

Unlocking the power of a patient's own biology for the treatment of rare disease

**Investor Presentation** January 2025



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# **Quince Therapeutics investment highlights**



) Risk-mitigated pivotal Phase 3 clinical trial of lead asset EryDex underway in pediatric rare disease



EryDex targets Ataxia-Telangiectasia (A-T) with no currently approved treatments and estimate \$1+ billion\* global peak commercial opportunity



) Encouraging Phase 3 clinical trial results in prior study of patients with A-T



 Selected Duchenne muscular dystrophy (DMD) as second indication for EryDex given high unmet need

S Current cash runway through pivotal Phase 3 topline results into 2026

\*\$1+ billion estimated global peak commercial opportunity is based on IQVIA Medical Claims (Dx), PharmetricsPlus (P+), and IQVIA Analytics in the U.S. and the company's internal estimates and assumptions outside the U.S.

# Corticosteroids encapsulated in autologous red blood cells designed to significantly alter drug characteristics

Autologous red blood cells (RBCs) ideal vehicle for drug delivery with *potential* for:

- Improved biodistribution that may enable slow release of drug while circulating through tissues, organs, and capillary beds where therapeutic effect is desired
- ✓ Altered pharmacokinetics and pharmacodynamics, including long circulating half-life, and altered or improved tissue distribution, may significantly increase desired therapeutic effect and/or improve safety profile
- ✓ Improved biocompatibility through use of autologous RBCs, thereby avoiding issues with donor compatibility (no engineered or donor RBCs utilized)
- Mitigating chronic toxicity and adrenal suppression associated with long-term corticosteroid use

Autologous Intracellular Drug Encapsulation (AIDE) Technology



20+ years of research & development and \$100 million invested in AIDE technology



# Lead asset EryDex encapsulates dexamethasone sodium phosphate (DSP) for once monthly treatment



# Why are conventional corticosteroids toxic?

#### Well-described dose-limiting toxicity of corticosteroids

#### Adrenal suppression

- Low cortisol levels
- Cushingoid appearance
- Hirsutism
- Loss of bone mineral density
- Growth retardation in pediatrics
- Delay in puberty
- Delay in puberty

- Elevated glucose resulting in hyperglycemia and diabetes
- Immunosuppression resulting in infections



Note: Information represented does not reflect a completed comparative study of EryDex versus oral/IV administration of dexamethasone, but rather provides a comparison of published corticosteroid pharmacokinetic information relative to company data regarding EryDex. IC50 and SC50 refer to pharmacodynamic parameters of which IC50 reflects drug concentration eliciting 50% of the maximum inhibition and SC50 reflects drug concentration eliciting 50% of the maximum stimulation References: Krzyzanski, Journal of Pharmacokinetics and Pharmacodynamics (2021) 48: 411-438; Aljebab, PLoS ONE 12(1):e0170259. doi:10.1371/journal.pone.0170259, January 26, 2017; Montanha et al, Frontiers in Pharmacology (2022) 13: 814134.

# **EryDex designed to optimize dexamethasone delivery through once monthly dosing in A-T patients**

Average concentration-time profile for plasma dexamethasone in EryDex



— Average Concentration EryDex monthly dose = 17.4 mg



Note: Pharmacokinetic (PK) curve from Population PK model (smoothed) based on company's prior studies of EryDex. IC50 and SC50 refer to pharmacodynamic parameters of which IC50 reflects drug concentration eliciting 50% of the maximum inhibition and SC50 reflects drug concentration eliciting 50% of the maximum stimulation. References: Montanha et al, Frontiers in Pharmacology (2022) 13: 814134; Krzyzanski et al, Journal of Pharmacokinetics and Pharmacodynamics (2021) 48: 411-438.

### No currently approved treatments for A-T patients



A-T is an inherited rare neurodegenerative and immunodeficiency disorder caused by mutations in ATM gene

 Estimated prevalence of approximately 10,000 patients with A-T in U.S., U.K., and EU4 countries\*

Neurological symptoms worsen until patients are wheelchair dependent, usually by age 12 – with teenage years typically marked by repeated infections, pulmonary impairment, and malignancies

Median lifespan of approximately 25-30 years

Currently no approved treatments for A-T and no currently known effective approaches to delay progression of disease



\*Patient population based estimated A-T patient population are based on IQVIA Medical Claims (Dx), PharmetricsPlus (P+), and IQVIA Analytics in the U.S. and the company's internal estimates and assumptions outside the U.S.

# **Rapid neurological progression in A-T**

Symptoms progress quickly from 6 to 9 years of age





\*Scores based on the Crawford Quantitative Neurologic A-T Scale (100=normal). References: Rothblum-Oviatt C, et al. Orphanet J Rare Dis. 2016;11(1):159; Crawford TO, et al. Neurology. 2000;54(7):1505–1509.

# **Encouraging EryDex Phase 3 clinical trial results in prior ATTeST study**



- Improvement observed in
   6 to 9 year-old subgroup
   across multiple endpoints
- At 12 months, EryDex well-tolerated with no serious safety concerns
- 3+ years of ATTeST OLE observed no serious safety concerns
- Apply key learnings from ATTeST to pivotal NEAT study





Note: Company ATTeST clinical trial data (ClinicalTrials.gov ID: NCT02770807) presented reflect nominal p-values for ICARS values in ITT populations. Values reflect Least Square Means (LSM) difference from placebo and the P value presented • ICARS = International Cooperative Ataxia Rating Scale • mICARS = Modified International Cooperative Ataxia Rating Scale • mICARS = Rescored Modified International Cooperative Ataxia Rating Scale.

#### **Pivotal Phase 3 NEAT study design**

- Pivotal study being conducted under Special Protocol Assessment (SPA) agreement with FDA Allows for NDA submission, assuming positive results, following a single global Phase 3 NEAT study
- Multicenter, randomized, double-blind, placebo-controlled study with six infusions scheduled once every 21 to 30 days Enrolled first patient in global Phase 3 NEAT clinical trial of EryDex in June 2024 Topline data expected in fourth guarter of 2025

#### **32 patients with A-T enrolled as of mid-November 2024**

Plan to enroll approximately 86 patients with A-T ages 6 to 9 years old (primary analysis population) Approximately 20 additional patients with A-T ages 10 years or older also will be included Participants will be eligible to transition to an open label extension (OLE) study

#### > Primary efficacy endpoint - RmICARS

RmICARS measures primarily focused on posture and gait disturbance



# Attractive commercial opportunity for EryDex lead indication

# **\$1+ billion**\*

estimated global peak commercial opportunity for A-T indication alone

#### **EryDex for A-T**

Sestimated prevalence of approximately 10,000 patients with A-T\* in U.S., U.K., and EU4 countries with no currently approved A-T therapies

First-to-market potential and granted orphan drug designation from FDA and EMA, and Fast Track designation from FDA for the treatment of A-T

Attractive rare disease pricing comparables with recently approved treatment for Friedreich's ataxia indication (Biogen's Skyclarys WAC pricing at \$370K/year)

Highly scalable manufacturing infrastructure in place with low direct cost of goods

CE mark in Europe and strong patent protections with IP exclusivity until at least 2034 globally and 2035 in U.S.



\*\$1+ billion estimated global peak commercial opportunity and estimated A-T patient population are based on IQVIA Medical Claims (Dx), PharmetricsPlus (P+), and IQVIA Analytics in the U.S. and the company's internal estimates and assumptions outside the U.S.

# A-T represents significant U.S. commercial opportunity



**Physicians expect usage of EryDex in broad A-T Population** 

Given high unmet need and limited treatment options, HCPs expected utilization across all patient segments

Uptake in Ambulatory Patients	Uptake in Non-Ambulatory Patients
~90% OF PATIENTS	~75% OF PATIENTS
<ul> <li>Physicians were encouraged by the clinically meaningful data in ambulatory patients and expected broad utilization</li> <li>Physicians anticipated use in both classical and mild patients</li> </ul>	<ul> <li>Given limited treatment options, physicians were largely compelled to try EryDex in non- ambulatory patients, despite lack of trial data in this segment</li> </ul>



## **Selected DMD as second development program for EryDex**

EryDex

For indications beyond A-T where chronic steroid treatment is – or has the potential to become – a standard of care Duchenne muscular dystrophy (DMD) ideal second indication for EryDex given well-described clinical benefits of steroids in patients with DMD

Generating Phase 2 clinical trial study design to evaluate EryDex for the potential treatment of patients with DMD in 2025

Potential to start Phase 2 clinical study in 2025 in corticosteroid intolerant populations, representing majority of patients with DMD

Investigating other potential indications for EryDex spanning across ataxias, neurology, neuromuscular, hematology, and autoimmune diseases, with a focus on severe rare diseases



Prioritized list of rare disease indications where chronic corticosteroid treatment is – or has the potential to become – a standard of care if there were not corticosteroid-related safety concerns

Potential to advance directly into Phase 2 clinical studies for broad range of rare disease indications

#### Neurology/Neuromuscular

- Ataxia telangiectasia
   (1<sup>st</sup> indication)
- Myasthenia Gravis
- **Becker muscular dystrophy**
- Duchenne Muscular Dystrophy (2<sup>nd</sup> indication)
- S Limb-girdle muscular dystrophy



#### Inflammation & Immunology

- > Autoimmune hepatitis
- Hashimoto's encephalopathy

- Dermatomyositis
- > Pemphigus vulgaris

) Chronic inflammatory demyelinating polyradiculoneuropathy

#### Rheumatology

**Pediatric lupus** 

**Pulmonary sarcoidosis** 

Juvenile idiopathic arthritis



#### **Seasoned leadership team**





Strong cash position to reach meaningful milestones with approximately \$47.8 million in cash, cash equivalents, and short-term investments as of September 30, 2024

Well-capitalized with sufficient cash runway into 2026



#### Lean operating model and disciplined spending funds:

- EryDex through Phase 3 NEAT topline results and preparing for potential NDA and MAA submissions, assuming positive study results
- ~\$20 million NEAT study and ~\$15 million OLE direct trial costs
- Investigation of other potential indications for EryDex, including DMD



**Evaluate potential strategic partnerships to out-license of ex-U.S. rights to provide additional operating runway** 

### Key clinical and corporate milestones

2024	2025				
S First patient enrolled in Phase 3 NEAT clinical trial	S Completion of Phase 3 NEAT study enrollment				
Selected DMD as second indication for EryDex and generating Phase 2 study design	> Phase 3 NEAT clinical trial topline results in Q4 2025				
Ompleted identification of other potential rare disease indications for EryDex	Prepare for potential NDA and MAA submissions in 2026, assuming positive study results				
Received Fast Track designation for A-T from FDA	Initiate DMD Phase 2 clinical study for second EryDex indication				
Initiation of Phase 3 NEAT open label extension	> Potential out-licensing of ex-U.S. regional territories to				
Phase 3 ATTeST data published in The Lancet Neurology Sep 2024	provide runway through approval				

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#### Key investment takeaways

#### **O** Compelling clinical proposition

- Pivotal Phase 3 clinical trial of EryDex for A-T underway to evaluate lead rare disease asset with topline results expected in fourth quarter of 2025
- Risk-mitigated clinical and regulatory approach supported by optimized clinical trial design, special protocol assessment (SPA) agreement with FDA, Fast Track designation from FDA, and encouraging Phase 3 clinical trial results in prior study

#### > Attractive commercial opportunity

- Lead asset EryDex targets rare disease A-T with no currently approved treatments and estimated \$1+ billion\* global peak commercial opportunity
- Selected DMD as second indication for EryDex given high unmet need and welldescribed clinical benefits of steroids in patients with DMD

#### **Well-positioned to execute**

- Current cash runway through pivotal Phase 3 topline results into 2026
- Seasoned and experienced leadership team

\*\$1+ billion estimated global peak commercial opportunity is based on IQVIA Medical Claims (Dx), PharmetricsPlus (P+), and IQVIA Analytics in the U.S. and the company's internal estimates and assumptions outside the U.S.

# Appendix

# **Neurological manifestations in classic A-T**

Marked by gradual loss of mobility



At any age, patients with A-T develop increasing difficulty with: Involuntary movements | Chewing and swallowing | Articulation



# **EryDex designed to optimize dexamethasone delivery through once monthly dosing in A-T patients**

Average concentration-time profile for plasma dexamethasone in EryDex



# **Comparison of pharmacokinetic profiles between EryDex and monthly dexamethasone oral/IV administration using published PK information**

Average concentration-time profile for plasma dexamethasone in EryDex



Average Concentration EryDex monthly dose = 17.4 mg



Note: Pharmacokinetic (PK) curve from Population PK model (smoothed) based on company's prior studies of EryDex. Information represented does not reflect a completed comparative study of EryDex versus oral/IV administration of dexamethasone, but rather provides a comparison of published corticosteroid pharmacokinetic information relative to company data regarding EryDex. References: Montanha et al, Frontiers in Pharmacology (2022) 13: 814134; Świerczek A, Jusko WJ., Clinical and Translational Science (2023) 16(9):1667-1679.

# Daily dexamethasone administration led to peaks above IC50 associated with toxicity

1,000 Average plasma concentration (ng/mL) 100 Glucose sensitivity parameter (SC50) - 17.9 ng/mL 10 Lymphocyte sensitivity parameter (SC50) - 14 ng/ml 1 0.1 Cortisol sensistivity parameter (IC50) - .05 ng/mL 0.01 0.001 Sustained Efficacy Window 5 10 15 20 25 0 30 Days

Pharmacokinetic profile of oral/IV daily administration of dexamethasone (6 mg)

Average Concentration EryDex monthly dose = 17.4 mg

Note: Pharmacokinetic (PK) curve from Population PK model (smoothed) based on company's prior studies of EryDex. Information represented does not reflect a completed comparative study of EryDex versus oral/IV administration of dexamethasone, but rather provides a comparison of published corticosteroid pharmacokinetic information relative to company data regarding EryDex. IC50 and SC50 refer to pharmacodynamic parameters of which IC50 reflects drug concentration eliciting 50% of the maximum inhibition and SC50 reflects drug concentration eliciting 50% of the maximum stimulation. References: Krzyzanski, Journal of Pharmacokinetics and Pharmacodynamics (2021) 48: 411-438; Montanha et al, Frontiers in Pharmacology (2022) 13: 814134; Krzyzanski et al, Journal of Pharmacokinetics and Pharmacodynamics (2021) 48: 411-438; Świerczek A, Jusko WJ., Clinical and Translational Science (2023) 16(9):1667-1679.

# **Encouraging EryDex Phase 3 clinical trial results in prior ATTeST study**



Ocompleted largest global study of A-T patients in Phase 3 ATTeST clinical trial and OLE

- Double-blind, placebo-controlled study (N=175) over 6-month treatment period with 12-month OLE (N=104)
- Patients randomized 1:1:1 to EryDex low dose, high dose, or placebo
- Primary endpoint: mICARS Secondary endpoints: CGI-C QOL VABS
- Study observed EryDex slowed neurological deterioration in all ages of A-T patients with improvement observed in 6- to 9-year-old subgroup across multiple endpoints
- > 12-month safety analysis observed EryDex well-tolerated with no serious safety concerns typically associated with chronic steroid administration
- O CE mark obtained in Europe for treatment device and consumables kit



Note: mICARS = Modified International Cooperative Ataxia Rating Scale • CGI-C = Clinical Global Impression – Change • QOL = Quality of Life • VABS = Vineland Adaptive Behavior Scales. Company ATTeST clinical trial: ClinicalTrials.gov ID: NCT02770807.

Prior Phase 3 study observed EryDex slowed neurological deterioration in all ages of A-T patients



#### **ATTeST Primary Endpoint (All Ages) in Intent to Treat Population (ITT)**



# Prior Phase 3 study observed EryDex improvement in 6- to 9-year-old subgroup across multiple endpoints



Primary population selected for Phase 3 NEAT clinical trial

**ATTeST 6-9 Year Subgroup, mICARS** 6 mICARS change (worsening) from baseline (local rater) -4.8 from 4 placebo to high dose 2 (LSM: P=0.0016) 0 -2 **Baseline** Month 3 Month 6 Placebo Low Dose -High Dose

Note: mICARS = Modified International Cooperative Ataxia Rating Scale by Local Rater • LSM = Least Square Means. Company ATTeST clinical trial: ClinicalTrials.gov ID: NCT02770807.

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# Prior Phase 3 study observed EryDex well-tolerated with no serious safety concerns



	ATTeST: Initial Treatment Period			ATTeST: Through Month 12		
	EDS-EP Low Dose (N=59)	EDS-EP High Dose (N=57)	Placebo (N=59)	EDS-EP Low Dose (N=59)	EDS-EP High Dose (N=57)	Non-switch Placebo (N=19)
Patients With Any TEAE (%)	73%	82%	73%	76%	88%	79%
Patients With Any Treatment-Related TEAE (%)	25%	37%	25%	32%	44%	26%
Patients With Any Serious TEAE (%)	10%	12%	12%	14%	16%	21%
Patients With Any Serious Treatment-Related TEAE (%)	0	2%	0	2%	2%	5%
Patients With Any TEAE Leading to Discontinuation (%)	0	4%	0	2%	4%	0
Patients With Any TEAE Leading to Death (%)	0	0	0	0	0	0

Note: TEAE = Treatment Emergent Adverse Event • EDS-EP = EryDex System End Product. Company ATTeST clinical trial: ClinicalTrials.gov ID: NCT02770807.

#### ICARS and modified scales used to assess neurological symptoms

#### **Full ICARS**

#### **100 points**, 19 items

- **Posture and gait disturbance** (34 points)
- Kinetic function (52 points)
- Speech disorder (8 points)
- Oculomotor disorders (6 points)

#### mICARS

#### () 54 points, 11 items

- **Posture and gait disturbance** (34 points)
- Kinetic function (12 points)
- Speech disorder (8 points)

#### **RmICARS\***

#### > **29 points**, 9 items

- **Posture and gait disturbance** (23 points)
- Kinetic function (2 points)
- Speech disorder (4 points)

\*RmICARS requested by the FDA; individual criteria collapsed to better reflect clinical meaningfulness of changes



Note: ICARS = International Cooperative Ataxia Rating Scale • mICARS = Modified International Cooperative Ataxia Rating Scale • RmICARS = Rescored Modified International Cooperative Ataxia Rating Scale.

# **ICARS primary endpoint measurement criteria**

Full ICARS 100 points 19 Items		mICARS 54 points 11 items		Rescored mICARS (FDA) 29 Points 9 items		
Posture and Gait Disturbance (34 points)		Posture and Gait Disturbance (34 points)		Posture and Gait Disturbance (23 points)		
1. Walking capacities	0-8	1. Walking capacities	0-8	1. Walking capacities	0-4	
2. Gait Speed	0-4	2. Gait Speed	0-4	2. Gait Speed	0-3	
3. Standing Capacities eyes open	0-6	3. Standing Capacities eyes open	0-6	3. Standing Capacities eyes open	0-4	
4. Spread of feet eyes open	0-4	4. Spread of feet eyes open	0-4	4. Spread of feet eyes open	0-3	
5. Body sway feet together eyes open	0-4	5. Body sway feet together eyes open	0-4	5. Body sway feet together eyes open	0-3	
6. Body sway feet together eyes closed	0-4	6. Body sway feet together eyes closed	0-4	6. Body sway feet together eyes closed	0-3	
7. Quality of sitting position	0-4	7. Quality of sitting position	0-4	7. Quality of sitting position	0-3	
Kinetic Function (52 points)		Kinetic Function (12 points)		Kinetic Function (2 points)		
test left & right except drawing		test left & right except drawing		test left & right except drawing		
8. Knee tibia test	0-4					
9. Action tremor	0-4					
10. Finger to nose test (dysmetria)	0-4					
11. Finger to nose test (intention tremor)	0-4					
12. Finger finger test	0-4					
13. Pronation supination	0-4	13. Pronation supination	0-4			
14. Drawing	0-4	14. Drawing	0-4	14. Drawing	0-2	
peech Disorder (8 points) Speech Disorder (8 points)		Speech Disorder (4 points)				
15. Fluency of speech	0-4	15. Fluency of speech	0-4			
16. Clarity of speech	0-4	16. Clarity of speech	0-4	16. Clarity of speech	0-4	
Oculomotor Disorders (6 points)						
17. Gave evoked nystagmus	0-3					
18. Abnormalities of ocular pursuit	0-2					
19. Dysmetria of the saccade	0-1					
Total	0-100	Tota	l 0-54	Tota	al 0-29	

