



# Jefferies Global Healthcare Conference Presentation

June 2025

*Transform Therapies. Reimagine Lives.*

## Forward-Looking Statements

This presentation contains forward looking statements within the meaning of federal securities laws, including the “safe harbor” provisions of the Private Securities Litigation Reform Act of 1995. Such statements are based upon current plans, estimates and expectations of management of Alumis Inc. (“Alumis”) in light of historical results and trends, current conditions and potential future developments, and are subject to various risks and uncertainties that could cause actual results to differ materially from such statements. The inclusion of forward-looking statements should not be regarded as a representation that such plans, estimates and expectations will be achieved. Words such as “anticipate,” “expect,” “project,” “intend,” “believe,” “may,” “will,” “should,” “plan,” “could,” “continue,” “target,” “contemplate,” “estimate,” “forecast,” “guidance,” “predict,” “possible,” “potential,” “pursue,” “likely,” and words and terms of similar substance used in connection with any discussion of future plans, actions or events identify forward-looking statements. All statements, other than statements of historical facts, including express or implied statements regarding the sufficiency of our capital resources; our cash runway, which is preliminary, unaudited and subject to change; our competitive ability and position; our clinical pipeline; and any assumptions underlying any of the foregoing, are forward-looking statements.

Risks and uncertainties include, among other things, the risk that Alumis may be adversely affected by economic, business and/or competitive factors; the risk that the anticipated benefits and synergies of the recent merger with ACELYRIN, Inc. may not be fully realized or may take longer to realize than expected, including the risk that the combined company may not be able to be successfully integrated and achieve the growth prospects expected from the transaction; the impact of legislative, regulatory, economic, competitive and technological changes; the implementation of our business model and strategic plans for our product candidates and pipeline, and challenges inherent in developing, commercializing, manufacturing, launching, marketing and selling potential existing and new products and product candidates; the scope, progress, results and costs of developing our product candidates and any future product candidates, including conducting preclinical studies and clinical trials, and otherwise related to the research and development of our pipeline; the timing and costs involved in obtaining and maintaining regulatory approval for current or future product candidates, and any related restrictions, limitations and/or warnings in the label of any product, if and once approved; the market for, adoption (including rate and degree of market acceptance) and pricing and reimbursement of our product candidates, if approved, and their respective abilities to compete with therapies and procedures that are rapidly growing and evolving; uncertainties in contractual relationships, including collaborations, partnerships, licensing or other arrangements and the performance of third party suppliers and manufacturers; our ability to establish and maintain intellectual property protection for products or avoid or defend claims of infringement; and (xxi) potential delays in initiating, enrolling or completing preclinical studies and clinical trials.

While the list of factors presented here are considered representative, no such list should be considered to be a complete statement of all potential risks and uncertainties. For additional information about other factors that could cause actual results to differ materially from those described in the forward-looking statements, please refer to our periodic reports and other filings with the Securities and Exchange Commission (the “SEC”), including the risk factors identified in our most recent Quarterly Report on Form 10-Q. The risks and uncertainties described above and in the SEC filings cited above are not exclusive and further information concerning us and our businesses, including factors that potentially could materially affect our business, financial conditions or operating results, may emerge from time to time. Readers are urged to consider these factors carefully in evaluating these forward-looking statements, and not to place undue reliance on any forward-looking statements, which speak only as of the date hereof. Readers should also carefully review the risk factors described in other documents we file from time to time with the SEC.

The forward-looking statements included in this presentation are made only as of the date hereof. Alumis assumes no obligation and does not intend to update these forward-looking statements, even if new information becomes available in the future, except as required by law.

This presentation contains trademarks, service marks, trade names and copyrights of Alumis and other companies which are the property of their respective owners. This presentation discusses product candidates that are under clinical study and which have not yet been approved for marketing by the U.S. Food and Drug Administration. No representation is made as to the safety or effectiveness of these product candidates for the uses for which they are being studied. This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. These data involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. We have not independently verified the data generated by independent parties and cannot guarantee their accuracy or completeness. In addition, projections, assumptions, and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

This presentation shall not constitute an offer to sell or the solicitation of an offer to buy any securities, nor shall there be any sale of these securities in any state or jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or jurisdiction. Sales and offers to sell our securities will only be made in accordance with the Securities Act of 1933, as amended, and applicable SEC regulations, including written prospectus requirements.

### Additional Information and Where to Find It

Copies of documents filed with the SEC by Alumis are available free of charge under the SEC Filings heading of the Investor Relations section of Alumis’ website at <https://investors.alumis.com/>.

A decorative graphic on the left side of the slide features a microscopic view of several cells with purple and red internal structures, set against a light blue background. This graphic is partially enclosed by a white, rounded rectangular shape. Below this, there are several overlapping circles in various shades of blue, creating a layered, abstract effect.

# Well Capitalized Company with Multiple Upcoming Expected Development Milestones and Extended Runway into 2027

- › **Alumis – ACELYRIN merger created a late-stage clinical biopharma company** dedicated to innovating, developing and commercializing transformative therapies for immune-mediated diseases
- › Differentiated pipeline with multiple upcoming milestones expected, including:
  - Topline data from **Phase 3 ONWARD trials** for Alumis' ESK-001 in moderate-to-severe plaque psoriasis **expected for readout in early 1Q 2026**
  - Topline data from **Phase 2b LUMUS trial in systemic lupus erythematosus** on track for **readout in 2026**
  - **Phase 2 clinical trial initiation** for Alumis' **A-005 in MS**
  - Addition of **lonigutamab**, a subcutaneously delivered anti-IGF-1R for thyroid eye disease (TED), with committed capital for a clinical development plan to evaluate its potential differentiation
- › **Pro forma cash of ~\$619 million** as of March 31, 2025, provides **runway into 2027 beyond multiple expected clinical readouts**; post merger closing, Alumis will have **103M total shares outstanding**
- › Combined company to benefit from **world-class leadership team with proven record of operating discipline and capital efficiency**

# Late-Stage Pipeline with Multiple Near-Term Catalysts

TARGET		DEVELOPMENT				ANTICIPATED MILESTONES
		PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	
<b>ESK-001</b> (TYK2)	Moderate-to-Severe Plaque Psoriasis (PsO)					<i>Early 1Q 2026: Phase 3 topline data</i>
	Systemic Lupus Erythematosus (SLE)					<i>2026: Phase 2b topline data</i>
	Add'l indications TBD PsA, IBD, etc.	<i>Other suitable development opportunities for ESK-001 include expanded Psoriasis indication, and/or other immunological indications outside the CNS</i>				
<b>Lonigutamab</b> (anti-IGF-1R)	Thyroid Eye Disease (TED)					<i>Clinical Development Plan to be finalized mid-2025</i>
<b>A-005</b> (TYK2)	Multiple Sclerosis (MS)					<i>2025: Initiate Phase 2 in MS</i> <i>2026: Phase 2 topline data</i>
	Add'l indications TBD PAR, AD, etc.	<i>Expanded opportunities for A-005 include other neuroinflammatory or neurodegenerative indications</i>				
<b>IRF5, Additional Targets</b>	Undisclosed					<i>YE25: New clinical candidate</i>

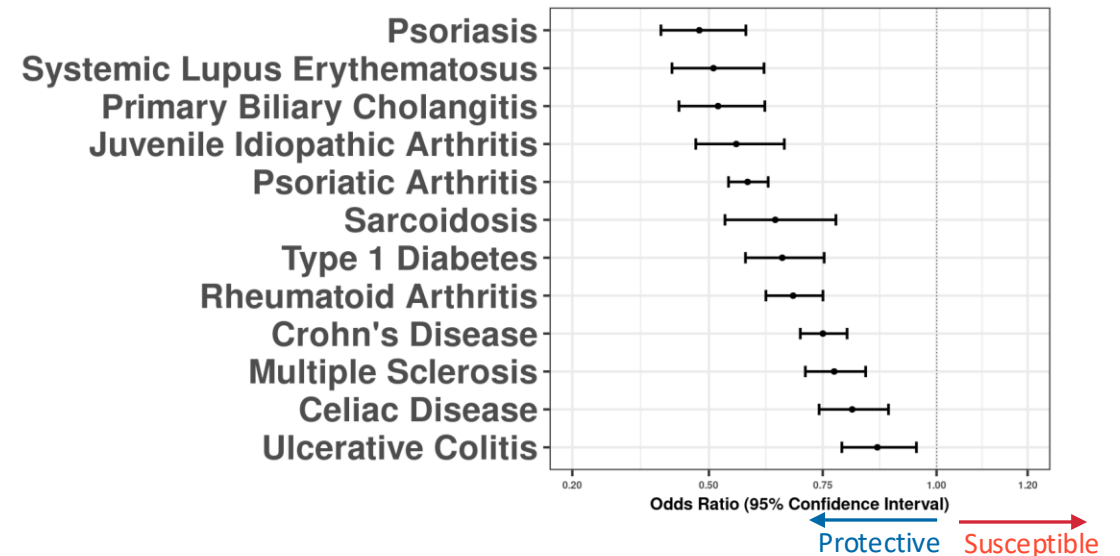
# ESK-001: TYK2i Achieving Maximal Target Inhibition



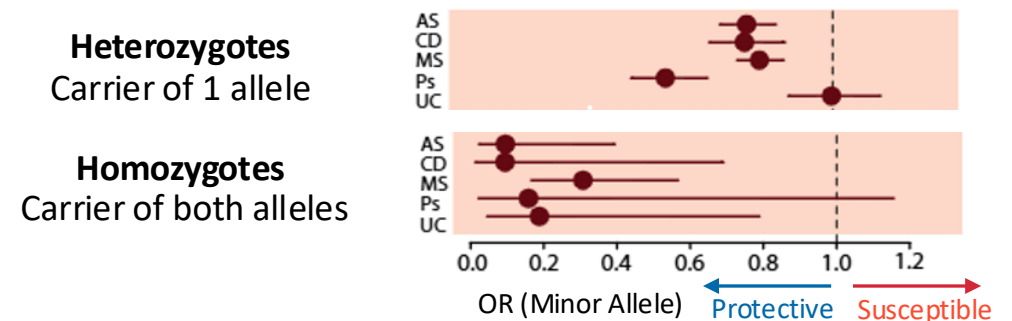
# Extensive Genetic Insights Inform TYK2 Indications

- > TYK2 P1104A Loss-of-kinase-function variant stands out in the human genome, conferring **powerful** protection from broad array of **immune-mediated diseases**
- > Out-sized protection conferred by carriers of **two P1104A variants** (homozygotes) reinforces requirement of full target inhibition to realize full therapeutic benefit
- > No known association of P1104A with serious infections, malignancy, cardiovascular events or venothromboembolism<sup>1</sup>

## TYK2 P1104A variant protective across indications of interest



## TYK2 P1104A homozygotes show greater disease protection<sup>2</sup>



# ESK-001 and A-005: A Highly Differentiated TYK2i Portfolio

## ESK-001

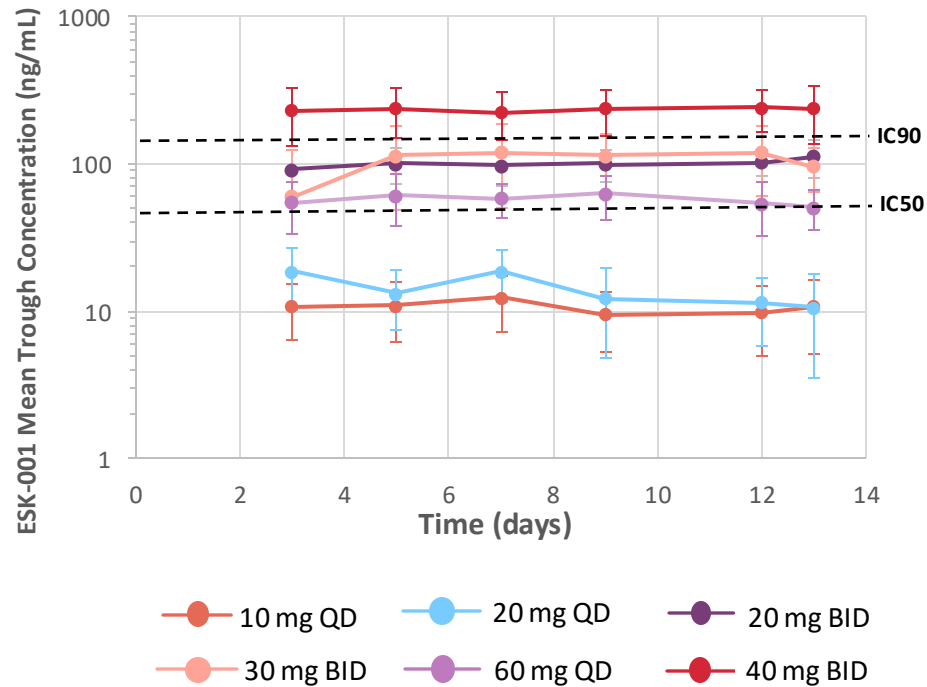
- › **Maximal Target Inhibition** Phase 3 dose fully inhibits TYK2 by every measure in skin and blood\*
- › **High Response Oral** Long term PASI and sPGA response rates competitive with high efficacy biologics
- › **Long Term Safety** No major safety signals to date with up to two years of active therapy

## A-005

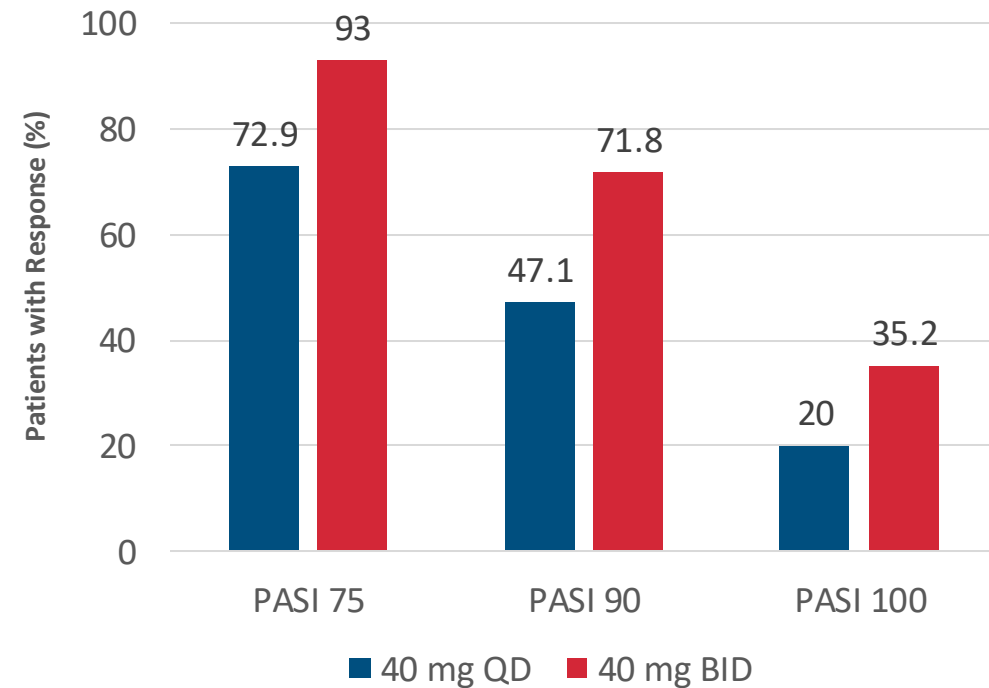
- › **Full CNS Penetration** Significant and prolonged cerebral spinal fluid (CSF) exposure
- › **Maximal Target Inhibition** High peripheral and CSF exposure achieves maximal target inhibition
- › **Phase 2 Ready** Chronic tox ongoing, CMC and clinical pharmacology support Phase 2

# Maximal Target Inhibition Led to 15-20% Increase in Clinical Response (PASI)

## Maximal Target Inhibition Maintained Across 24-hour Dosing Period (Phase 1 multidose trough PK)

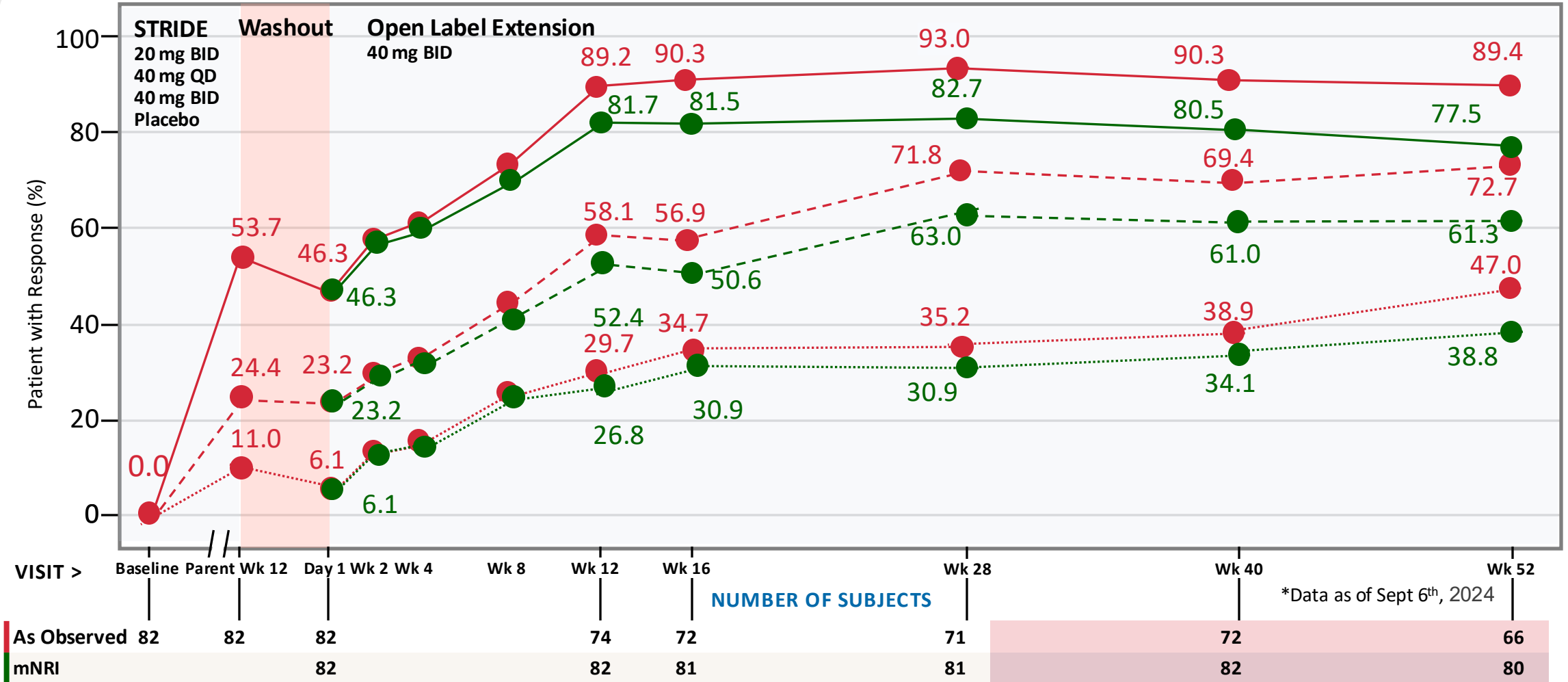


## Clinical Outcomes at 28 Weeks (OLE Phase 2, PASI as observed)



# OLE BID: Consistent Results Supporting Robustness of Methodology

OLE Treatment: ESK-001 40 mg BID



mNRI: Modified Non-Responder Imputation

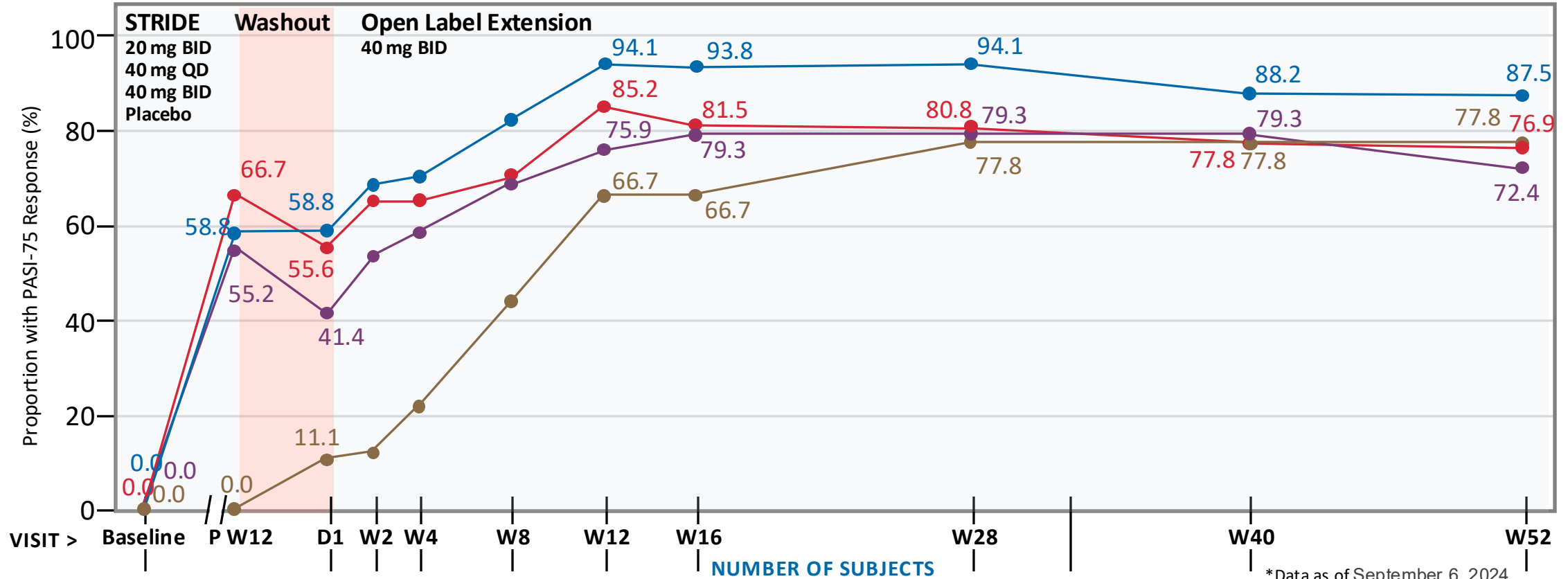


- Patient Achieving PASI-75 (AO) (%)
- - -●- - - Patient Achieving PASI-90 (AO) (%)
- .....●..... Patient Achieving PASI-100 (AO) (%)
- Patient Achieving PASI-75 (mNRI) (%)
- - -●- - - Patient Achieving PASI-90 (mNRI) (%)
- .....●..... Patient Achieving PASI-100 (mNRI) (%)

# PASI-75 Over Time for OLE 40 mg BID Cohort by STRIDE Study Dose

*Includes Patients from STRIDE Placebo, 20 mg BID, 40 mg QD and 40 mg BID Cohorts (mNRI)*

## OLE Treatment: ESK-001 40 mg BID



\*Data as of September 6, 2024

	Baseline	P	W12	D1	W2	W4	W8	W12	W16	W28	W40	W52
40mg QD (mNRI)	17	17	17	17	16	17	17	17	16	17	17	16
20mg BID (mNRI)	29	29	29	29	26	29	29	29	29	29	29	29
40mg BID (mNRI)	27	27	27	27	26	26	27	27	27	26	27	26
Placebo (mNRI)	9	9	9	9	8	9	9	9	9	9	9	9



ESK-001 40mg QD

ESK-001 20mg BID

ESK-001 40mg BID

Placebo

# Safety Profile of ESK-001 at Week 52: No Significant Safety Findings Throughout 52 Weeks

	ESK-001 40 mg QD (N=82)		ESK-001 40 mg BID* (N=147)		Overall (N=164)	
	n (%)	EAIR	n (%)	EAIR	n (%)	EAIR
Subjects with ≥ 1 TEAE	50 (61)	122.76	73 (50)	102.33	108 (66)	108.18
Subjects with ≥ 1 TE SAE <sup>1</sup>	2 (2)	3.10	4 (3)	3.39	6 (4)	3.29
Subjects with TEAE related to study drug	12 (15)	20.19	15 (10)	13.83	26 (16)	15.70
Subjects with SAE related to study drug	2 (2)	3.10	2 (1)	1.67	4 (2)	2.17
Subjects with TEAE leading to death	0	-	0	-	0	-
Subjects with TEAE leading to study drug discontinuation <sup>2</sup>	1 (1)	1.55	5 (3)	4.19	6 (4)	3.26
Subjects with TEAE ≥ Grade 3	3 (4)	4.66	6 (4)	5.12	8 (5)	4.42
<b>Most frequent TEAEs (≥5% in any treatment group)</b>						
Nasopharyngitis	10 (12)	16.88	6 (4)	5.15	14 (9)	8.09
Upper respiratory tract infection	3 (4)	4.71	13 (9)	11.66	16 (10)	9.20
Headache	5 (6)	8.28	5 (3)	4.28	10 (6)	5.71
COVID-19	3 (4)	4.74	8 (5)	6.88	11 (7)	6.17

Data are based on the safety analysis population (all treated patients). Safety data displayed are based on 06 SEP 2024 data cut of ongoing OLE study.

\*Includes subjects who were randomized to ESK-001 40 mg BID from the start of OLE and who switched from 40 mg QD to 40 mg BID.

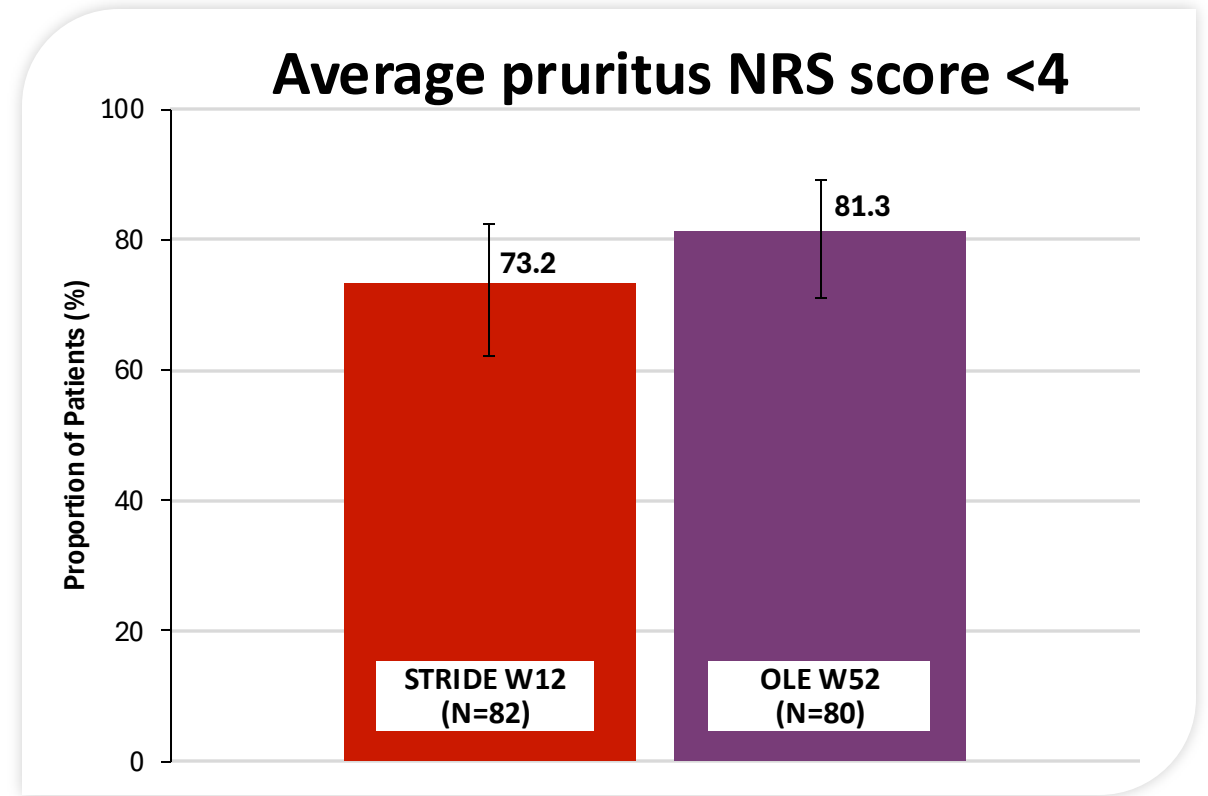
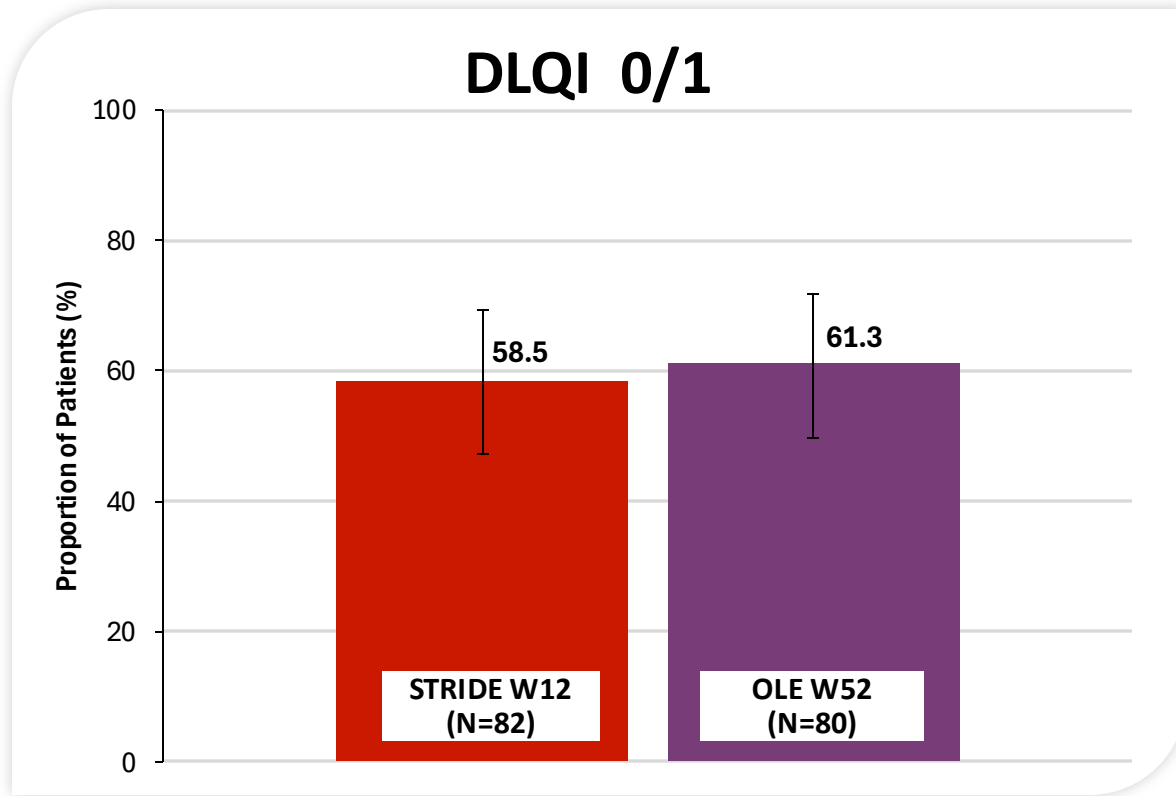
<sup>1</sup>TE SAE: inflammatory arthritis, asthma exacerbation, cellulitis, peritonsillar abscess, septic shock, sepsis, non-small cell lung carcinoma, renal cell carcinoma.

<sup>2</sup>40 mg QD: non-small cell lung carcinoma; 40 mg BID: dyspepsia, hypersensitivity, osteomyelitis, pruritus, renal cell carcinoma.

TEAE, treatment-emergent adverse event; SAE, serious adverse event; EAIR, exposure-adjusted incidence rate per 100 patient years.

# Patient-reported Outcomes Throughout Week 52 for Original 40 mg BID

*Robust and rapid improvements in quality of life and control of itch maintained over time*



Based on the modified intention-to-treat analysis population.

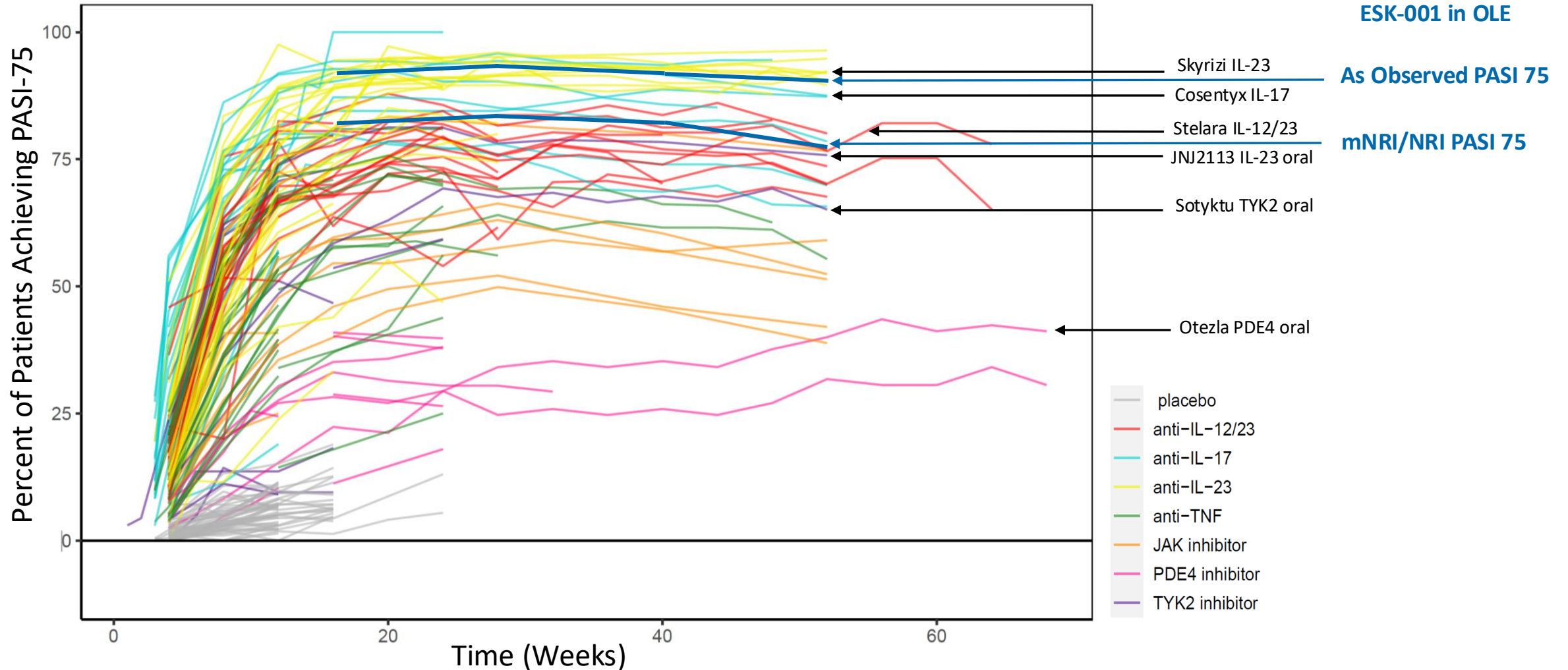
mNRI analysis: if patient discontinued due to AE or inadequate response, then imputed as a non-responder; if discontinued for other reasons, then imputed using LOCF (i.e., last observation carried forward).

DLQI, Dermatology Life Quality Index; NRS, numerical rating scale.

# Psoriasis: Current Treatment Landscape

*Maximal response is Achieved at Week 24 and Beyond*

### PASI 75 Outcomes for Recent Psoriasis Studies (79 studies, 13 molecules)



# Psoriasis: Large Market with Significant Unmet Need for High Efficacy Oral

## PLAQUE PSORIASIS

**~16M**

**MODERATE-TO-SEVERE  
PATIENTS WORLDWIDE<sup>1</sup>**

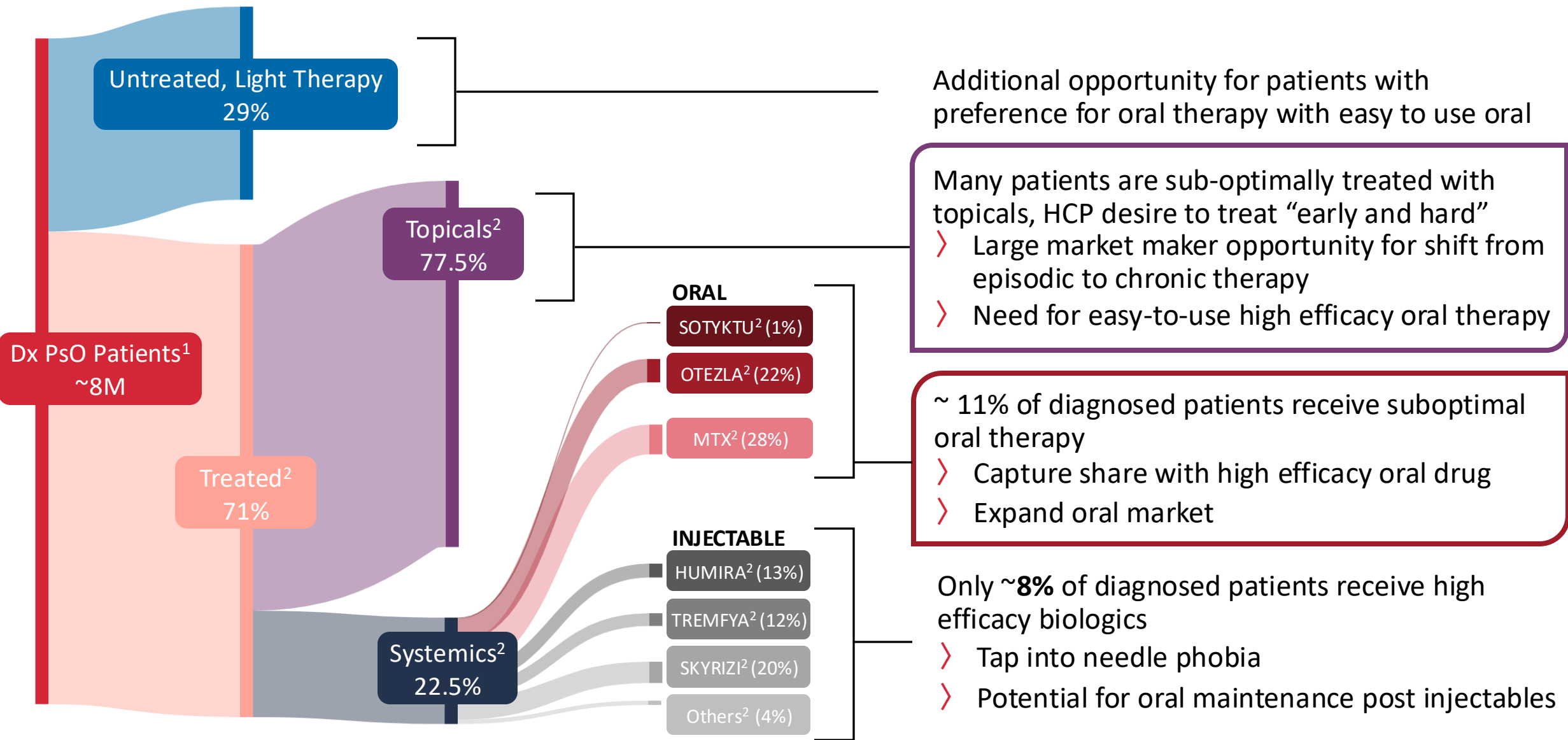
**\$25B+**

**GLOBAL MARKET<sup>2</sup>**

- > ~8M adults have plaque psoriasis in the United States, 1.5M with moderate-to-severe disease<sup>1</sup>
- > Treatment dominated by injectable biologics and sub-effective orals
  - Less than 10% of diagnosed patients receive an injectable biologic
- > Introductions of high efficacy orals are poised to drive market growth

**ESK-001 is a next-generation TYK2i with differentiated profile for oral treatment in psoriasis**

# Psoriasis: 92% of Diagnosed Psoriasis Patients are Not Treated with a Biologic Therapy\*



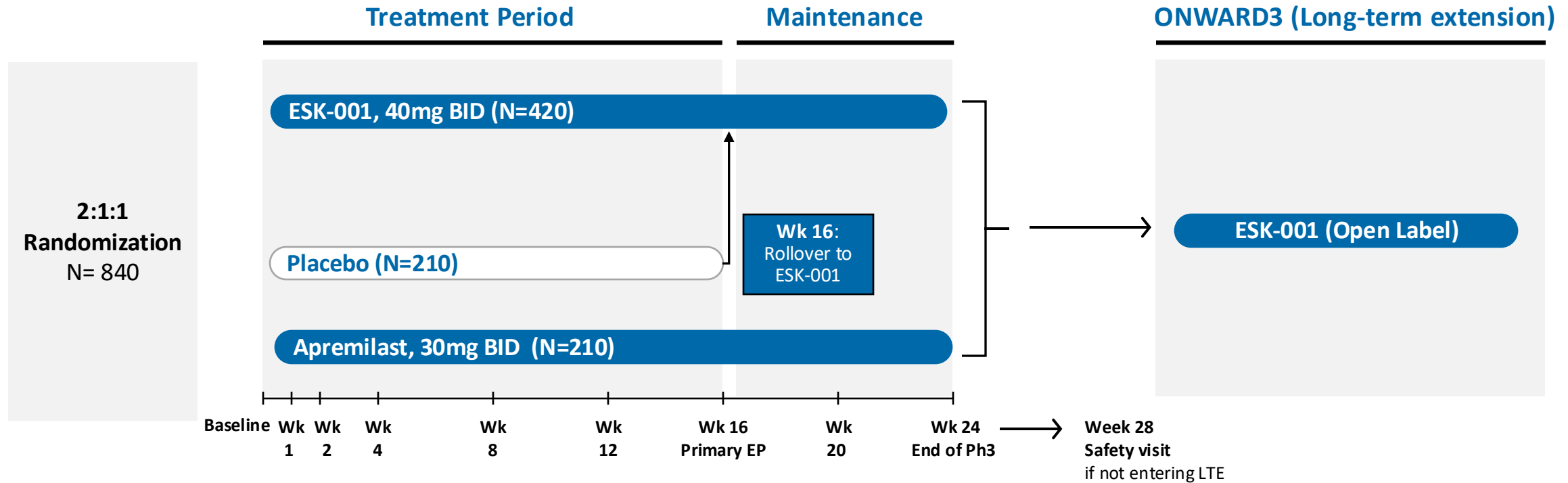
<sup>1</sup> National Psoriasis Foundation

<sup>2</sup> IQVIA Analysis, Stable and eligible newly diagnosed patients from April 2021– March 2022 utilized for longitudinal analysis; all patients have at least 24M of look forward post-Dx

\* Last data March 2024; product and market dynamics since March 2024 not reflected here

# Psoriasis: ESK-001 Phase 3 ONWARD Program

Three Studies: Two parallel Phase 3 studies and a long-term extension (LTE) study



## ESK-001-016 (ONWARD1) & ESK-001-017 (ONWARD2):

> 24-week duration, apremilast active comparator

## ESK-001-018 (ONWARD3)

> Long term extension (LTE) study, includes treatment withdrawal period

# SLE: Ongoing Phase 2b Program (LUMUS) is Designed for Speed to Market and Probability of Clinical Success


- › **High unmet need for safe and effective treatment in SLE**
  - No oral targeted treatments available at this time
  - Opportunity to expand into lupus nephritis, cutaneous lupus
- › **Multiple points of validation for TYK2 and associated pathways in SLE**
  - Strong genetic rationale from P1104A loss of function mutation
  - Strong scientific rationale for inhibition of Type I Interferon preclinically and from Saphnelo<sup>®</sup>
  - Positive Phase 2 results from competitive TYK2 molecule
- › **Ongoing global Phase 2b LUMUS trial, expected topline readout in 2026**
  - Designed as first of two potentially pivotal trials
  - Primary endpoint BICLA at week 48, target enrollment: n=388 patients
  - Includes OLE for long term safety database
- › **Potential for accelerated regulatory pathway with one additional confirmatory Phase 3 trial prior to seeking approval**

# LUMUS Trial Incorporates Key Learnings from Past SLE Trials

## Lupus Clinical Development Challenges

- › High placebo response rates responsible for failed SLE trials driven by:
  - Insufficient disease activity
  - Excessive concomitant medications
  - Incorrect/inconsistent use of composite outcome measures
  - Trial design and/or conduct issues (inexperienced sites, lack of enrollment and outcome adjudication processes, inadequate investigator training)

## Alumis Success Factors to Mitigate Challenges

- › LUMUS trial requires stringent disease activity criteria
  - › Enrollment and outcome adjudication processes, real time data consistency checks implemented
  - › Concomitant medications minimized; steroid taper incorporated
  - › Extensive and ongoing site training in endpoint assessments
- 

## Alumis-Kaken Collaboration for ESK-001 in Dermatology in Japan

- › Collaboration underscores ESK-001's commercial potential in PsO and leverages Kaken's regional capabilities and expertise in novel dermatology treatments
- › Non-dilutive capital extends current runway through Phase 3 PsO data readout
- › Maintains optionality for global commercialization strategy, including potential global partnering

## Deal Background and Terms

- › **Kaken:** Specialty pharmaceutical company in Japan with strong experience in developing and commercializing novel pharmaceuticals with a focus on dermatology
- › **Upfront and Near-Term Payments to Alumis:** \$40M (\$20M upfront, \$20M in 2025-2026 non-contingent payments)
- › **Additional Regulatory and Commercial Milestones and Option Fees:** Approx. \$140M in aggregate
- › **Tiered Royalties:** Low double-digits to mid-twenties on aggregate net sales in Japan
- › **Indications Covered:** Dermatological indications including PsO, PsA, CLE, etc.
- › **Expansion:** Options for rheumatology and GI diseases

› *Alumis receiving \$40M near-term for Japan, <5% of Worldwide Psoriasis Market (estimated at \$600M in 2024)<sup>1</sup>, highlighting significant opportunity for Alumis in ROW*

**Lonigutamab:  
Next Generation Anti-IGF-1R**



# Lonigutamab

*A Next-Generation Subcutaneous Anti-IGF-1R Therapy With Best-in-Class Potential in TED*



## Best-In-Class Potential

- › Uniquely differentiated MOA: non-competitively binding IGF-1R antagonist in TED
- › Robust and compelling Phase 1/2 clinical data that may enable selection of dose that optimizes efficacy and safety
- › Potential for commercially attractive product profile with IV-like efficacy and reduced safety barriers for adoption

## Lonigutamab Development Plan

- › **Capital Investment:** Initial commitment of approximately \$25-\$50M to evaluate potential differentiation in TED; investment has been included in plan for cash runway into 2027
- › **Development Plan:** Goal is to design well-informed clinical development plan to assess and maximize the opportunity for lonigutamab. Intend to utilize the combined companies' deep scientific, development, and program expertise.
- › **Timing:** Expect to finalize well-informed and capital efficient clinical development program mid 2025

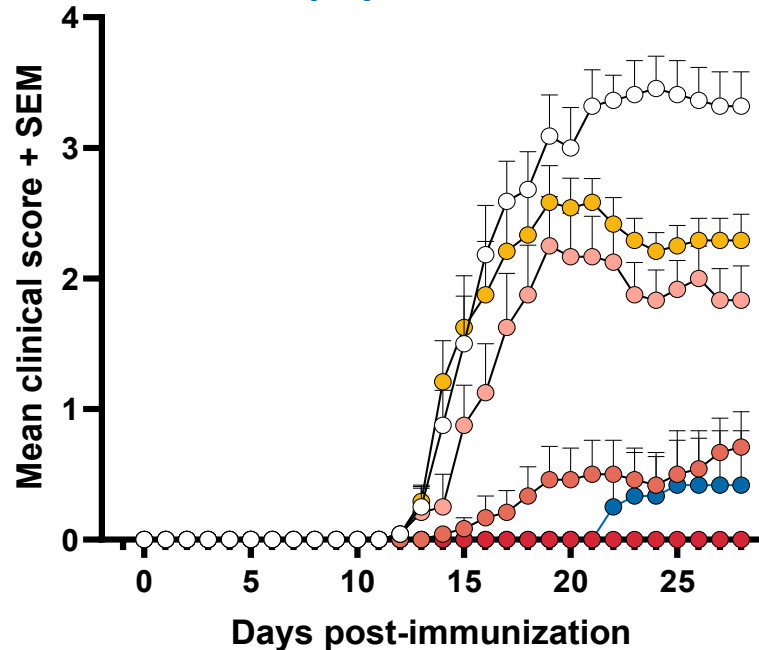
**A-005: First-in-Class,  
CNS-Penetrant  
Allosteric TYK2 Inhibitor**



# A-005 Achieved Significant Dose-Dependent Response Preclinically

*In Both Prophylactic and Therapeutic EAE Models (MOG peptide) with Once-Daily Oral Dosing*

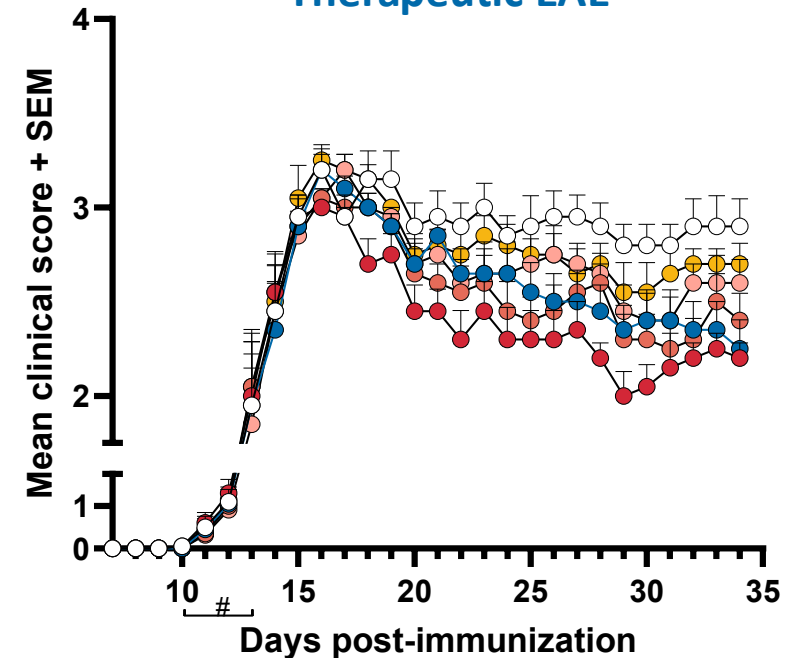
## Prophylactic EAE



Once daily oral dosing initiated 1 day prior to EAE induction; Mann-Whitney U test vs vehicle,  $p < 0.05$  for 1 mg/kg (day 20-28), 3 mg/kg (day 20-28), 10 mg/kg (day 14-28), 30 mg/kg (day 14-28)

- Vehicle (n=10)
- 1 mg/kg A-005 (n=10)
- 3 mg/kg A-005 (n=10)
- 10 mg/kg A-005 (n=10)
- 30 mg/kg A-005 (n=10)
- 3 mg/kg Fingolimod (n=10)

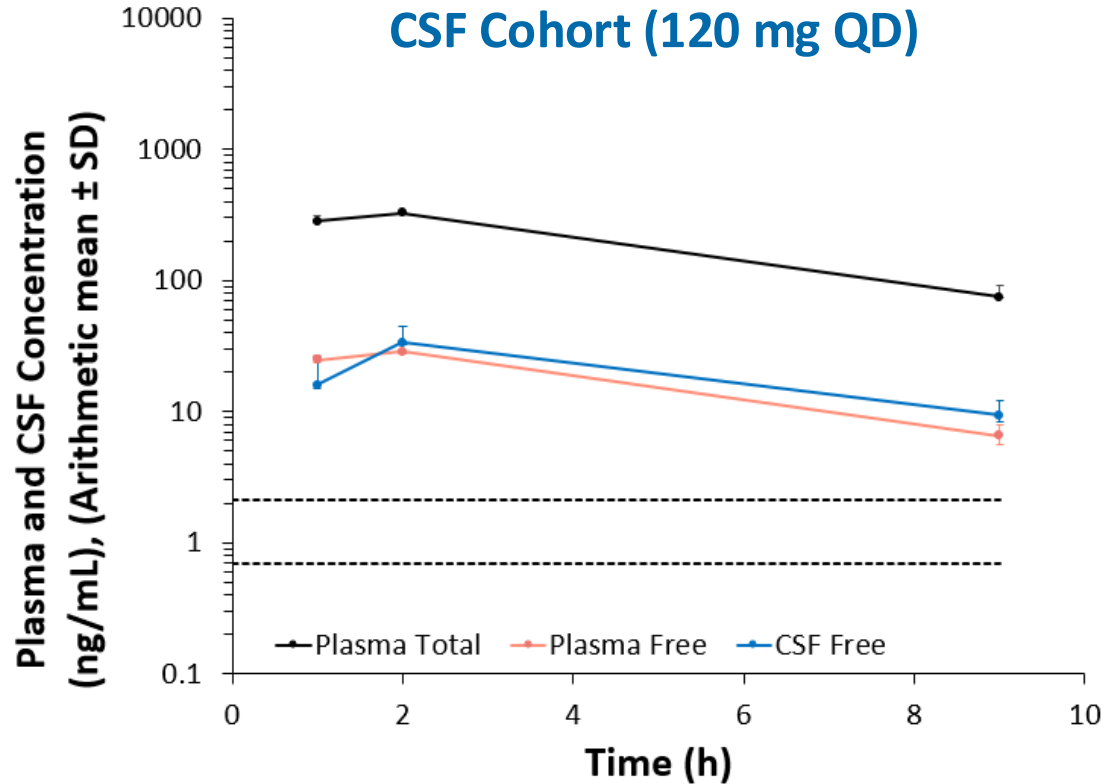
## Therapeutic EAE



Once daily oral dosing initiated the onset of EAE clinical signs (# enrollment period, days 10-13). Experience continued until each mouse had been dosed for at least 21 days (day 34). Mann-Whitney U-test vs vehicle,  $p < 0.05$  for 10 mg/kg (day 21, 25-27, 29-32, 34), 30 mg/kg (day 18-34)

- > Complete suppression of EAE achieved in prophylactic EAE model, and significantly effective in a therapeutic EAE model
- > A-005 recapitulates TYK2 human loss-of-function variant knock-in mouse EAE data

# A-005 Demonstrated Ability to Cross Blood-Brain Barrier with High Levels of Exposure in Cerebral Spinal Fluid (CSF) in Phase 1



## PK Summary: CSF Cohort (120 mg QD)

	$T_{max}$ (h)	$C_{max}$ (ng/mL)	$C_{9h}$ (ng/mL)
<i>Plasma<sub>Total</sub>, mean (SD)</i>	1.5 (NA)	327 (0.6)	75 (16)
<i>Plasma<sub>Free</sub>, mean (SD)</i>	1.5 (NA)	29 (0.1)	7 (1.4)
<i>CSF<sub>Free</sub>, mean (SD)</i>	2.0 (NA)	34 (10.9)	9 (2.7)
<i>Ratio (CSF<sub>free</sub>/Plasma<sub>free</sub>)</i>	NA	1.2	1.4

> A-005 concentration in CSF significantly above IC90 levels, >4 times higher than IC<sub>90</sub> measured in microglia cells in vitro.

# Clinical Development Strategy for A-005

**Goal:** Establish Clinical Proof-of-Concept in First Neuroinflammatory Indication by 2026

## Positive Phase 1 Clinical Trial Completed

- › Established CSF exposure and ability to maximally inhibit TYK2 across broad range of Ph2 doses
- › Favorable safety profile at all doses tested with no series treatment emergent adverse events

## Phase 2 Readiness: Nonclinical CMC and toxicology programs ready to enable Ph2 initiation in 2025

- › Enables range of studies including treatment beyond 3 months and long-term extension studies

## Future Clinical Development

- › Phase 2 study in MS patients currently expected to be initiated in 2H25 with readout in 2026
- › Potential expansion into neurodegenerative diseases

# Recent Achievements and Anticipated Multiple Near-Term Milestones

2025



- 1Q25 ESK-001 – PsO 52-Wk Phase 2 OLE Data for Late-Breaker Presentation at AAD
- 2Q25 Alumis / ACELYRIN Merger Close
- Mid-25 Finalize Plan for Lonigutamab
- 2H25 A-005 – MS Phase 2 Initiation
- 2H25 IND Filing for 3rd Clinical Candidate
- 2025 Once-daily formulation established for ESK-001

2026



- 1Q26 ESK-001 – PsO Phase 3 Topline Data
- 2026 ESK-001 – SLE Phase 2b Topline Data
- 2026 A-005 – MS Phase 2 Topline Data

Thank You!

