



# Corporate Presentation

JULY 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; risks arising from our technology transfer of ARCALYST drug substance manufacturing; 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 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.

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# Portfolio of Immune-Modulating Assets

Program	Target	Preclinical	Phase 1	Phase 2	Phase 3	Commercial
<b>CARDIOVASCULAR FRANCHISE</b>						
<b>ARCALYST® (rilonacept)<sup>1,2</sup></b> IL-1α & IL-1β	<i>Recurrent Pericarditis</i>					
<b>Mavrimumab<sup>3</sup></b> GM-CSFRα	<i>Evaluating Development in Rare Cardiovascular Diseases</i>					
<b>AUTOIMMUNE FRANCHISE</b>						
<b>KPL-404</b> CD40/CD154	<i>Rheumatoid Arthritis</i>					

Program	Licensee	Exclusive Licensed Territory
<b>OUT-LICENSING AGREEMENTS</b>		
<b>ARCALYST® (rilonacept)<sup>1,2</sup></b> IL-1α & IL-1β	<i>Huadong Medicine</i>	<i>Asia Pacific Region, Excluding Japan</i>
<b>Mavrimumab<sup>3</sup></b> GM-CSFRα	<i>Huadong Medicine</i>	<i>Asia Pacific Region, Excluding Japan</i>
<b>Vixarelimab</b> OSMRβ	<i>Roche and Genentech</i>	<i>Worldwide</i>

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

# 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 **\$220-\$230M** in 2023, representing ~84% growth at the midpoint
- **Significant opportunity** 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 study
- Pursuing collaborative study agreements for **mavrilimumab** in rare cardiovascular diseases

### Strong Financial Position to Support Growth

- **\$185.0M Q223** cash position
- **Cash runway into at least 2027** 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**

# 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, as well as the efficacy and safety of mavrilimumab, 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 Phase 2 study

## Kiniksa is in a Strong Financial Position to Support Growth

- **Well-capitalized, with \$185.0M** of cash<sup>1</sup>
- Profitable ARCALYST collaboration, non-dilutive capital from strategic out-licensing transactions, and continued financial discipline provide **cash runway into at least 2027**



1) As of June 30, 2023

# Out-Licensing Agreements

## 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 2022
  - \$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, of which approximately \$585 million remains
- 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

# ARCALYST®



## IL-1 $\alpha$ AND IL-1 $\beta$ CYTOKINE TRAP

**DISEASE AREA:** Recurrent pericarditis<sup>1</sup>; painful and debilitating auto-inflammatory cardiovascular disease

**COMPETITION**<sup>2</sup>: 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

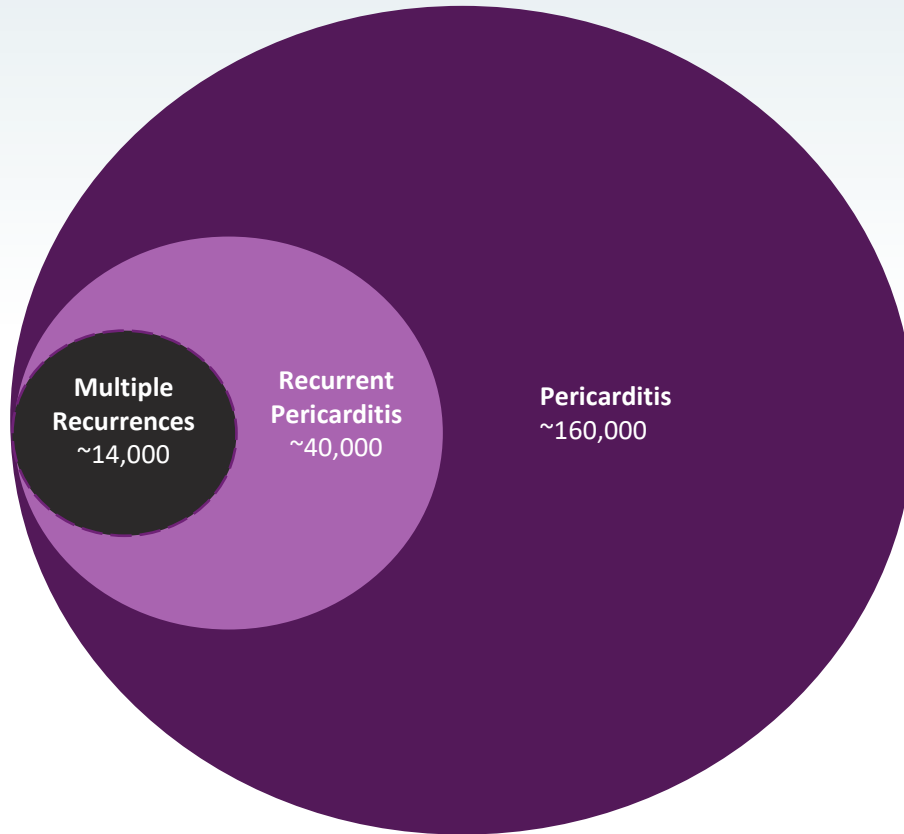
**ECONOMICS:** 50/50 split on profit and third-party proceeds

**RIGHTS:** Kiniksa has worldwide rights<sup>3</sup> (excluding MENA) for all indications outside those in oncology and local administration to the eye or ear



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-1 $\alpha$  = interleukin-1 $\alpha$  ; IL-1 $\beta$  = interleukin-1 $\beta$ ; 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<sup>1</sup>***

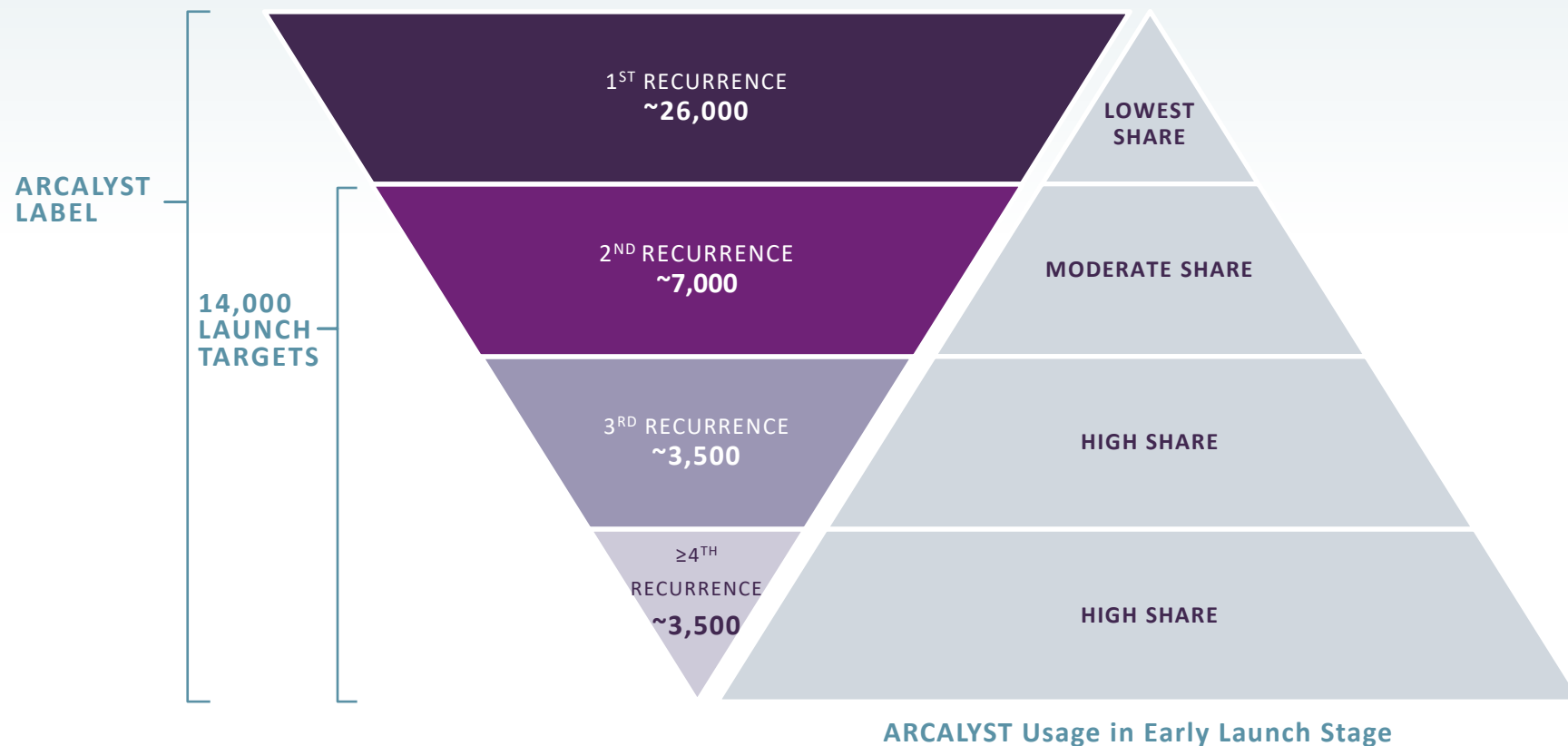
- **~ 160,000:** Epidemiological analysis using large national surveillance databases to calculate the pooled annualized prevalence of pericarditis (***Basis for Orphan Drug Designation approval***)<sup>2</sup>
- **~40,000:** Up to 30% experience at least one recurrence; some recur over multiple years<sup>6,7</sup>
- **~14,000:** Nearly 50% annual turnover with ~7,000 patients coming into the pool each year<sup>8</sup>



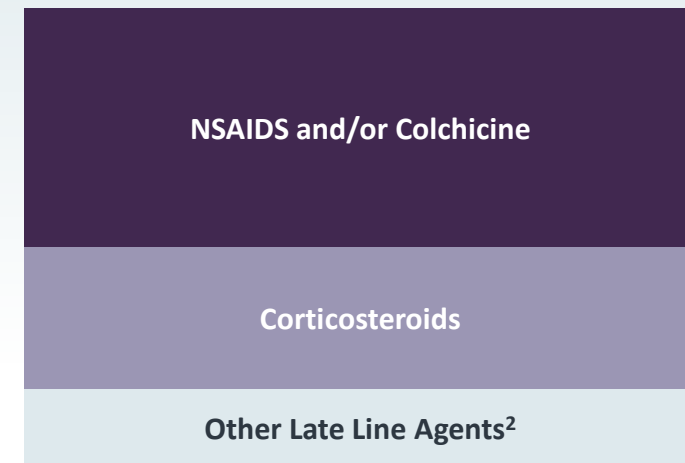
1) Cremer et al. American Journal of Cardiology. 2016;2311-2328; 2) DOF, Kiniksa Pharmaceuticals, Ltd.; 3) Brucato A, Maestroni S, Cumetti D, et al. Autoimmun Rev. 2008; 8:44-47; 4) Lange R, Hills L. N Engl J Med. 2004; 351: 2195-2202; 5) Imazio M, Cecchi E, Demichelis B, et al. Circulation. 2007; 115: 2739-2744; 6) Imazio et al. Circulation. 2005;112:2012-2016; 7) Adler et al. Circulation. 1998;97:2183-2185; 8) Klein A, Cremer P, Kontzias A, et al. US database study of clinical burden and unmet need in recurrent pericarditis. J Am Heart Assoc. 2021; 10:e018950. doi:10.1161/JAHA. 120.018950

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

Recurrent Pericarditis Annual Epidemiology: ~40,000



ARCALYST PATIENTS BY PRIOR PRODUCT<sup>1</sup>



ARCALYST PATIENTS BY FLARE STATUS @ INITIATION<sup>1</sup>

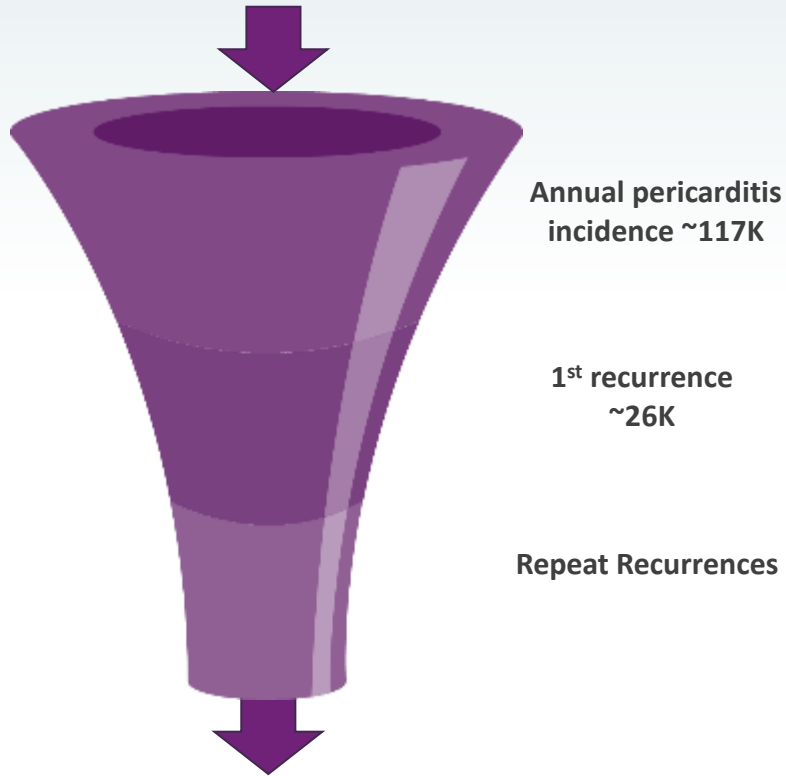


Klein A, Cremer P, Kontzias A, Furqan M, Tubman R, Roy M, Magestro M. Annals of Epidemiology. 2019;36:71; 2) Lin D, Majeski C, DerSarkissian M, Magestro M, Cavanaugh C, Laliberte F, Lejune D, Mahendran M, Duh M, Klein A, Cremer P, Kontzias A, Furqan M, Tubman R, Roy M, Mage. (Nov, 2019). Real-World Clinical 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

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

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



- ~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 (1 <sup>st</sup> episode) <sup>1</sup>	117K	117K	117K	117K	117K
Incidence of initial RP patients (1 <sup>st</sup> recurrence) <sup>2</sup>	26K	26K	26K	26K	26K
Ongoing recurrent from year-1 <sup>3</sup>				7K	7K
Ongoing recurrent from year-2 <sup>3</sup>			7K	3.5K	3.5K
Ongoing recurrent from year-3 <sup>3</sup>		7K	3.5K	1.8K	1.8K
Ongoing recurrent from year-4 <sup>3</sup>	7K	3.5K	1.8K	0.9K	0.9K
Ongoing recurrent from year-5 <sup>3</sup>	3.5K	1.8K	0.9K	0.5K	0.5K
Ongoing recurrent from year-6 <sup>3</sup>	1.8K	0.9K	0.5K	0.2K	0.2K
Ongoing recurrent from year-7 <sup>3</sup>					0.1K

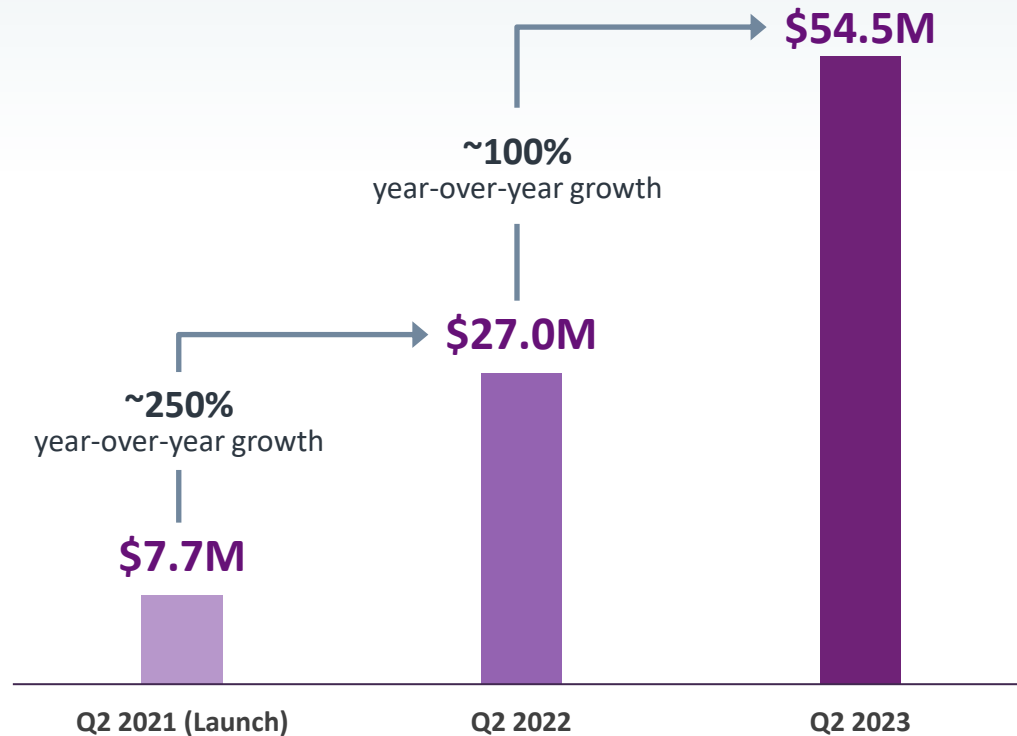
*Addressable Opportunity in U.S.*



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

# Strong Q2 2023 Revenue Growth Driven by Robust Commercial Execution

## Total Net Revenue Growth per Quarter



**Total Prescribers** >1,250

**Repeat Prescribers** (~23%)  
(% of Total)

**Payer Approval** >90%  
(% of Completed Cases)

**Average Total Duration of Therapy** 20 months

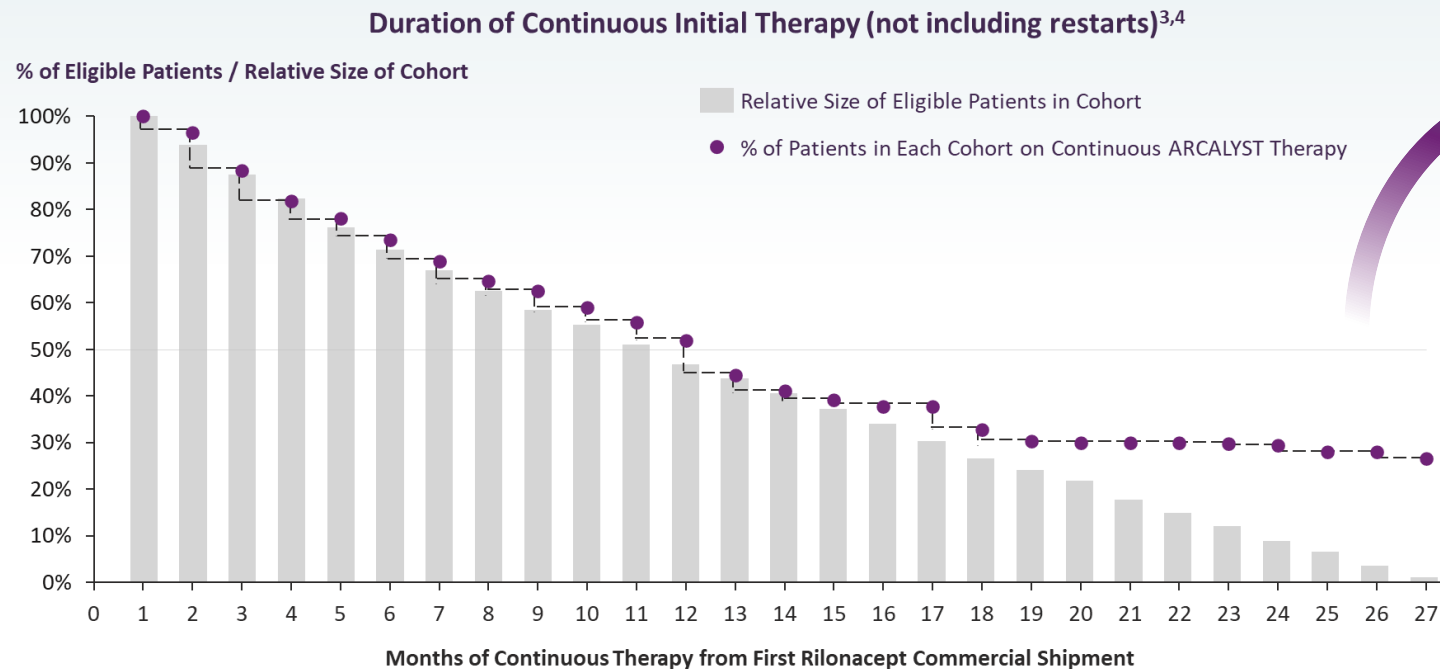
**Compliance** >85%

# Average Total Duration of ARCALYST Therapy Increased to ~20 Months<sup>1</sup>

Advancing the treatment paradigm to treat continuously throughout disease duration (median 3 years<sup>2</sup>)

Average  
*Initial*  
Duration of Therapy  
**~14 Months<sup>1</sup>**

Median  
*Initial*  
Duration of Therapy  
**~12 Months<sup>1</sup>**



**~45%**

Of Patients  
Restarted  
Therapy  
Following Initial  
Discontinuation

(Within ~8 weeks)

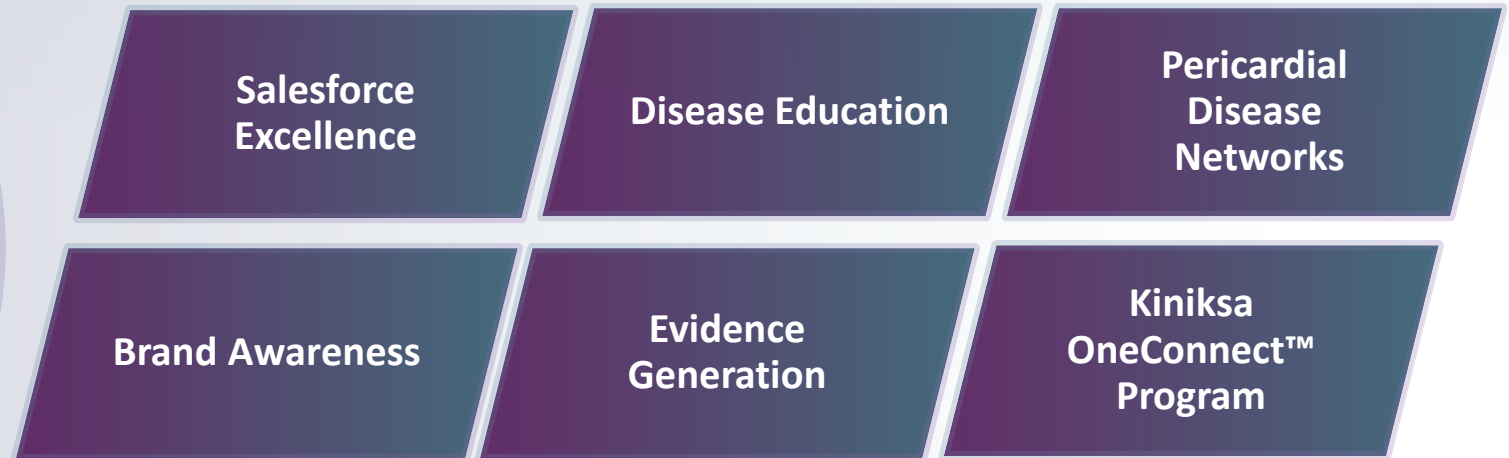
**~20 Months Average *Total* Duration of Therapy After Accounting for Patient Restarts**



1) As of Q2 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 6/30/2023 (patient restarts are not included in the chart)

# Expanding Breadth & Depth of ARCALYST Use for Recurrent Pericarditis

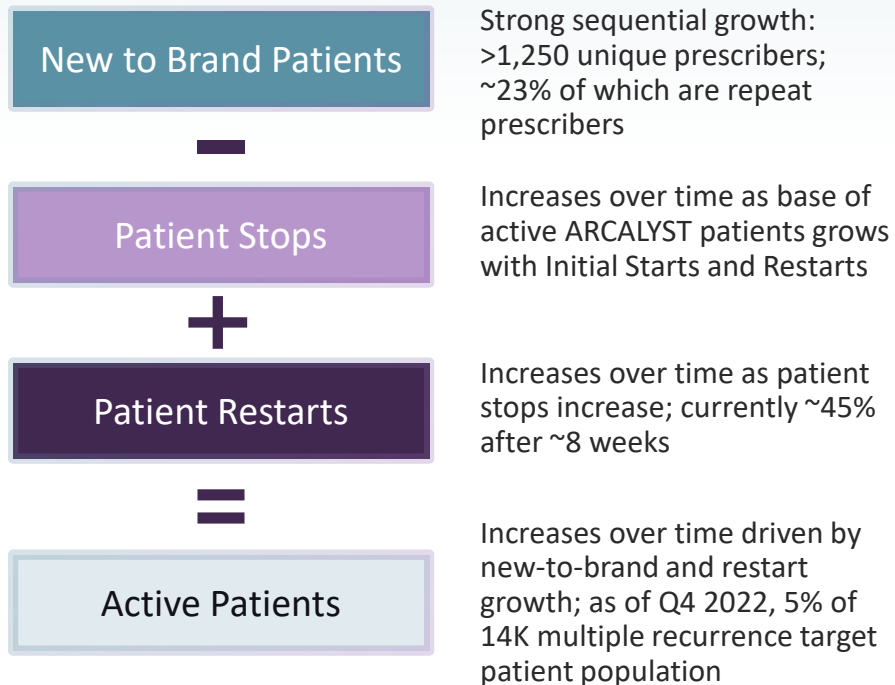
## Expanding Base of New Prescribers



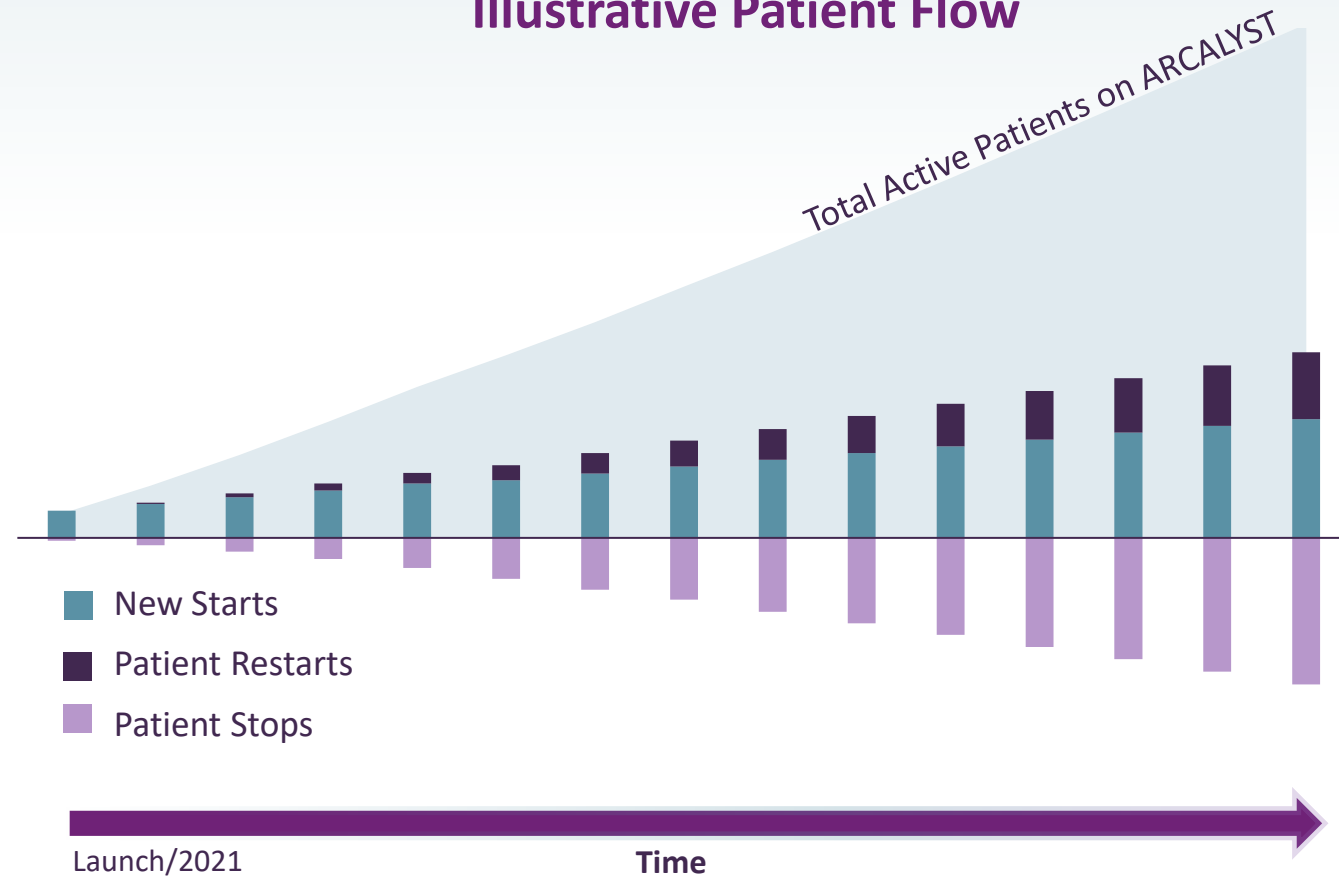
## Driving Growth with Existing Prescribers

# 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

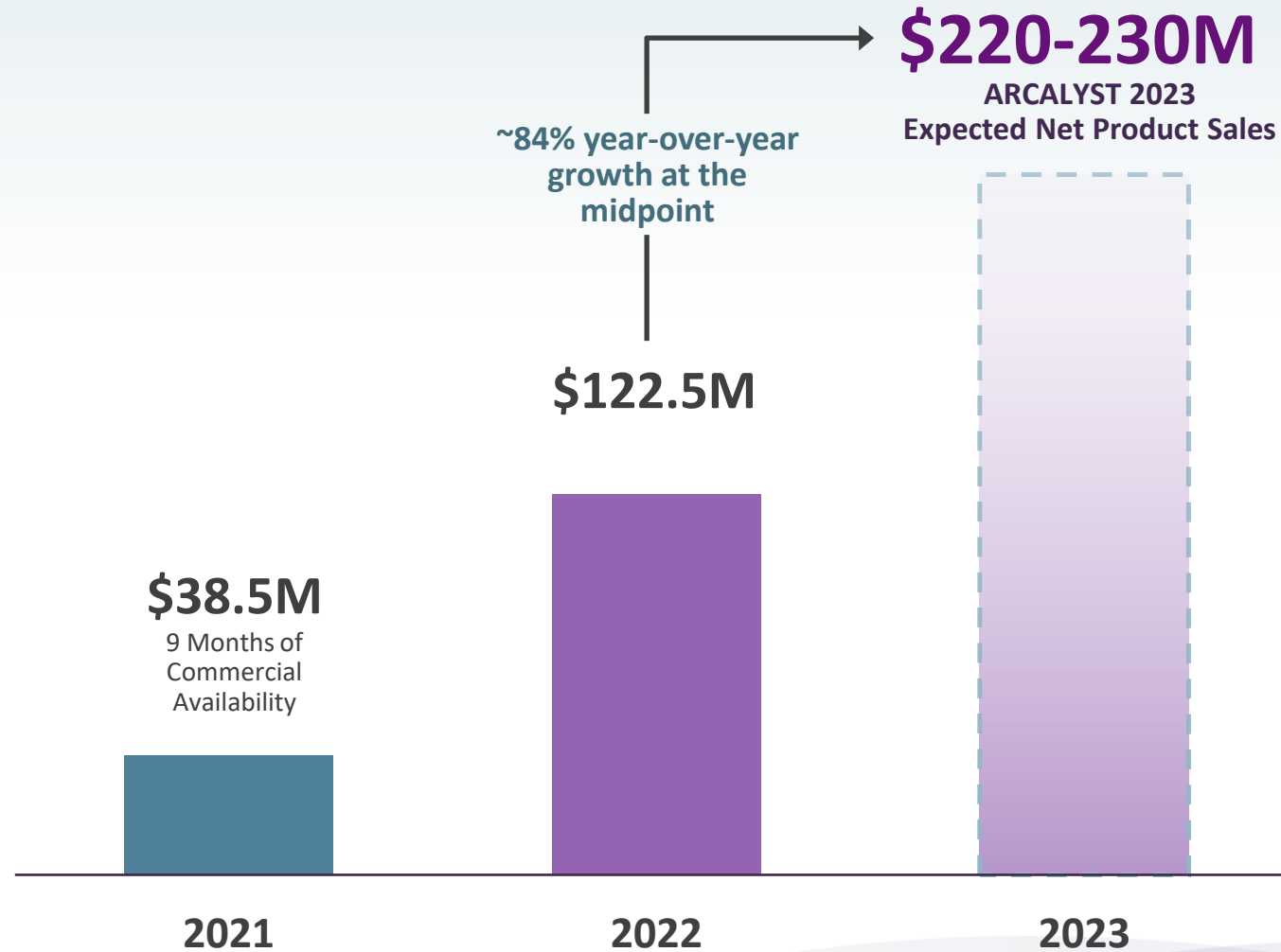


## Illustrative Patient Flow



# 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

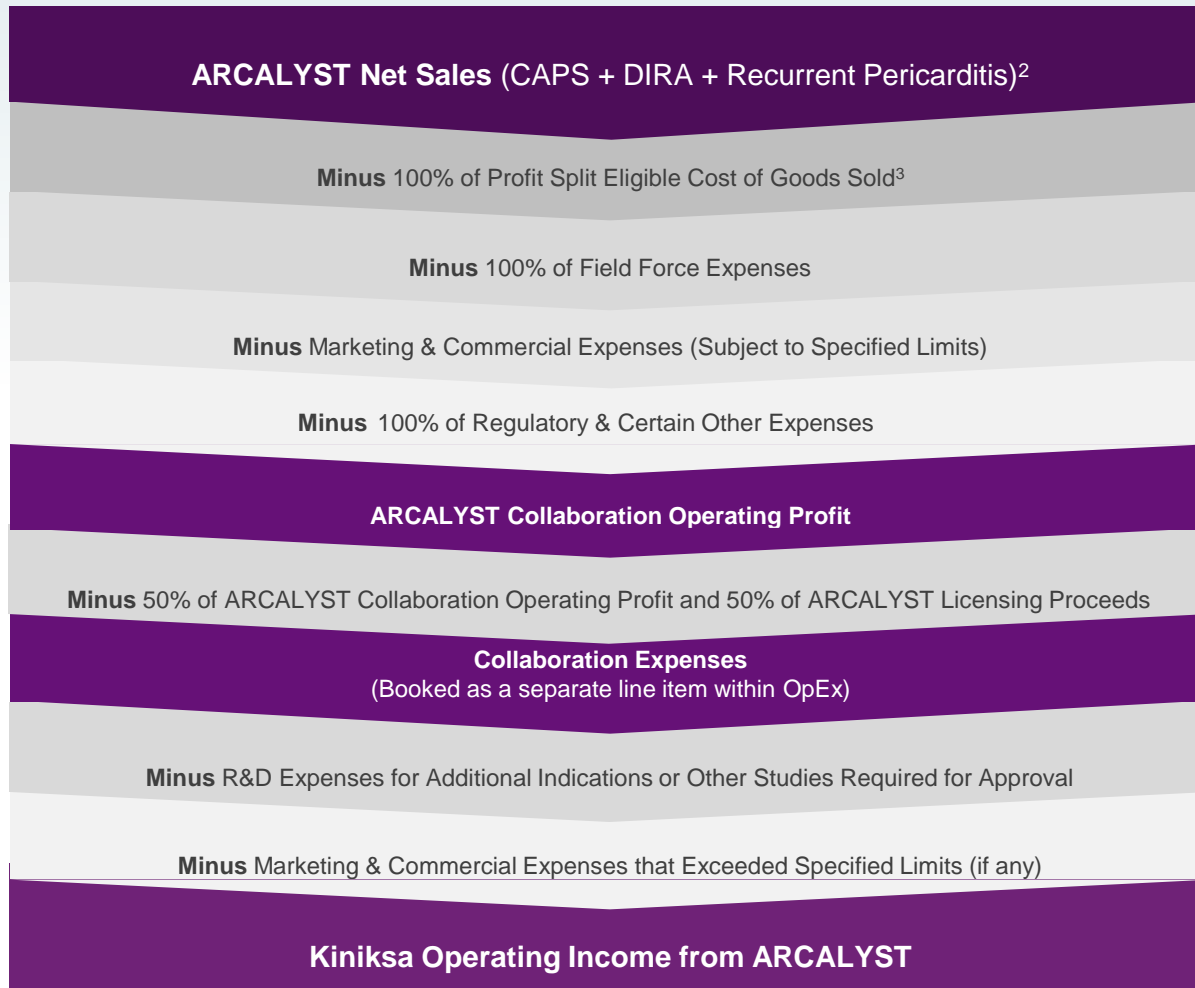
## Distribution

- 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<sup>1</sup>



- 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<sup>1</sup>

**SCIENTIFIC RATIONALE<sup>2,3</sup>:** 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

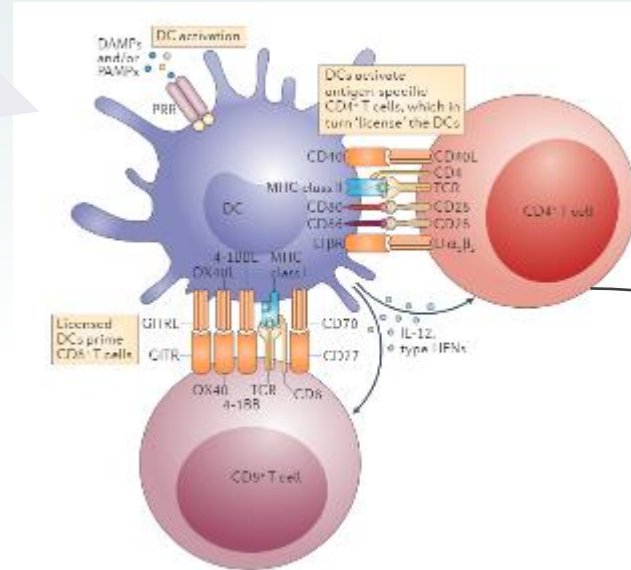
**RIGHTS:** Worldwide



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

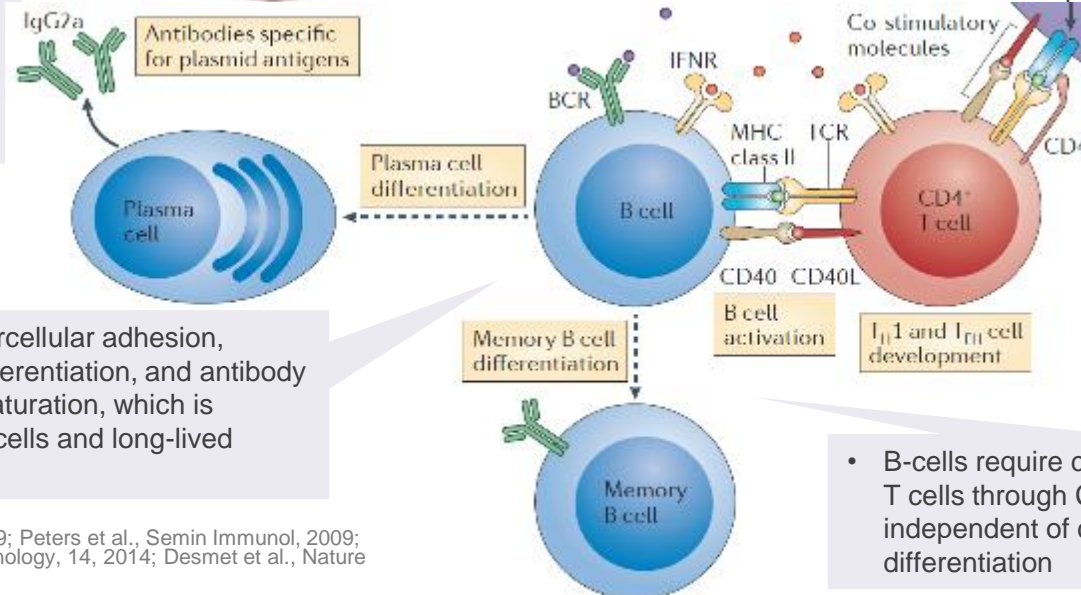
# CD40/CD154 is an Essential Immune Pathway for T-Cell Priming and T-Cell Dependent B-Cell Responses

- 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



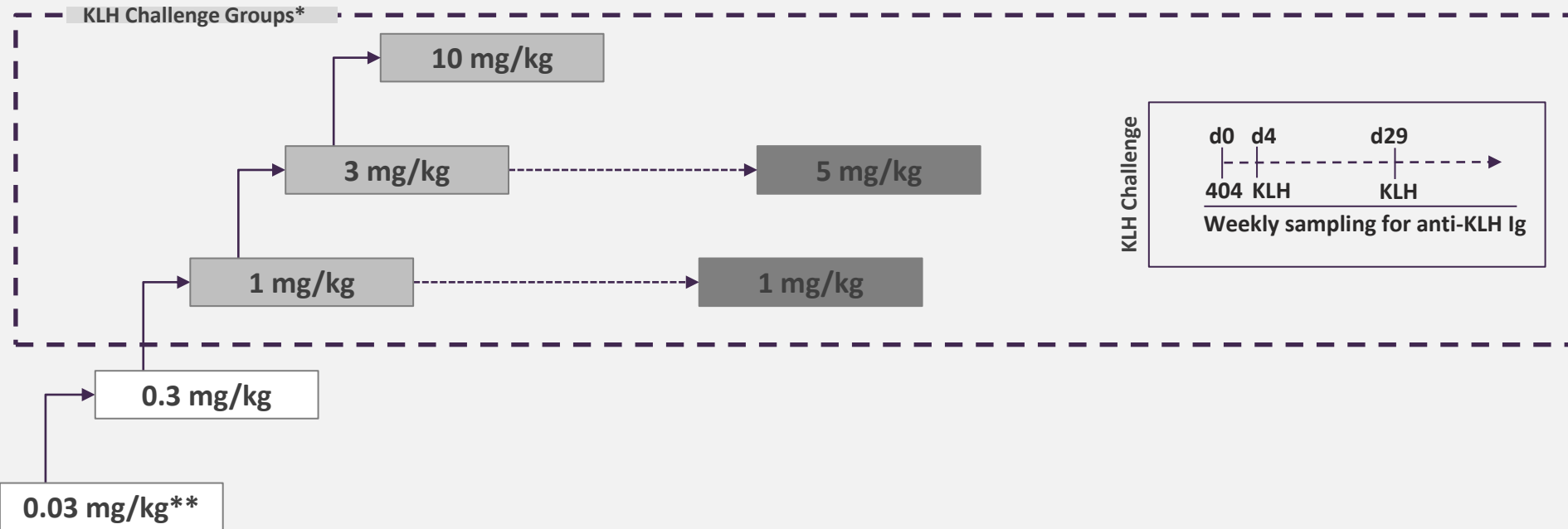
- CD40 engagement triggers B-cell intercellular adhesion, sustained proliferation, expansion, differentiation, and antibody isotype switching leading to affinity maturation, which is essential for generation of memory B cells and long-lived plasma cells

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

# KPL-404 Single-Ascending-Dose Phase 1 Study

Part A (Single IV dose)

Part B (Single SC Dose)



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

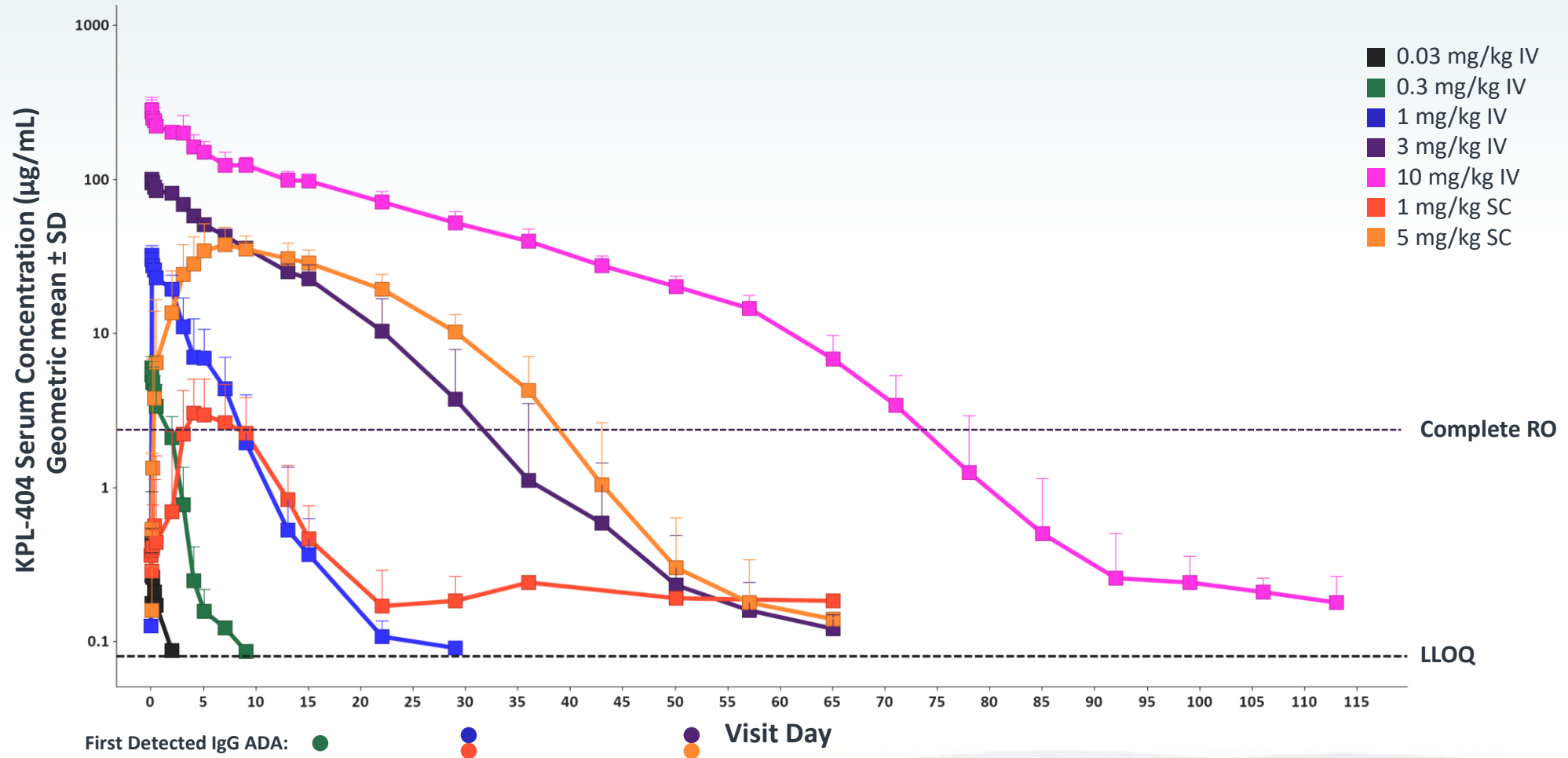
**Notes:** Unless otherwise noted dose groups included 6 active/2 placebo subjects; \*1° KLH challenge for all SAD dose groups except 0.03 and 0.3 mg/kg, 2° KLH re-challenge only in 1, 3, and 10 mg/kg IV; \*\* Cohort included 2 active and 2 placebo subjects



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

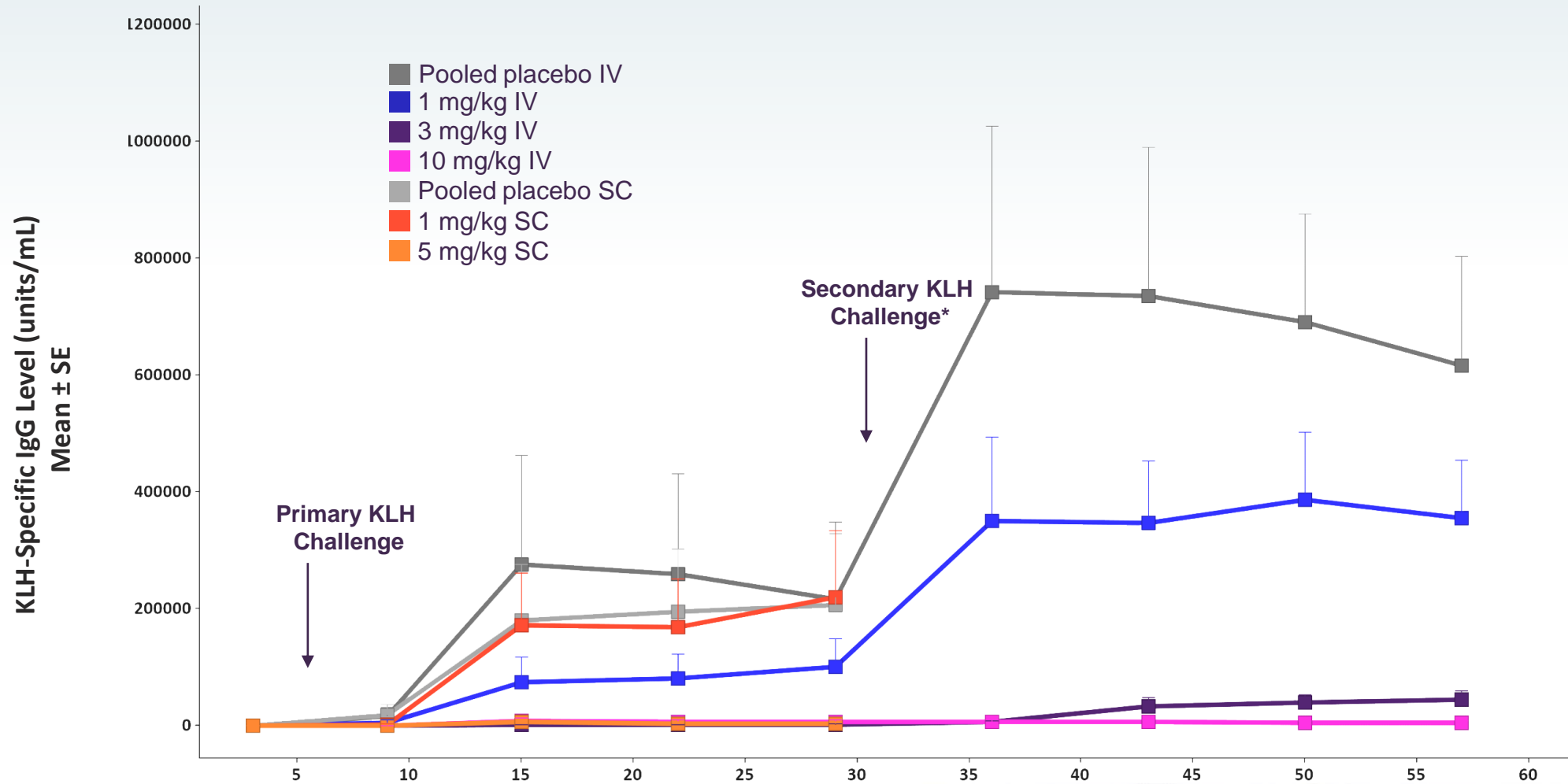
# Final Data from KPL-404 Single-Ascending-Dose Phase 1 Study

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

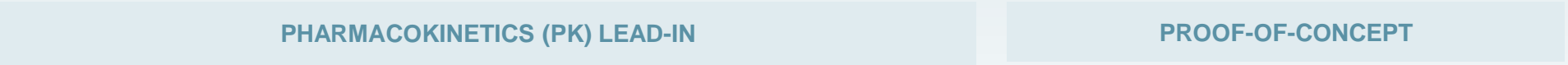


KLH = keyhole limpet hemocyanin

\*Only IV cohorts were rechallenged with KLH on day 29

# 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)**

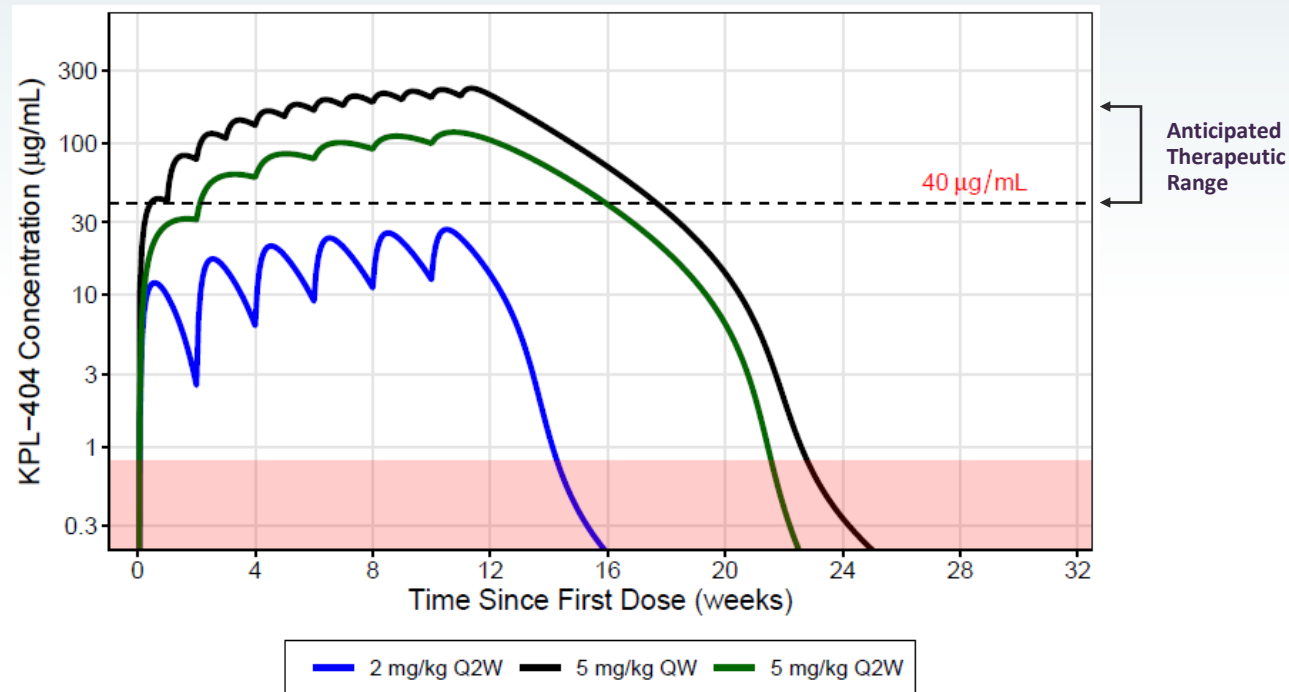
- Cohort 3 will randomize up to 75 patients
- Primary Endpoint:
  - Change from baseline in DAS28-CRP at Week 12
- Secondary Endpoints :
  - Incidence of treatment-emergent adverse events (TEAEs)
  - Pharmacokinetics ( $C_{max}$ ,  $AUC_{(0-t)}$ )

**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









# 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 Data Generated To Date Suggest it is Well-Positioned Against Competitors

Company	Product	Phase	Target	Format	Routes of Administration Being Studied	Key Dosing Regimens Being Studied
 KINIKSA	KPL-404	P2	CD40	mAb	SC	5mg/kg (~400mg) SC qwk / q2wk <sup>1</sup>
 NOVARTIS	ISCALIMAB	P2	CD40	mAb	IV SC	10mg/kg IV q4wk Up to 300mg SC qwk / q2wk <sup>2</sup>
 HORIZON	DAZODALIBEP	P2	CD154	Tn3-fusion protein	IV-only	1,500mg IV induction period transition to q4wk maintenance period <sup>3</sup>
 sanofi	FREXALIMAB	P2	CD154	mAb	IV SC	Undisclosed IV dose/regimen Undisclosed SC dose/regimen <sup>4</sup>
 ucb	DAPIROLIZUMAB PEGOL	P3*	CD154	Pegylated-Fab	IV-only	~30mg/kg IV q4wk <sup>5</sup>
 Eledon Pharmaceuticals	TEGOPRUBART	P2	CD154	mAb	IV-only	8mg/kg IV q2wk <sup>6</sup>
 Bristol-Myers Squibb Company	BMS-986325	P1	CD40	mAb	IV SC	Unknown / Various <sup>7</sup>
 Lundbeck	Lu AG22515	P1	CD154	(scFv)2-Fab	IV SC	Unknown / Various <sup>8</sup>

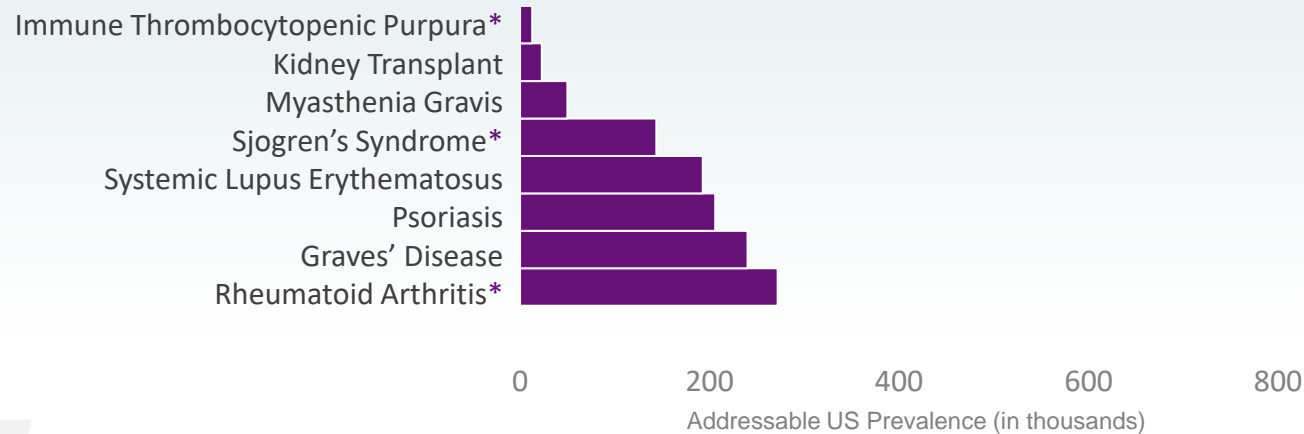


\*Dapirolizumab pegol achieved p=0.06 in SLE P2 study and Biogen / UCB are pursuing P3 (N=450); 1. Kiniksa Pharmaceuticals (NCT05198310); 2. Novartis AG (NCT03610516, NCT03905525, NCT03656562, NCT04541589, NCT04129528, NCT03827798); 3. Horizon Therapeutics (NCT04129164, NCT04163991, NCT05201469, NCT05306353); 4. Sanofi S.A. (NCT05039840, NCT04572841, NCT04879628); 5. UCB S.A. (NCT04294667); 6. Eledon Pharmaceuticals (NCT04322149); 7. Bristol-Myers Squibb (NCT05813717, NCT04684654); 8. H. Lundbeck A/S (NCT05136053).

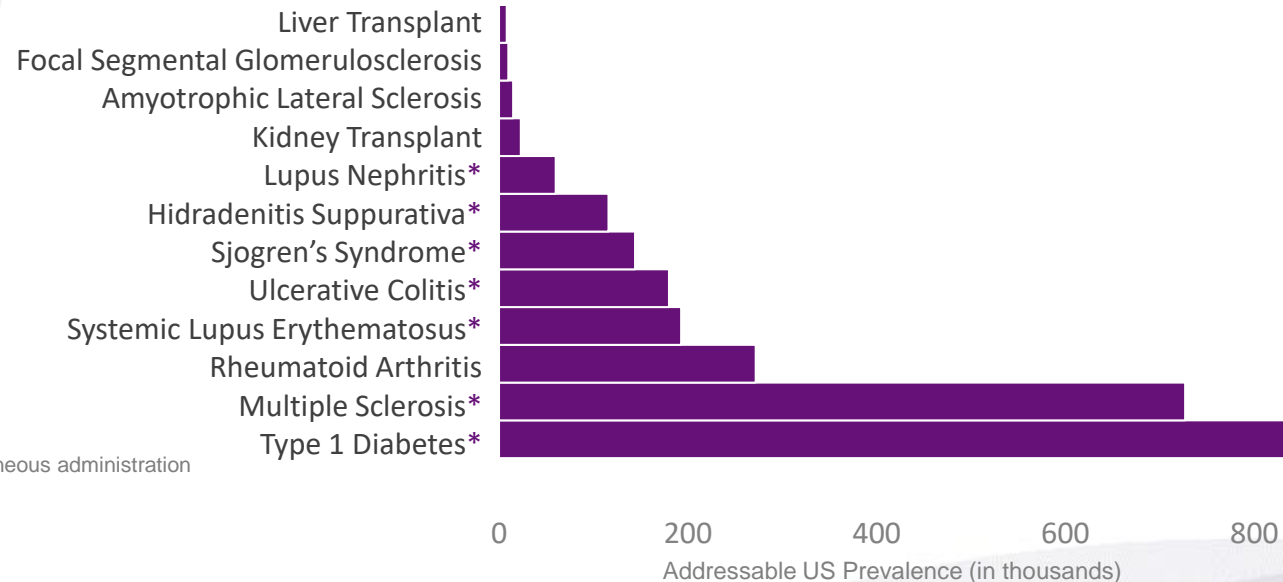
# Potential for Evaluation of KPL-404 in a Broad Range of Autoimmune Diseases

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



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 Sjogren'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: 2686; 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 et al. 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

## Second Quarter 2023

# Second Quarter 2023 Financial Results

Income Statement	Three Months Ended June 30,	
	2023	2022
Product Revenue	\$54.5M	\$27.0M
License and Collaboration Revenue	\$17.0M	\$0.0M
<b>Total Revenue</b>	<b>\$71.5M</b>	<b>\$27.0M</b>
Cost of Goods Sold	\$7.7M	\$5.0M
Collaboration Expenses <sup>1</sup>	\$14.0M	\$3.7M
Research and Development	\$23.8M	\$13.8M
Selling, General and Administrative	\$29.2M	\$23.8M
<b>Total Operating Expenses</b>	<b>\$74.6M</b>	<b>\$46.3M</b>
Income Tax Benefit (Provision)	\$16.2M	(\$0.7M)
<b>Net Income (Loss)</b>	<b>\$15.0M</b>	<b>(\$20.0M)</b>

Collaboration Expenses <sup>1</sup>	Three Months Ended June 30,	
	2023	2022
<b>ARCALYST Net Sales (RP + CAPS + DIRA)</b>	<b>\$54.5M</b>	<b>\$27.0M</b>
Profit Split-Eligible Cost of Goods Sold	(\$7.4M)	(\$4.8M)
Commercial, Marketing, Regulatory and Other Expenses	(\$19.1M)	(\$14.9M)
<b>ARCALYST Collaboration Operating Profit</b>	<b>\$28.0M</b>	<b>\$7.4M</b>
ARCALYST Licensing Proceeds	\$0.0M	\$0.0M
<b>Collaboration Expenses<sup>1</sup></b>	<b>\$14.0M</b>	<b>\$3.7M</b>

Balance Sheet	June 30, 2023	December 31, 2022
Cash, Cash Equivalents and Short-term Investments	\$185.0M	\$190.6M

**Cash reserves expected to fund current operating plan into at least 2027**



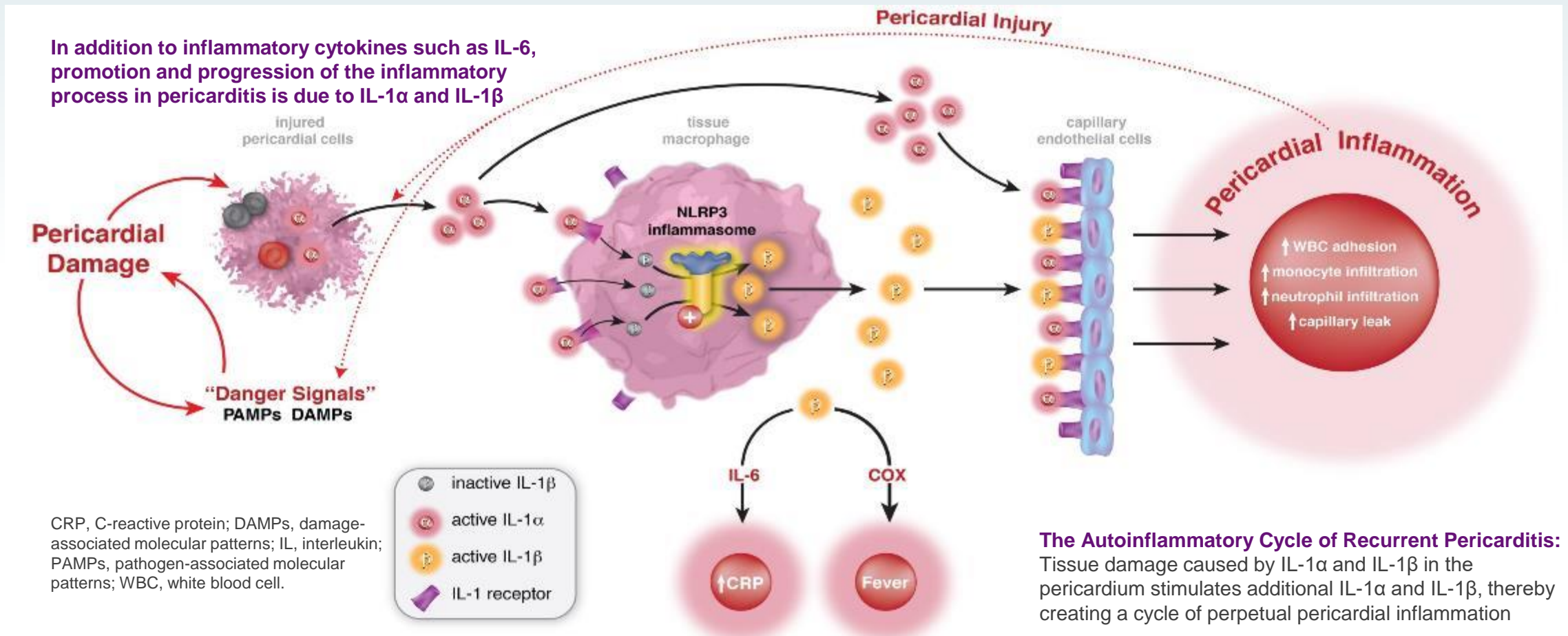
1) Subject to the terms of the definitive agreements between Kiniksa and Regeneron; 50% of ARCALYST Collaboration Operating Profit plus 50% of ARCALYST Licensing Proceeds  
 RP = Recurrent Pericarditis, CAPS = Cryopyrin-Associated Periodic Syndromes, DIRA = Deficiency of Interleukin-1 Receptor Antagonist



# Appendix

# ARCALYST (rilonacept)

# Role of IL-1 $\alpha$ and IL-1 $\beta$ in the Autoinflammatory Cycle of Recurrent Pericarditis



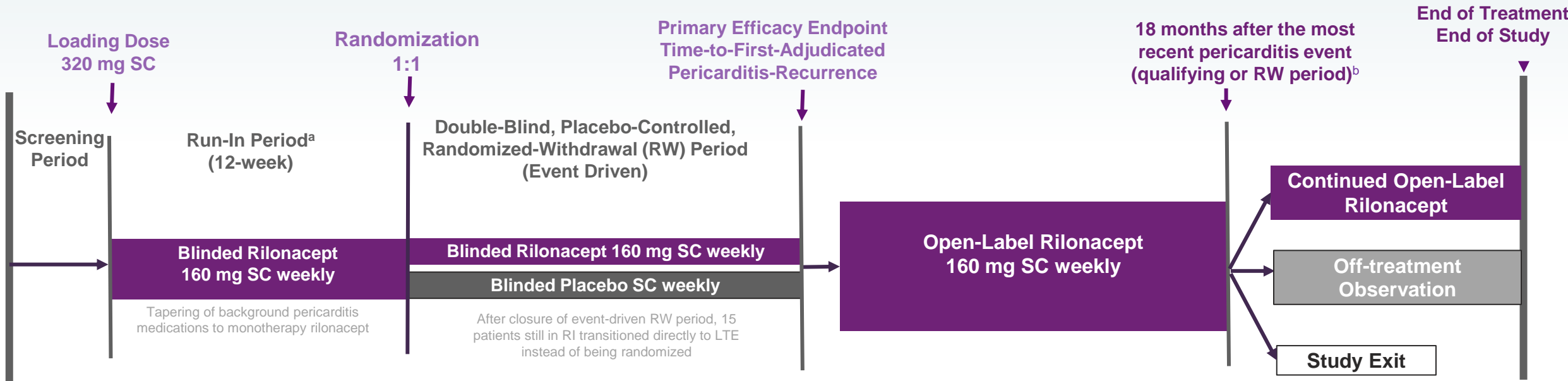
Brucato A, et al. Int Emerg Med 2018 <https://doi.org/10.1007/s11739-018-1907-x>  
Dinarello CA, et al. Nat Rev Drug Discov 2012;11:633-652

# 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)



<sup>a</sup> The duration of the run-in period was concealed from patients, so that they were blinded to the timing of randomization

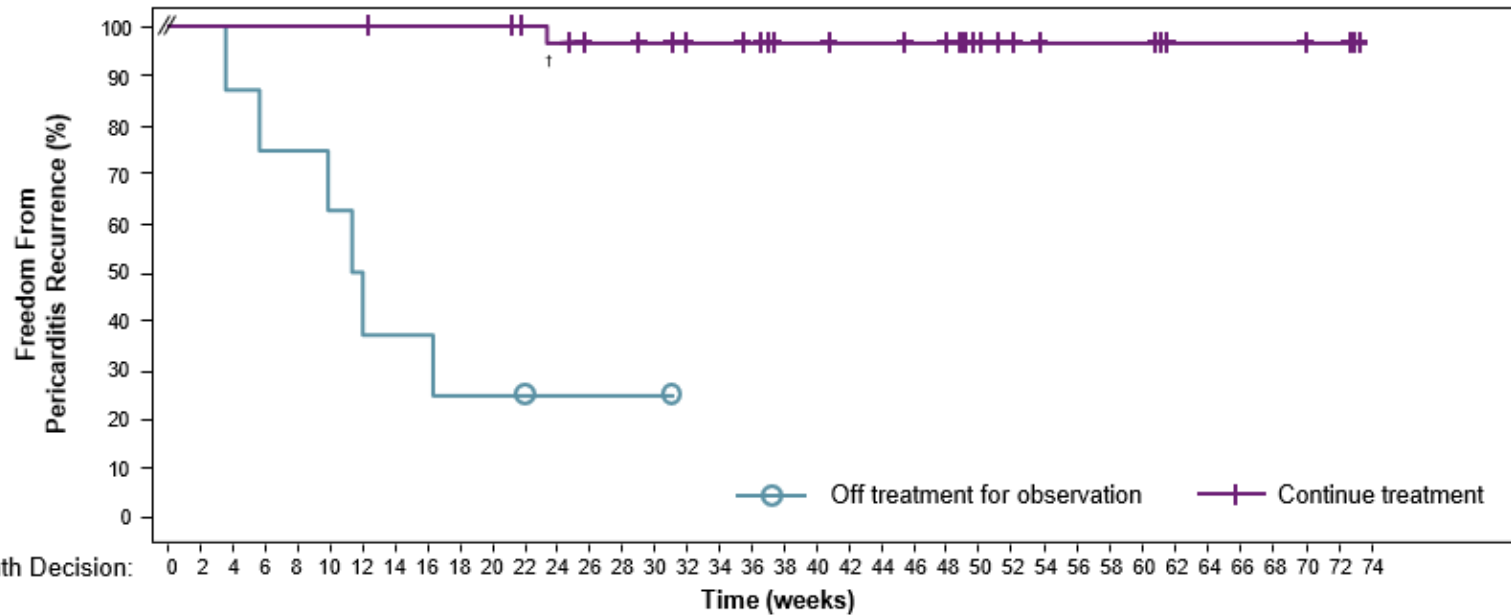
<sup>b</sup> For each patient in the LTE, a decision was made 18 months after the most recent pericarditis recurrence (Qualifying or RW period) based on clinical status and one of the following actions was taken at the investigator's discretion:

- 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<sup>1</sup>



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

	N	Patients with Recurrence, <sup>a</sup> n (%)	Weeks to Recurrence, <sup>a</sup> Median (95% CI)
Continued rilonacept treatment	33	1 (3)	NE (NE-NE)
Off treatment for observation	8	6 (75)	11.8 (3.7-NE)

<sup>a</sup>After 18-month decision. CI, confidence interval; NE, not estimable.

Week after 18-Month Decision: 0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 34 36 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	33	33	33	33	33	33	33	32	32	32	32	30	29	27	27	25	24	23	22	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	8	8	7	6	6	6	4	3	3	2	2	2	1	1	1	1	0																						

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





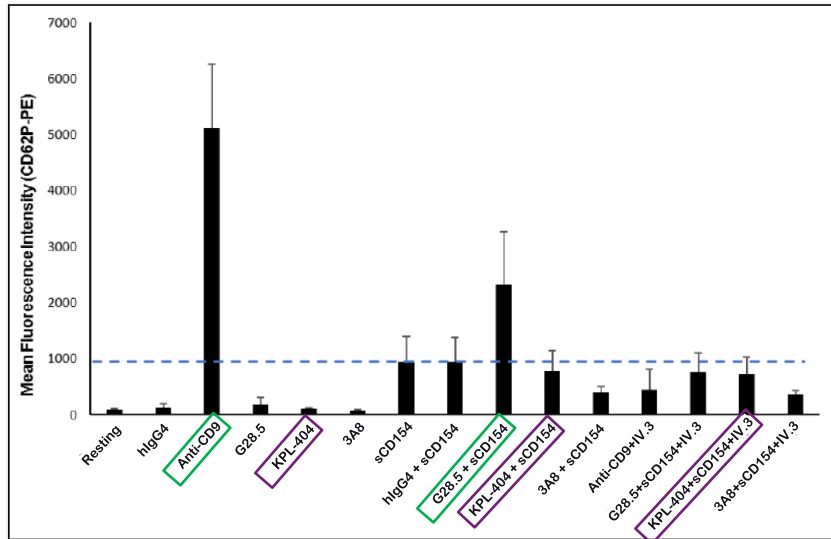
# Appendix KPL-404

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

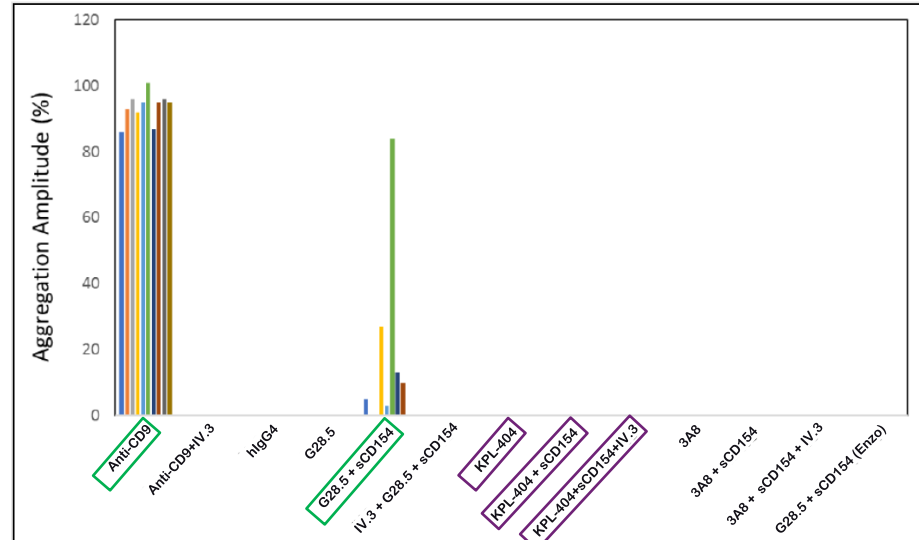
- At least three first-generation IgG1 anti-CD154 mAbs\* were associated with thromboembolic events in humans and NHPs<sup>1</sup>
- **Mechanism:** Activation of platelets through cross-linking mediated by IgG-Fc/FcγRIIa interaction
  - Platelet activation observed *in vivo* with anti-CD154 mAbs with 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<sup>1,2</sup>

**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<sup>3</sup>**

**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 (%)**



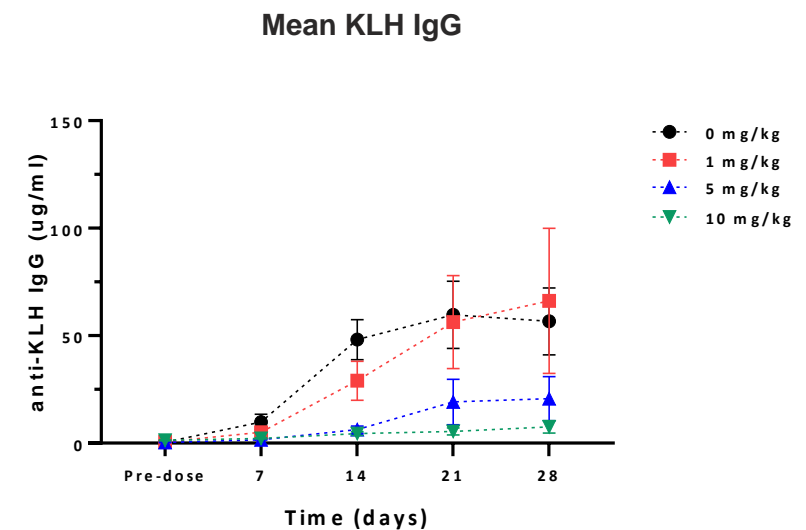
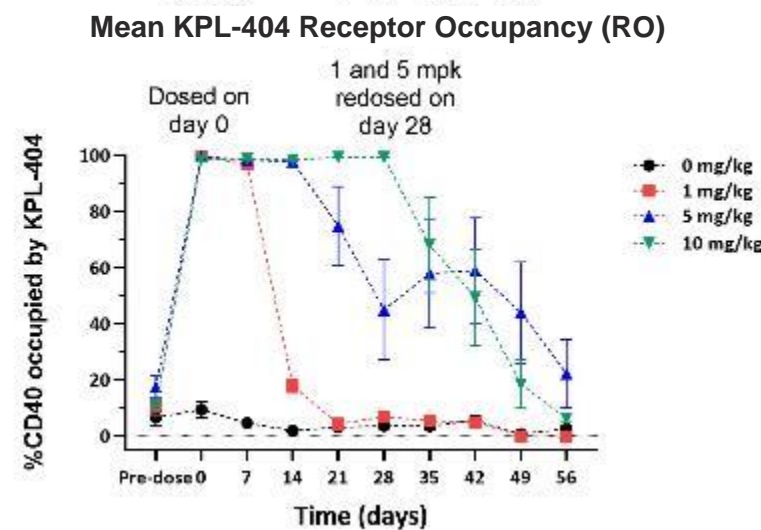
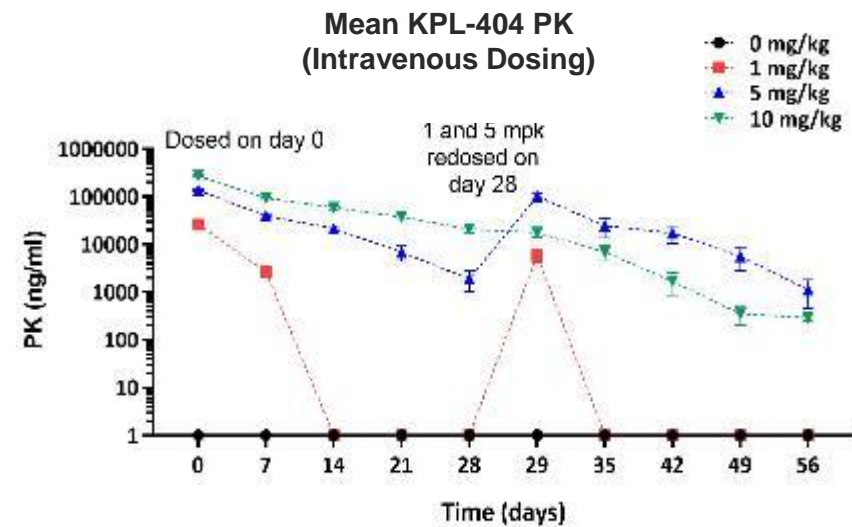
- Positive controls:
- G28.5: anti-CD40 mAb – causes sCD40L-dependent platelet activation (Langer et al., Thromb Haemost 2005; 93(06): 1137-1146)
  - Anti-CD9: mAb – causes sCD40L-independent platelet activation
  - IV.3 - anti-FcγRIIa antibody



\*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



*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*



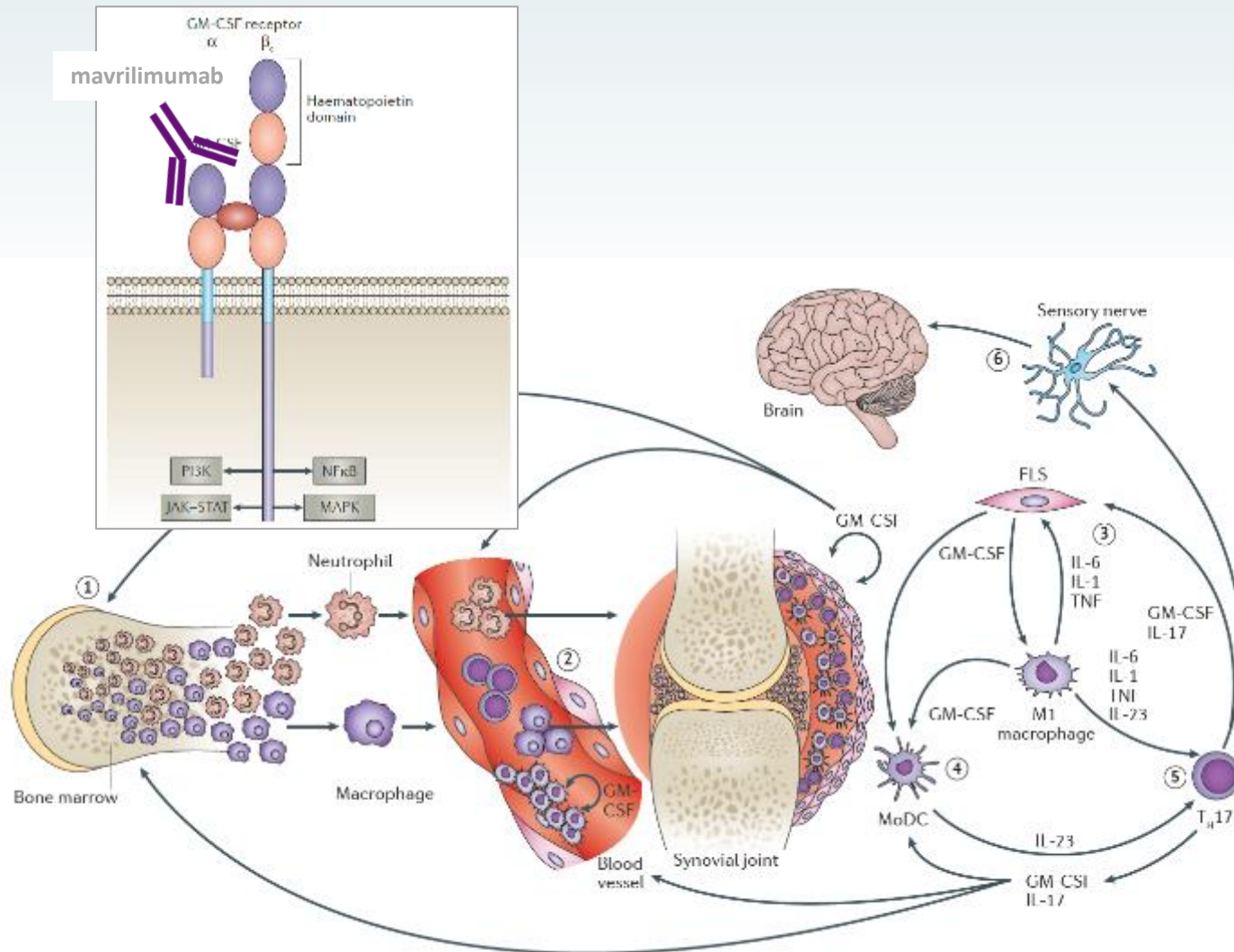
Source = 1) Poster presentation at the Keystone Symposia: Antibodies as Drugs: New Horizons in the Therapeutic Use of Engineered Antibodies: KPL-404, a CD40 antagonist, blocked antigen-specific antibody responses in an in vivo NHP model and demonstrated strong PK/PD correlation; 2) Muralidharan et al. 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



# Appendix

# Mavrilimumab

# Mavrilimumab, a GM-CSFR $\alpha$ 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- $\kappa$ B, 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



# Corporate Presentation

JULY 2023