTE already had a history of 2.5 years of disease duration (mean 3.8 pericarditis recurrences) before entering RHAPSODY
- At the end of the event-driven RW study, the median duration of rilonacept therapy had reached 9 months (maximum 14 months)
- In May 2020, 74 of 75 eligible patients continued into the RHAPSODY open-label LTE
- At the 1-year anniversary of the LTE (April 2021), the median duration of continuous rilonacept treatment had reached 20 months
- All patients were followed in the LTE until geography-specific study closure
  - Total LTE—all geographies (n = 74)
    - Median rilonacept treatment duration from run-in baseline was 23 months (maximum 35 months)
  - US patients (n = 45)
    - In April 2021, the LTE was concluded in the United States, and all US patients either switched to commercial ARCALYST® (rilonacept) therapy (n = 32) or discontinued rilonacept (n = 12)
    - Median continuous rilonacept treatment duration from run-in baseline was 18 months (maximum 27 months)
  - Non-US (Italy, Israel, Australia) patients (n = 29)
    - In June 2022, the non-US LTE was concluded, and all patients discontinued rilonacept
    - Median rilonacept treatment duration from run-in baseline was 29 months (maximum 35 months)

RHAPSODY LTE Patient Disposition (Consort Diagram)



Imazio M, Klein AL, et al. Prolonged Rilonacept Treatment in Rhapsody Long-term Extension Provided Persistent Reduction of Pericarditis Recurrence Risk. Poster 2223 (Presented at AHA Scientific Sessions 2022)

*Acute endocarditis. AE, adverse event; CRP, C-reactive protein; FDA, US Food and Drug Administration; LTE, long-term extension; NRS, numerical rating scale; RI, run-in; RW, randomized-withdrawal; SAE, serious adverse event.

Efficacy Up to 18-Month Decision Point

- During treatment with open-label rilonacept in the LTE (before 18-month decision point), continued rilonacept treatment resulted in continued treatment response
  - Pericarditis recurrences, inflammation signs (CRP levels), and severity of RP symptoms (Patient Global Impression of Pericarditis Severity [PGIPS]) remained low
  - At each study visit:
    - >95% of patients had CRP levels ≤1 mg/dL
    - >86% of patients reported absent or minimal pericarditis symptoms (PGIPS)
  - Only 3 investigator-assessed recurrences were reported
    - Annualized incidence: 0.04 events per patient-year

Imazio M, Klein AL, et al. Prolonged Rilonacept Treatment in Rhapsody Long-term Extension Provided Persistent Reduction of Pericarditis Recurrence Risk. Poster 2223 (Presented at AHA Scientific Sessions 2022)

Efficacy After the 18-Month Decision Point

- A total of 52 patients reached the 18-month decision point while on rilonacept (i.e., 18 months since most recent recurrence, whether qualifying episode or in the RW period)
  - 33 patients continued treatment with open-label rilonacept
  - 8 patients suspended rilonacept treatment and remained on study for observation (rilonacept rescue for recurrence was allowed)
  - 11 patients discontinued study participation
- Continued treatment with rilonacept past 18 months resulted in continued treatment response
  - There was a 98% reduction in risk of recurrence (hazard ratio, 0.02; *P*<0.0001[a])
    - Recurrence (investigator-assessed) rate was 3.0% (1/33) in the patients who continued rilonacept treatment. This recurrence occurred at 23.4 weeks into the LTE and was associated with a treatment interruption of 4 weeks
    - Recurrence (investigator-assessed) rate was 75.0% (6/8) in the patients who suspended rilonacept treatment for observation
  - The median (IQR) time to recurrence after suspending rilonacept treatment was 11.8 (3.7–not estimable [NE]) weeks
  - Reinitiation of rilonacept resulted in resolution of acute pericarditis recurrence
  - Annualized recurrence rate[b] (95% CI) was 0.18 (0.06–0.41) events per patient-year for the patients who remained on rilonacept and 2.18 (0.80–4.75) events per patient-year for the patients who interrupted rilonacept
- At the end of the LTE treatment period, patients stopped rilonacept treatment and were returned to standard of care for recurrent pericarditis. Patients were monitored in a posttreatment safety follow-up period (6 weeks post–last dose) for adverse events
  - 4 additional pericarditis recurrences occurred during the posttreatment follow-up period, at ~6 weeks post–rilonacept treatment (3 patients) and ~3 weeks post–rilonacept treatment (1 patient)

[a]Two-sided *P* value, log-rank test. [b]Number of recurrences in LTE periods for all patients/sum of patient-years in LTE periods for all patients. For patients who continued in study off treatment for observation, patient-years calculated as treatment, minimum (end-of-study date, cutoff date, first-dose date after observation -1) – LTE 18-month disposition date +1; for patients who continued treatment, patient-years calculated as minimum (end-of-study date, cutoff date) – LTE 18-month disposition date +1; 95% CI calculated using an exact method with Poisson distribution. Imazio M, Klein AL, et al. Prolonged Rilonacept Treatment in Rhapsody Long-term Extension Provided Persistent Reduction of Pericarditis Recurrence Risk. Poster 2223 (Presented at AHA Scientific Sessions 2022)

RHAPSODY LTE Safety & Adverse Experiences

- During the LTE period, treatment-emergent adverse events (TEAEs) were experienced by 83.8% of patients (n = 62)
- In most patients, the maximum severity of TEAEs was mild (37.8%) or moderate (37.8%)
- 2 patients experienced serious TEAEs (acute endocarditis, viral pneumonia) considered “related” to the study drug

TABLE 1. ADVERSE EVENTS REPORTED IN RHAPSODY LONG-TERM EXTENSION

TEAE Category,[a] n (%)	LTE Period (n = 74)
Any TEAE[b]	**62 (83.8)**
TEAE by maximum severity[c]	
Mild	28 (37.8)
Moderate	28 (37.8)
Severe	6 (8.1)
TEAE related to study drug[d]	**21 (28.4)**
Patients with serious TEAEs[e]	**5 (6.8)**
Serious TEAE related to study drug	2 (2.7)
Leading to dose interruption	2 (2.7)
Leading to study drug discontinuation	3 (4.1)
Leading to death	0
Infection or infestation	31 (41.9)
TEAE of upper respiratory tract infection	12 (16.2)
TEAE of injection-site reaction	4 (5.4)

[a]Patients with multiple events were counted once in same category. [b]Adverse event that starts or increases in severity from first study-drug dose to 6 weeks after last dose. [c]Each patient represented according to maximum severity. [d]Event was related, possibly related, or missing, as assessed by investigator. [e]5 patients experienced serious TEAEs: 1. Pneumothorax; 2. Acute endocarditis, aortic valve disease, acute myocardial infarction, pericarditis; 3. Transient ischemic attack, coronavirus infection; 4. Pneumonia, pneumonia viral (COVID-19); 5. Left ventricular failure, hip fracture, bile duct stone, cardiac-device malfunction. LTE, long-term extension; TEAE, treatment-emergent adverse event. Imazio M, Klein AL, et al. Prolonged Rilonacept Treatment in Rhapsody Long-term Extension Provided Persistent Reduction of Pericarditis Recurrence Risk. Poster 2223 (Presented at AHA Scientific Sessions 2022)

Conclusions from RHAPSODY LTE

- Patients with RP have a chronic autoinflammatory disease, characterized by multiple recurrences mediated by IL-1. This disease may last several years
- In patients with symptomatic RP failing standard of care:
  - Continued rilonacept treatment during the LTE (median 18 and 29 months in the US and non-US patients, respectively) resulted in continued treatment response
  - Rilonacept reduced the risk of pericarditis recurrence by 98% beyond 18 months of treatment
    - Suspension of rilonacept treatment even after 18 months of treatment resulted in unmasking of the underlying autoinflammation process, resulting in pericarditis recurrence
    - Reinitiation of rilonacept resulted in resolution of the acute pericarditis recurrences
  - Over treatment periods of 18 months and beyond in this study, rilonacept was generally well tolerated
  - In patients with similar disease characteristics, treatment beyond 18 months may be warranted to prevent pericarditis recurrence over the long term

Imazio M, Klein AL, et al. Prolonged Rilonacept Treatment in Rhapsody Long-term Extension Provided Persistent Reduction of Pericarditis Recurrence Risk. Poster 2223 (Presented at AHA Scientific Sessions 2022)

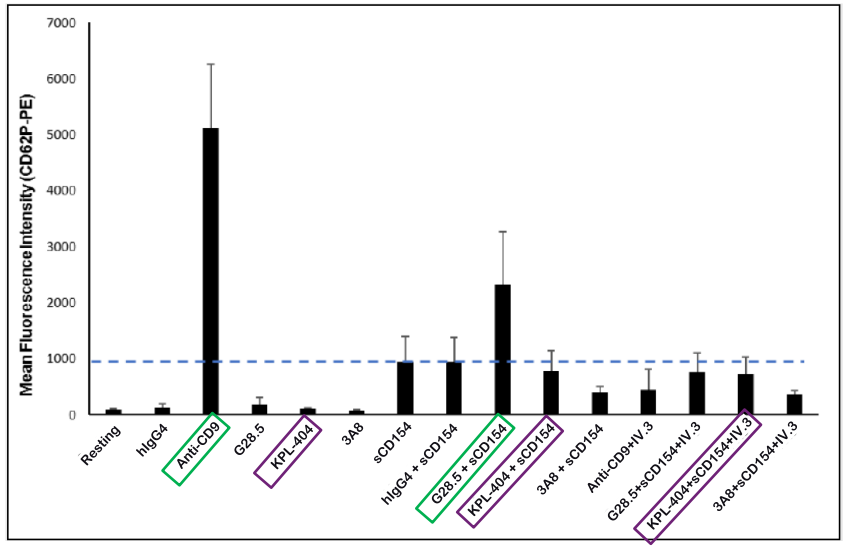
Appendix
KPL-404

KPL-404 Does Not Cause Platelet Activation or Aggregation *in vitro*

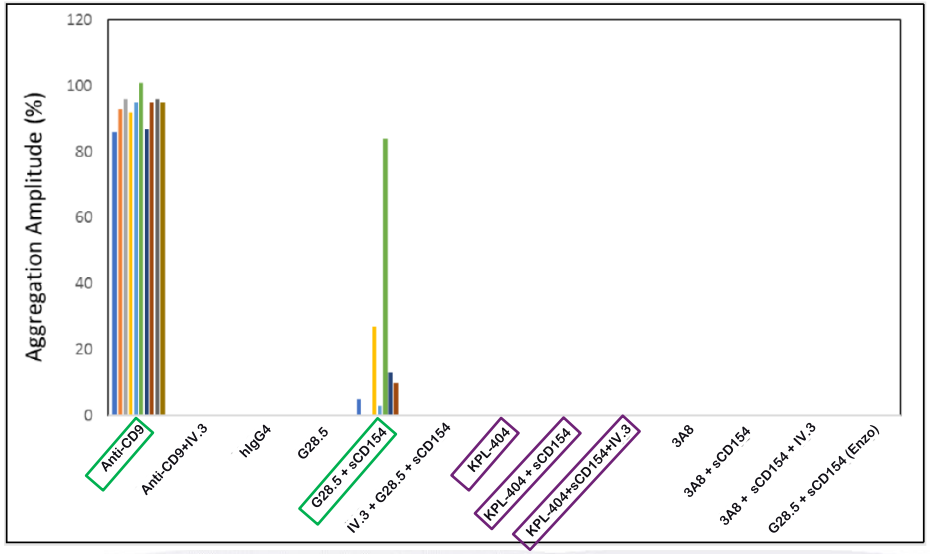
- At least three first-generation IgG1 anti-CD154 mAbs* were associated with thromboembolic events in humans and NHPs[1]
- **Mechanism:** Activation of platelets through cross-linking mediated by IgG-Fc/FcγRIIa interaction
  - Platelet activation observed *in vivo* with anti-CD154 mAbs with active Fc region
  - Platelet activation *in vitro* by anti-CD40 mAbs requires presence of sCD154 and active Fc region
  - Absence of an active Fc-region prevents platelet activation[1,2]

KPL-404 did not cause upregulation of the cell-surface platelet activation marker CD62P
KPL-404 did not induce platelet aggregation in the presence (or absence) of soluble CD154[3]

KPL-404 Alone and in Combination with sCD154 does not increase CD62P Expression on the Platelet Surface



KPL-404 Alone and in Combination with sCD154 does not increase Platelet Aggregation Amplitude (%)



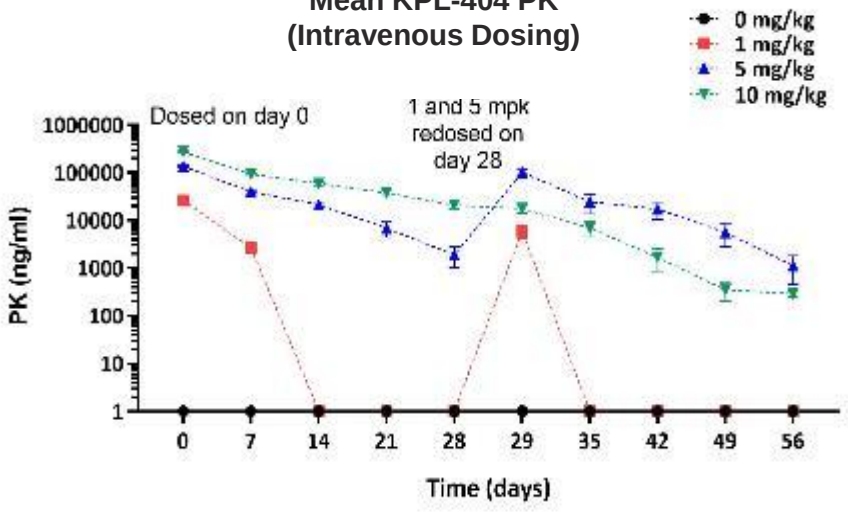
Positive controls:
- G28.5: anti-CD40 mAb – causes sCD40L-dependent platelet activation (Langer et al., Thromb Haemost 2005; 93(06): 1137-1146)
- Anti-CD9: mAb– causes sCD40L-independent platelet activation
- IV.3 - anti-FcγRIIa antibody

*ruplizumab/hu5c8, toralizumab/IDEC-131, ABI793

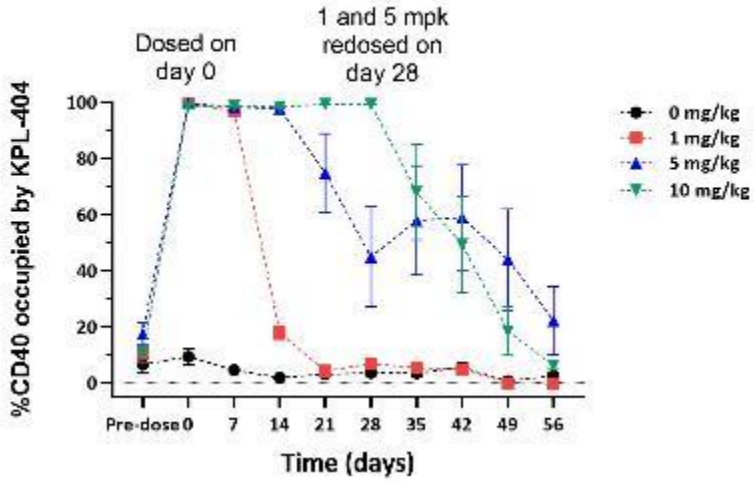
Sources: 1) Law & Grewal, Advances in Experimental Medicine and Biology, vol 647. Springer; 2) Shock et al., Arthritis Research & Therapy 17, Article Number: 234 (2015); 3) KNSA in-house data

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

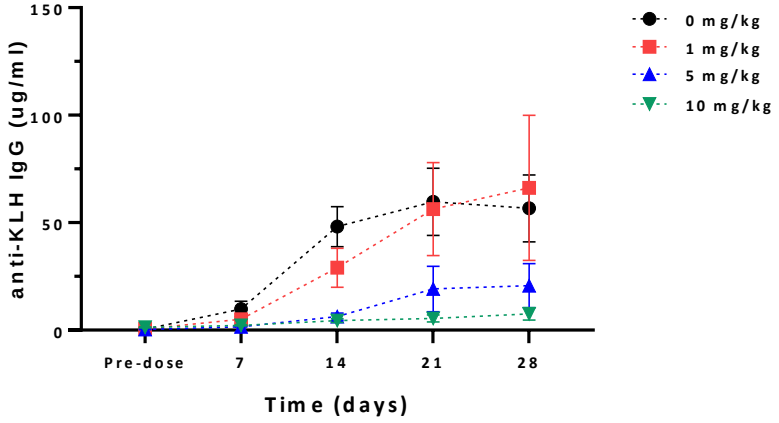
Mean KPL-404 PK (Intravenous Dosing)



Mean KPL-404 Receptor Occupancy (RO)



Mean KLH IgG



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

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; 2) Muralidharan et al. Preclinical immunopharmacologic assessment of KPL-404, a novel, humanized, non-depleting antagonistic anti-CD40 monoclonal antibody. J Pharmacol Exp Ther. 2022, 381(1):12-21; TDAR = T-cell dependent antibody response; KLH = keyhole limpet hemocyanin

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:

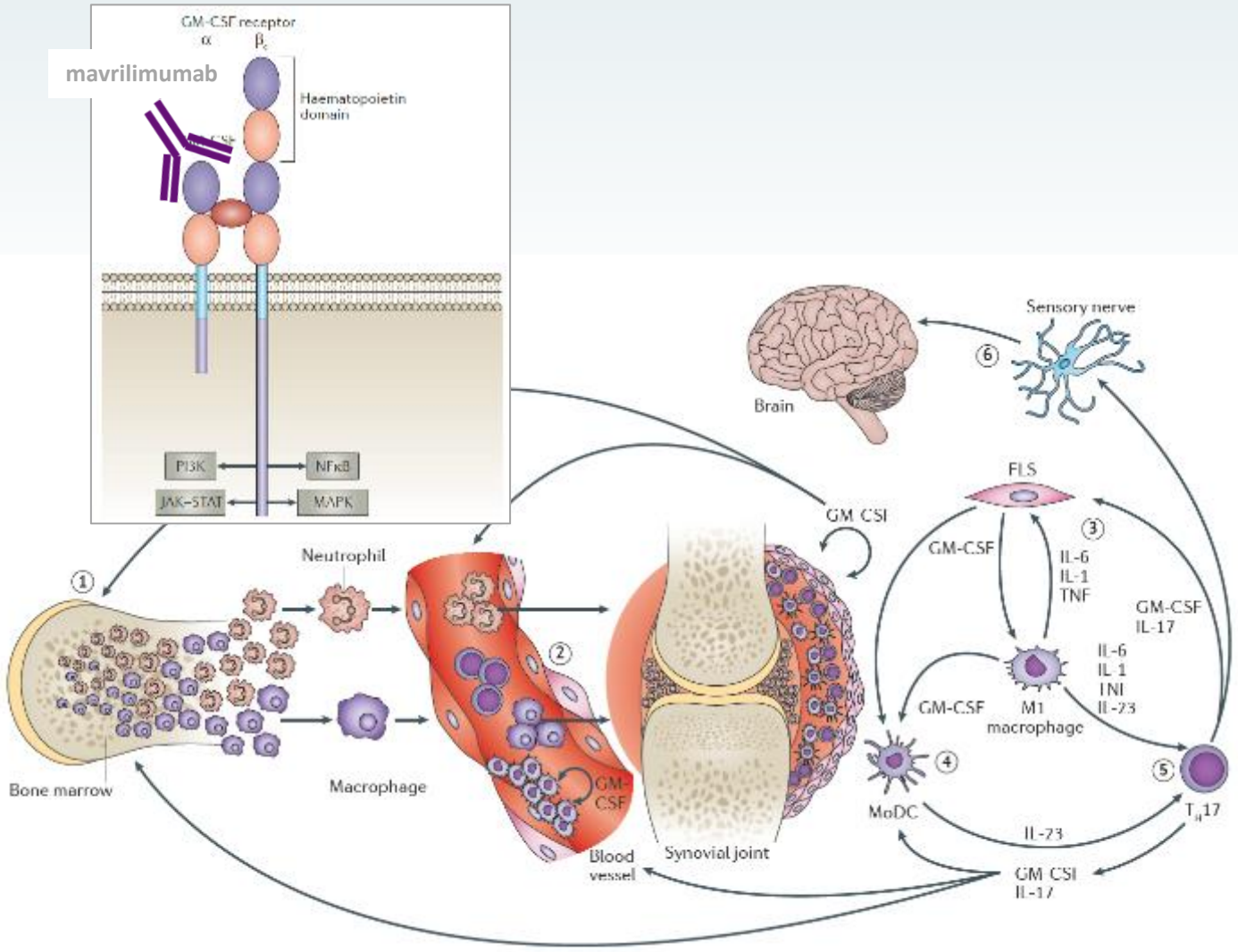
- All dose escalations occurred as per protocol with no dose limiting safety findings. All 6 subjects dosed with KPL-404 3 mg/kg IV showed full receptor occupancy through Day 29, which corresponded with complete suppression of the T-cell Dependent Antibody Response (TDAR) to KLH through Day 29. Consistent 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

Appendix Mavrilimumab

Mavrilimumab, a GM-CSFRα antagonist, blocks GM-CSF signaling; A Key Mediator of Inflammation and Autoimmunity



- **Granulocyte-macrophage colony stimulating factor (GM-CSF) is a growth factor first identified as an inducer of differentiation and proliferation of myeloid cells (neutrophils, eosinophils, and monocytes/macrophages) derived from hematopoietic progenitor cells**
  - Activated macrophages produce proinflammatory cytokines such as TNF, IL-6, IL1, lipid-derived mediators and chemokines
  - Downstream signaling is mediated by STAT5, JAK2, NF-kB, PI3K
- **Data suggest GM-CSF signaling plays a role in several additional cell types including, antigen-presenting cells, T-cells, and B-cells**
  - GM-CSF has a range of functions on mature eosinophils including dose-dependent eosinophil priming, migration, and degranulation
- **GM-CSF is involved in a wide range of biological processes in both innate and adaptive immunity; its functions span multiple tissues and biological processes allowing it to show potential as a therapeutic target for multiple inflammatory and autoimmune disorders**

Sources: Wicks, Roberts, Nature Review Immunology, 2015; Hamilton, Expert Review of Clinical Immunology, 11:4, 457-465

Corporate Presentation

MAY 2023