QUINCE THERAPEUTICS

Ataxia-Telangiectasia

Unlocking the power of a patient's own biology to address high unmet need for rare neurodegenerative and immunodeficiency disorder

Investor Webinar

February 7, 2025

Today's Agenda

Dr. Dirk Thye
- Quince Therapeutics overview

Dr. Mary Kay Koenig
- A-T natural history overview
- Symptomatic treatment approach
- Competitive landscape overview

Dr. Dirk Thye
- Evidence supporting EryDex potential treatment for A-T

Dr. Mary Kay Koenig
- Phase 3 NEAT clinical trial

Q&A

Addressing high unmet need in Ataxia-Telangiectasia

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Quince Therapeutics overview

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

- **A** Autologous
- **I** Intracellular
- **D** Drug
- **E** Encapsulation

- 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
- 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.

Mary Kay Koenig, M.D.

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A complex disorder first recognized nearly 70 years ago

Ataxia: Poor muscle control

Telangiectasia: Dilation of capillaries resulting in visible red lesions on the skin

1957

8 cases described by Boder and Sedgwick:

- Progressive ataxia
- Telangiectasia
- Shrinking of thymus
- Abnormalities in ovaries

1957-1966

Further development of clinical picture:

- Immune system abnormalities
- Increased risk of leukemias/ lymphomas
- Neurologic pathologies
- Confirmation of autosomal recessive inheritance

1988-1995

Identification of genetic defect:

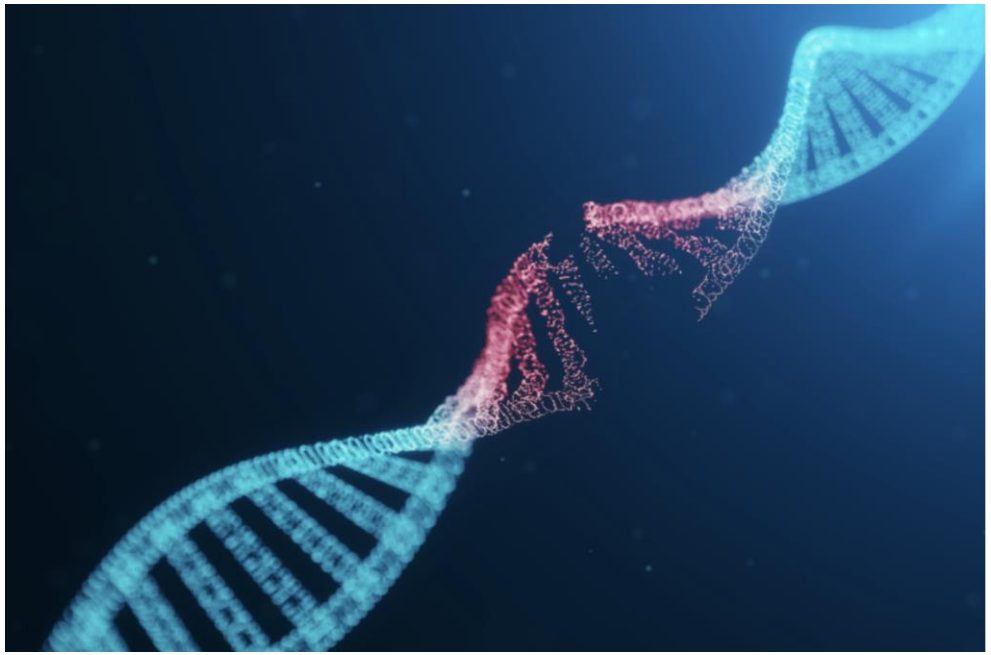
- Localized to chromosome 11
- Isolated to single gene coding for a protein kinase: ATM *(ataxia-telangiectasia mutated)*

References: 1. Crawford TO. *Semin Pediatr Neurol*. 1998;5:287-294. 2. Gatti RA, et al. *Nature*. 1988;336(6199):577–580. 3. Savitsky K, et al. *Science*. 1995;268(5218):1749–1753.

How defects in a single gene can cause a complex multisystem disorder

ATM is a master regulator of DNA repair and cellular stress responses[1-3]

ATM is required for repair of double-stranded DNA breaks (DSBs)



Each human cell acquires an estimated 25 DSB per day[3]

DSBs occur…

During normal cellular processes:

- ✓ Meiosis (cell division)
- ✓ Variable–diversity–joining (VDJ) recombination (needed to generate unique immune cell receptors required to recognize a vast array of pathogens)
- ✓ Generation of reactive oxygen species (ROS) from normal cellular metabolism

After exposure to:

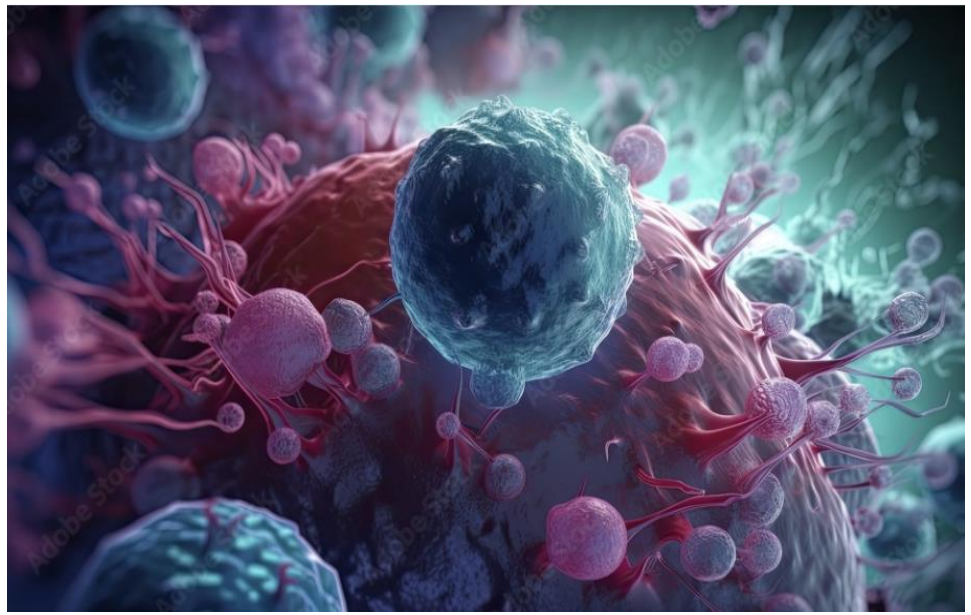
- ✓ Ionizing radiation
- ✓ Certain chemicals
- ✓ Ultraviolet (UV) light

Failure to correctly repair DSBs can lead to cell death or chromosomal rearrangements (which can result in cancer)

References: 1. Bensimon A, et al. *FEBS Letters*. 2011;585(11):1625-1639. 2. Donath H, et al. *Front. Pediat.* 2020;8:317. 3. Lee J-H, Paull TT. *Nat Rev Mol Cell Biol. 2021;22:796-814.*

ATM plays pivotal role in multiple signaling pathways

ATM is activated by oxidative stress and regulates levels of ROS[1]



ATM interacts with >700 other proteins– making additional roles likely[2]

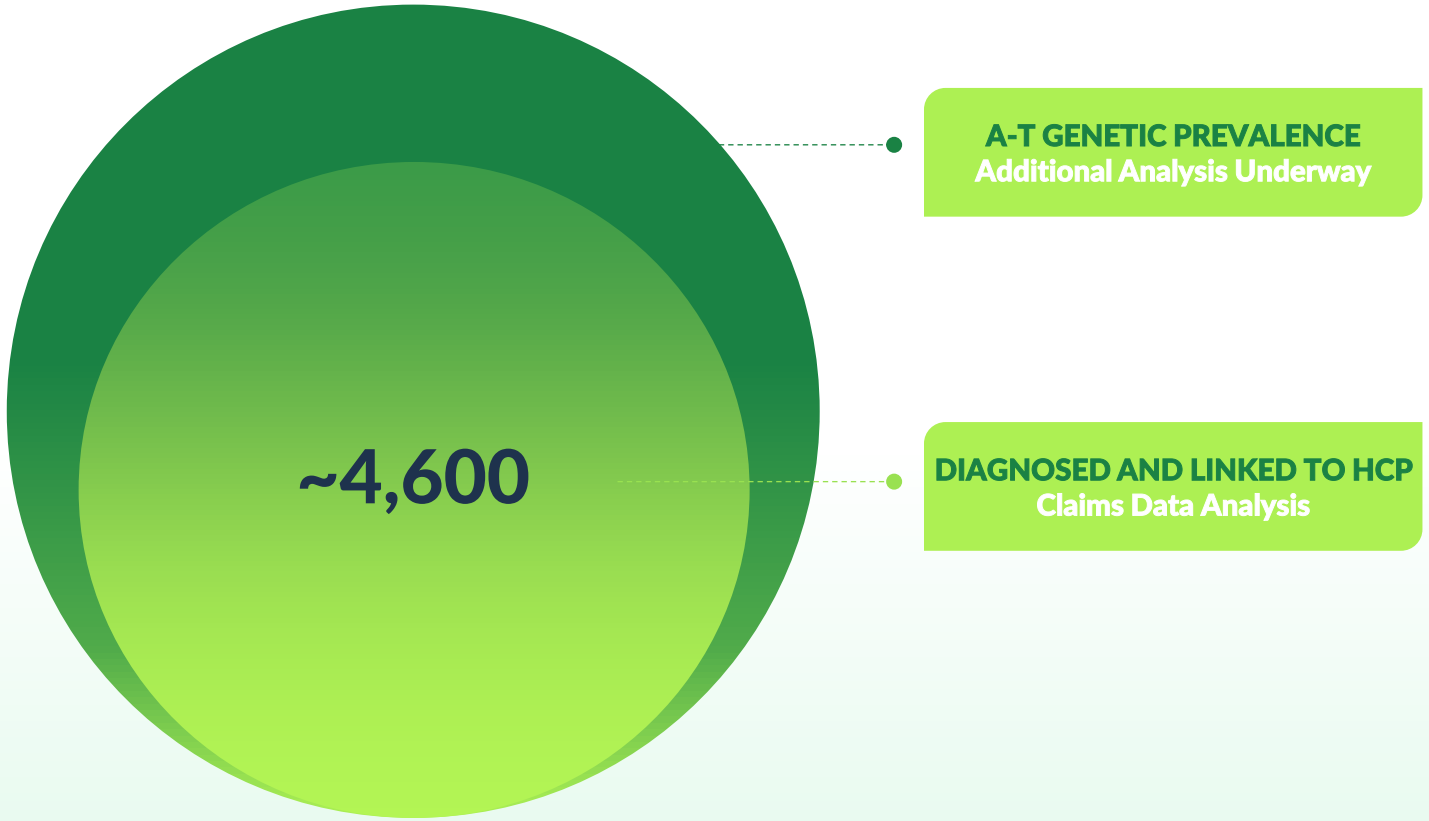
ATM also[1-4]:

- ✓ Regulates the cell cycle and apoptosis
- ✓ Is involved in insulin signaling
- ✓ Mediates epigenetic regulation
- ✓ May play role in intracellular vesicle transport

Decreased ATM activity has been implicated in the pathogenesis of neurological disorders including Alzheimer's, Huntington's and Parkinson's diseases[3,4]

References: 1. Bensimon A, et al. *FEBS Letters*. 2011;585(11):1625-1639. 2. Donath H, et al. *Front. Pediat.* 2020;8:317. 3. Lee J-H, Paull TT. *Nat Rev Mol Cell Biol.* 2021;22:796-814. 4. Pizzamiglio L, et al. *Cells.* 2020;9(9):1969.

A-T represents significant U.S. commercial opportunity



- Approximately 4,600 diagnosed U.S. patients with A-T
- No currently approved A-T treatments, potential to expand patient number with market development
- Benefit from engaged, connected A-T patient community
- A-T has similar epidemiology to Friedreich's ataxia

Source: IQVIA Medical Claims (Dx), PharmetricsPlus (P+), and IQVIA Analytics

Characteristic of classic A-T manifestation

Manifestation	Classic ("Typical" / "Early onset")
Neurological	Childhood onset
Cerebellar ataxia (inability to coordinate muscle movement)	+
Impaired motor control	+
Decreased ability to move/feel	+
Immunodeficiency	+
Pulmonary disease	+
Increased risk of malignancy	+ (median onset 12.5 years)
Sensitivity to ionizing radiation	+

Significantly reduced life expectancy due to pulmonary failure and malignancy (typically <30 years old)

Reference: 1. Veenhuis S, et al. Ataxia-telangiectasia. In: Adam MP, et al, eds. *GeneReviews® [Internet]*. University of Washington, Seattle; 1993-2024. March 19, 1999. [Updated October 5, 2023. Accessed April 12, 2024. https://www.ncbi.nlm.nih.gov/books/NBK26468.

Common features of classic A-T

Clinical picture becomes more challenging with age

	<5 years	5-15 years	15-20 years	>20 years
Ataxia	√	√	√	√
Neurologic deterioration		√		
Immunodeficiency	√	√	√	√
Infections	√	√	√	√
Sinopulmonary symptoms	√	√	√	√
Slurred speech		√	√	√
Difficulty swallowing		√	√	√
Telangiectasia		√	√	√
Faltering growth		√	√	
Nutritional compromise		√	√	√
Lymphoid cancers	√	√	√	√
Solid organ cancers				√
• Metabolic syndrome • Liver disease • Diabetes			√	√

Reference: McGrath-Morrow SA, et al. *J Multidiscipline Health.* 2021;14:1637-1644.

Neurological manifestations in classic A-T

Marked by gradual loss of mobility

Age	1-2	5	10	15
	• Walking begins at a normal age, but gait fails to improve • Difficulty standing or sitting still, sway side-to-side or backwards	• Walking becomes more difficult, walls or doorways used as support • Gait is quick, with a narrow stance	• Progression to wheelchair use • Increased difficulty reading due to impaired eye movement • Increased risk of silent aspiration	• Gross motor symptoms stop progressing after ages 12-15

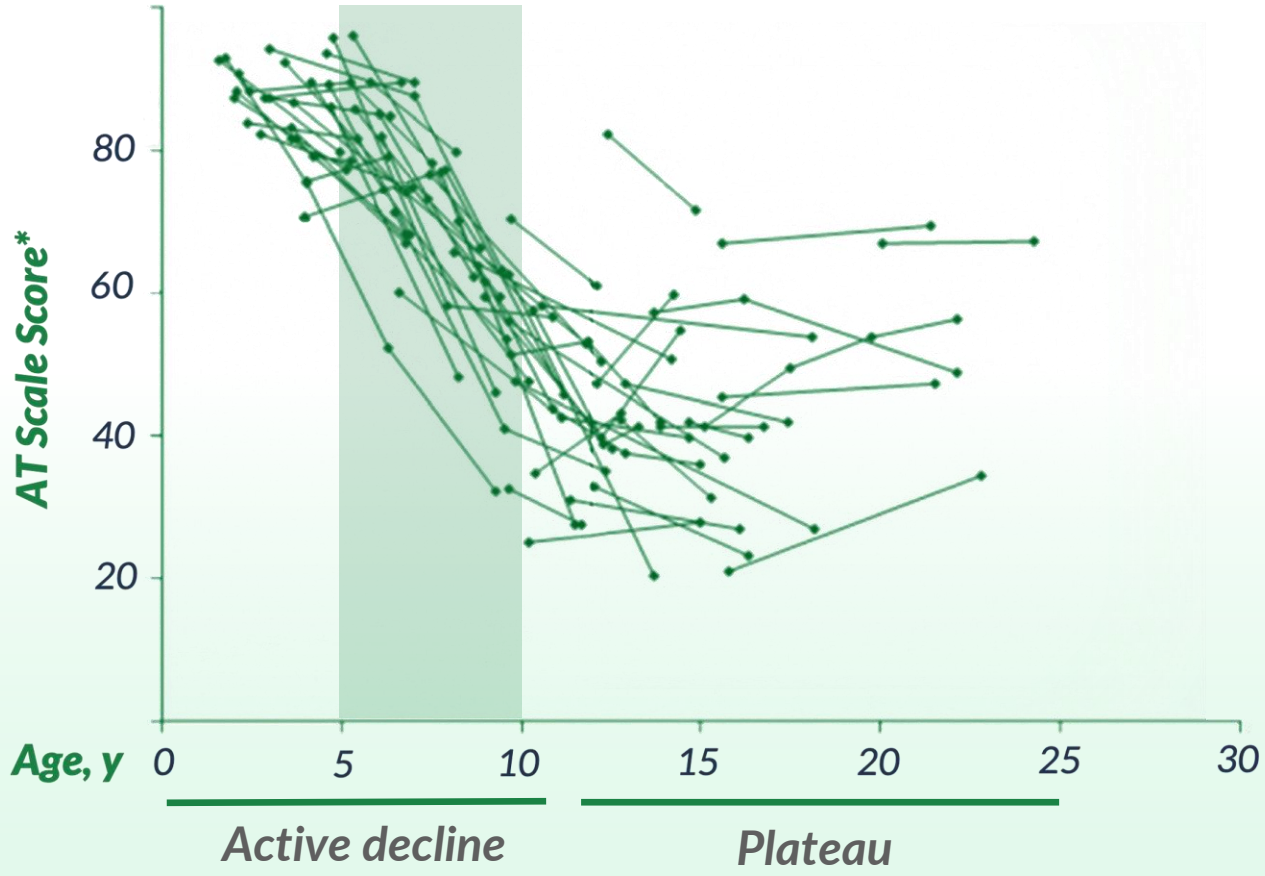
At any age, patients with A-T develop increasing difficulty with:

Involuntary movements | *Chewing and swallowing* | *Articulation*

Reference: 1. Rothblum-Oviatt C, et al. *Orphanet J Rare Dis.* 2016;11(1):159. doi:10.1186/s13023-016-0543-7. 2. Crawford TO. *Semin Pediatr Neurol.* 1998;5(4):287-294.

Rapid neurological progression in A-T

Symptoms progress quickly from 6 to 9 years of age, then plateau at 10-12 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.

No curative or disease-modifying therapies available

A-T treatment is generally supportive and includes:

Immunodeficiency	• Manage risk factors to prevent respiratory tract infections • Optimize vaccinations	• Provide prophylactic antibiotics, immune globulin (IG) replacement therapy
Recurrent pulmonary infections	• Antibiotics • IG replacement therapy	• Inhaled corticosteroids
Interstitial lung disease (pulmonary fibrosis)	• Systemic corticosteroids	
Oncology	• No consensus treatment protocols • Chemotherapy with dose-adjusted protocols	• Radiation therapy contraindicated • Radiomimetics (bleomycin) and neurotoxic drugs avoided
Ataxia	• Moderate evidence that amantadine may be effective	• Corticosteroids shown to improve ataxia, but are used with caution due to side effects

Reference: Van Os NJH, et al. *Dev Med Child Neurol.* 2017;59(7):680-689.

Recent publications in scientific journals

THE LANCET Neurology

September 2024

Articles

Safety and efficacy of intra-erythrocyte dexamethasone sodium phosphate in children with ataxia telangiectasia (ATTeST): a multicentre, randomised, double-blind, placebo-controlled phase 3 trial

Stefan Zielen, Thomas Crawford, Luca Benatti, Mauro Magnani, Matthias Kieslich, Monique Ryan, Isabelle Meyts, Sheffali Gulati, Rupam Borgohain, Ravi Yadav, Pramod Pal, Amaita Hegde, Suresh Kumar, Anand Venkateswar, Vrajesh Udani, Kollencheri PVinayan, Andreea Nissenkorn, Elisa Farzi, Vincenzo Leuzzi, Asbjørg Stray-Pedersen, Barbara Pietrucha, Samuel I Pascual, Riadh Gouider, Mary Kay Koenig, Steve Wu, Susan Perlman, Dirk Thye, Guenter Janhofer, Biljana Horn, William Whitehouse*, Howard Lederman*

Summary

Background Ataxia telangiectasia is a multisystem disorder with progressive neurodegeneration. Corticosteroids can improve neurological functioning in patients with the disorder but adrenal suppression and symptom recurrence on treatment discontinuation has limited their use, prompting the development of novel steroid delivery systems. The aim of the ATTeST study was to evaluate the efficacy and safety of intra-erythrocyte delivery of dexamethasone sodium phosphate compared with placebo in children with ataxia telangiectasia.

Methods This multicentre, randomised, double-blind, placebo-controlled, phase 3 trial was done at 22 centres in 12 countries (Australia, Belgium, Germany, India, Israel, Italy, Norway, Poland, Spain, Tunisia, the UK, and the USA). Eligible participants were children aged 6 years or older weighing more than 15 kg who met clinical criteria for ataxia telangiectasia but who had preserved autonomous gait. Participants were randomly assigned (1:1:1) to low-dose (approximately 5–10 mg), or high-dose (approximately 14–22 mg) intra-erythrocyte dexamethasone sodium phosphate, or placebo, using an independent interactive web response system, with minimisation for sex and age (6–9 years vs ≥10 years). Intravenous intra-erythrocyte dexamethasone sodium phosphate was administered once a month for 6 months. Participants, employees of the sponsor, investigators, all raters of efficacy endpoints, and central reviewers were masked to treatment assignment and dose allocations. The primary efficacy endpoint was change in the modified International Cooperative Ataxia Rating Scale (mICARS) from baseline to month 6, assessed in the modified intention-to-treat (mITT) population, which included all randomly assigned participants who received at least one dose of study drug and had at least one post-baseline efficacy assessment. This trial is registered with ClinicalTrials.gov (NCT02770807) and is complete.

Findings Between March 2, 2017, and May 13, 2021, 239 children were assessed for eligibility, of whom 176 were randomly assigned. One patient assigned to high-dose intra-erythrocyte dexamethasone sodium phosphate did not initiate treatment. 175 patients received at least one dose of treatment (59 patients received the low dose and 57 received the high dose of intra-erythrocyte dexamethasone sodium phosphate, and 59 received placebo). The mITT population comprised 164 participants (56 children in the low-dose group, 54 children in the high-dose group, and 54 in the placebo group). Compared with the placebo group, no differences were identified with regard to change in mICARS score from baseline to 6 months in the low-dose group (least squares mean difference −1·37 [95% CI −2·932 to 0·190]) or the high-dose group (−1·40 [−2·957 to 0·152]; p=0·0765). Adverse events were reported in 43 (73%) of 59 participants in the low-dose group, 47 (82%) of 57 participants in the high-dose group, and 43 (73%) of 59 participants in the placebo group. Serious adverse events were observed in six (10%) of 59 participants in the low-dose group, seven (12%) of 57 participants in the high-dose group, and seven (12%) of 59 participants in the placebo group. There were no reports of hyperglycaemia, hypertension, hirsutism, or Cushingoid appearance in any of the treatment groups, nor any treatment-related deaths.

Interpretation Although there were no safety concerns, the primary efficacy endpoint was not met, possibly related to delays in treatment reducing the number of participants who received treatment as outlined in the protocol, and potentially different treatment effects according to age. Studies of intra-erythrocyte delivery of dexamethasone sodium phosphate will continue in participants aged 6–9 years, on the basis of findings from subgroup analyses from this trial.

Funding EryDel and Quince Therapeutics.

Lancet Neurol 2024; 23: 871–82
See Comment page 846
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Long-term safety of dexamethasone sodium phosphate encapsulated in autologous erythrocytes in pediatric patients with ataxia telangiectasia

Mary Kay Koenig[1], Vincenzo Leuzzi[2], Riadh Gouider[3,4], Eppie M. Yiu[5,6], Barbara Pietrucha[7], Asbjørg Stray-Pedersen[8], Susan L. Perlman[9], Steve Wu[10], Trudy Burgers[11], Rupam Borgohain[12], Rukmini Mridula Kandadai[13], Isabelle Meyts[14], Giorgia Bucciol[14], Anaita Udwadia-Hegde[15], Ravi Yadav[16], Donna Roberts[17], Aaron Dane[18], Maureen Roden[19], Dirk Thye[19], Biljana Horn[19]*, Howard M. Lederman[20†] and William P. Whitehouse[21†]

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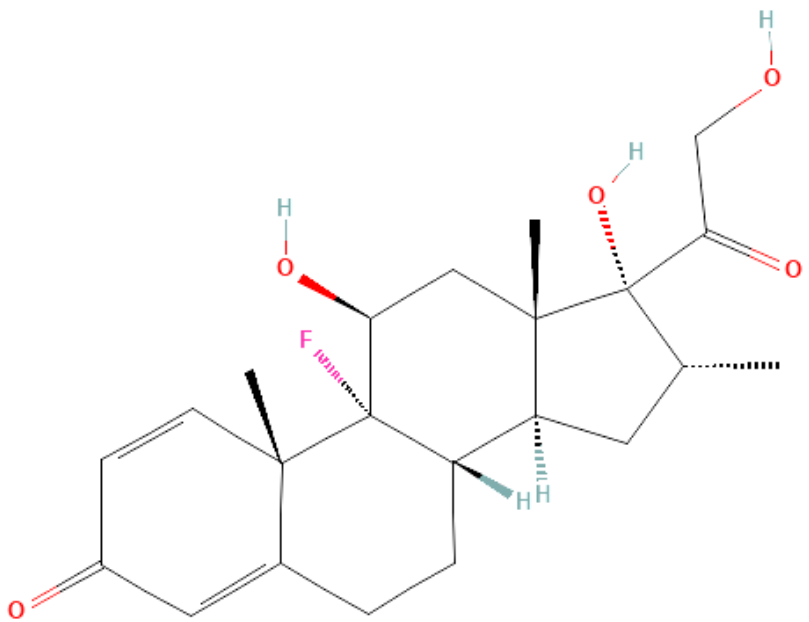
Background: Dexamethasone sodium phosphate (DSP) encapsulated in autologous erythrocytes (EryDex) was developed as an alternative to standard glucocorticoids in an effort to eliminate chronic steroid toxicity while preserving efficacy. The primary objective of this report is to describe the safety of long-term use of EryDex in treatment of pediatric patients with ataxia telangiectasia.

Methods: This is a post-hoc analysis of patients treated with EryDex for a minimum of 24 months in two prospective clinical trials. Outcomes include adverse events, growth, hemoglobin and serum iron, glucose levels, HbA1c, CD4+ lymphocytes, and bone mineral density.

References: Zielen, Stefan et al. *The Lancet Neurology*. Volume 23, Issue 9, 871 – 882. Koenig MK, et al. *Frontiers in Neurology*. 15:1526914, DOI=10.3389/fneur.2024.1526914.

Early evidence that corticosteroids ameliorate neurological symptoms in A-T

Parent observation led to initial studies



Betamethasone. Pubchem. *https://pubchem.ncbi.nlm.nih.gov/compound/9782*

Parents noticed neurological signs in their child with A-T improved when given short doses of betamethasone for bronchitis[1]

- Observation confirmed in subsequent reports in limited number of patients with A-T given oral betamethasone[2-4]
- Improvements are transient; once treatment is discontinued, neurological deterioration resumes
- Majority of patients exhibited some degree of toxicity from corticosteroid treatment, including:
  - ✓ Adrenal insufficiency
  - ✓ Cushingoid appearance (moon face)
  - ✓ Weight gain
  - ✓ Growth suppression

References: 1. Buoni S, et al. *Arch Neurol*. 2006;63(10):1479-1482. 2. Broccoletti T, et al. *Eur J Neurol*. 2011;18(4):564-570. 3. Zannolli R, et al. *Mov Dis*. 2012;27(10):1312-1316. 4. Hasegawa S, et al. *Pediatr Neurol*. 2019;100:60-66.

Encouraging EryDex Phase 3 clinical trial results in prior ATTeST study

EryDex
ATTeST Trial

- Completed 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

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.

ICARS and modified scales used to assess neurological symptoms

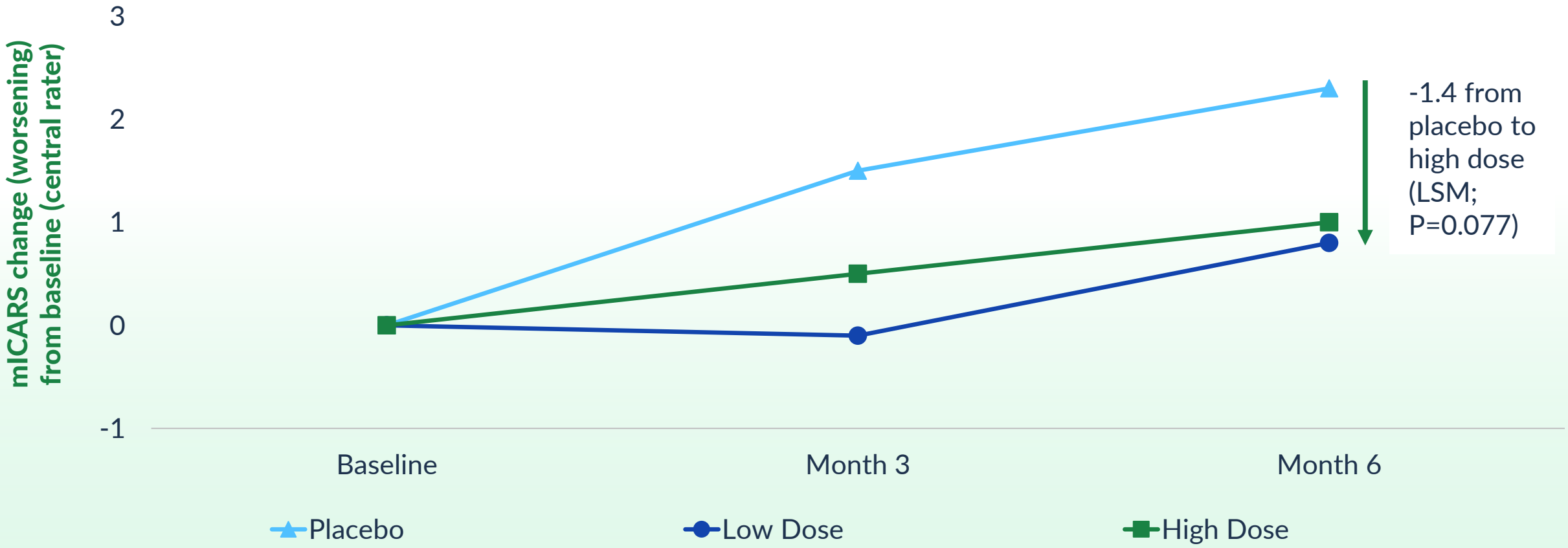
Full ICARS 100 points 19 Items		mICARS 54 points 11 items		Rescored mICARS (FDA) 29 Points 9 items	
Posture and Gait Disturbance (34 points)		Posture and Gait Disturbance (34 points)		Posture and Gait Disturbance (23 points)	
1. Walking capacities	0-8	1. Walking capacities	0-8	1. Walking capacities	0-4
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) test left & right except drawing		Kinetic Function (12 points) test left & right except drawing		Kinetic Function (2 points) 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
Speech 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	Total	0-54	Total	0-29

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

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

EryDex
ATTeST Trial

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



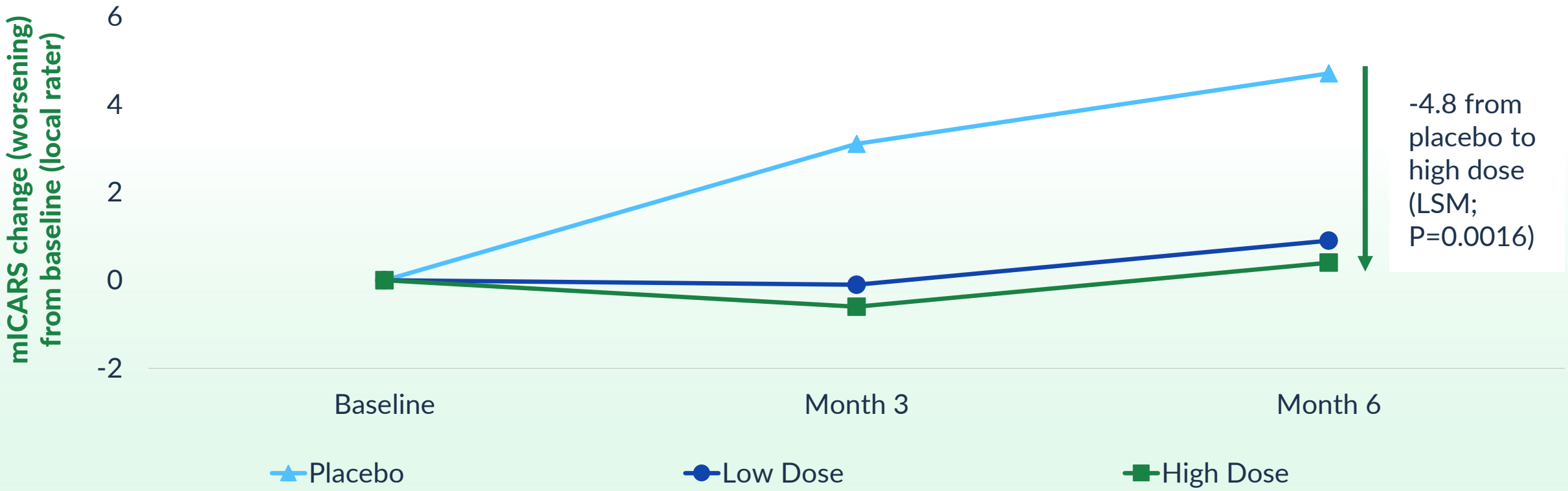
Note: mICARS = Modified International Cooperative Ataxia Rating Scale by Central Rater • LSM = Least Square Means. Company ATTeST clinical trial: ClinicalTrials.gov ID: NCT02770807.

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

EryDex
ATTeST Trial

Primary population selected for Phase 3 NEAT clinical trial

ATTeST 6-9 Year Subgroup, mICARS



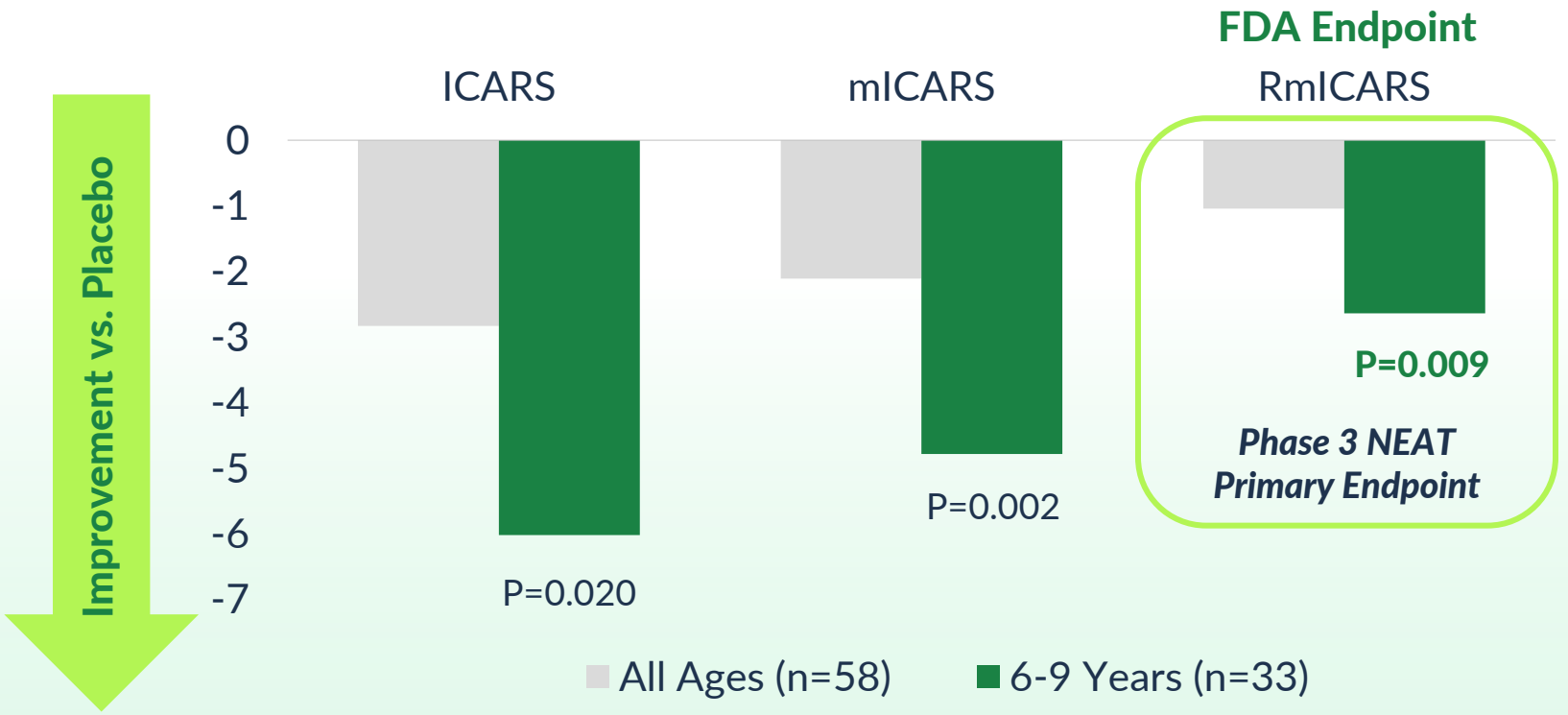
Note: mICARS = Modified International Cooperative Ataxia Rating Scale by Local Rater • LSM = Least Square Means. Company ATTeST clinical trial: ClinicalTrials.gov ID: NCT02770807.

Encouraging EryDex Phase 3 clinical trial results in ATTeST study

EryDex
ATTeST Trial

- 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

ATTeST ICARS Values in ITT Population



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 • RmICARS = Rescored Modified International Cooperative Ataxia Rating Scale

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

EryDex
ATTeST Trial

Three patients discontinued from the study, all unrelated to steroid toxicity

Two patients in high-dose group showed steroid-related TEAEs of pyrexia and tachycardia / pain and pruritus

	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.

Ataxia-Telangiectasia competitive landscape

Asset / Company	Stage	Drug / *MOA*	ROA and Dosing	Support Details
EryDex • Quince Tx	**Phase 3** (Initiated June 2024, conducted under SPA)	Dexamethasone *Glucocorticoid Receptor Antagonist*	Once monthly autologous cell infusion	• Positive prior P3 efficacy signals • Well tolerated and good safety profile • Current P3 study data expected in Q4 2025
IB1001 • IntraBio	**Phase 3** (Initiated November 2024)	N-acetyl-L-leucine *Modified Amino Acid*	Oral sachet 3x daily	• Theoretically affects mitochondrial function by improving ATP production • Failed P2 in A-T; Recently approved for NPC – priced in U.S. at $630K per year • Well tolerated and good safety profile
MBM-01 • Matrix BioMed	**Phase 2** (Last CT.gov update May 2021)	EPAS1/HIF1A Inhibitor	Oral	• Antioxidant drug shown to supplant the role of ATM by reducing oxidative stress, repair DNA damage, etc. • Also using for cancer treatment • Potential 20 patient IIT, no results posted
Triheptanoin • Univ of Queensland	**Phase 2** (Open label IIT)	Triheptanoin *Energy substrate replacement*	Oral ≥4x daily	• Unknown efficacy in small Phase 2 IIT • Patents by Ultragenyx until 2029 (not funded) • Will require government funding to get approved
Nicotinamide • Univ of Queensland	**Phase 2** (Open label IIT)	Nicotinamide *NF-κB modulatory*	Oral 3x daily	• Positive efficacy signals in small Phase 2 IIT • Will require government funding to get approved
Betamethasone • Acasti	**Phase 1 complete** (Development stalled, attempted out-license)	Betamethasone *Glucocorticoid Receptor Antagonist*	Oral spray for short term use	• No distinct advantages over common oral steroids • Higher Cmax than oral betamethasone, may lead to more Aes • Likely similar safety profile to steroids • Deprioritized by Acasti

Source: Company internal competitive analysis

Dirk Thye, M.D.

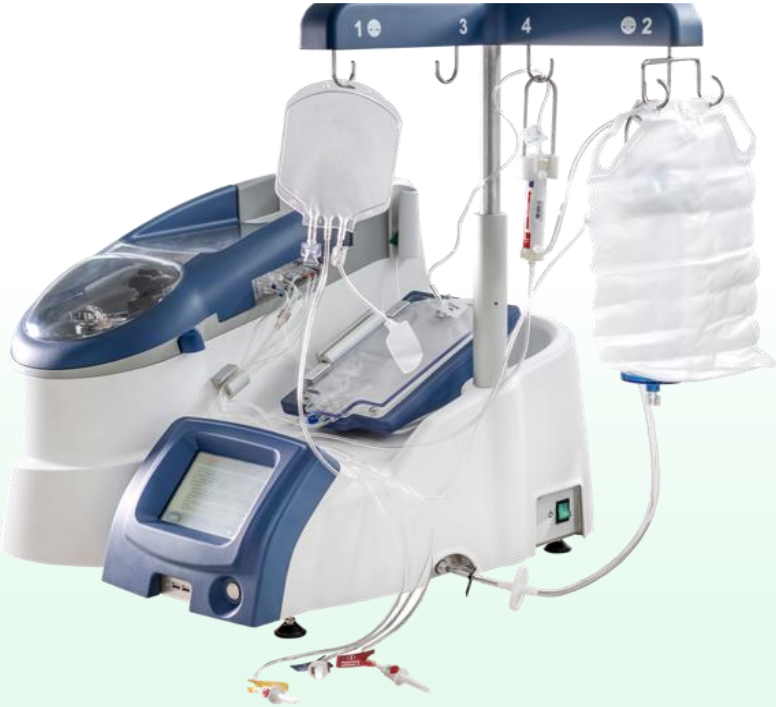
Chief Executive Officer and Chief Medical Officer
Quince Therapeutics

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:

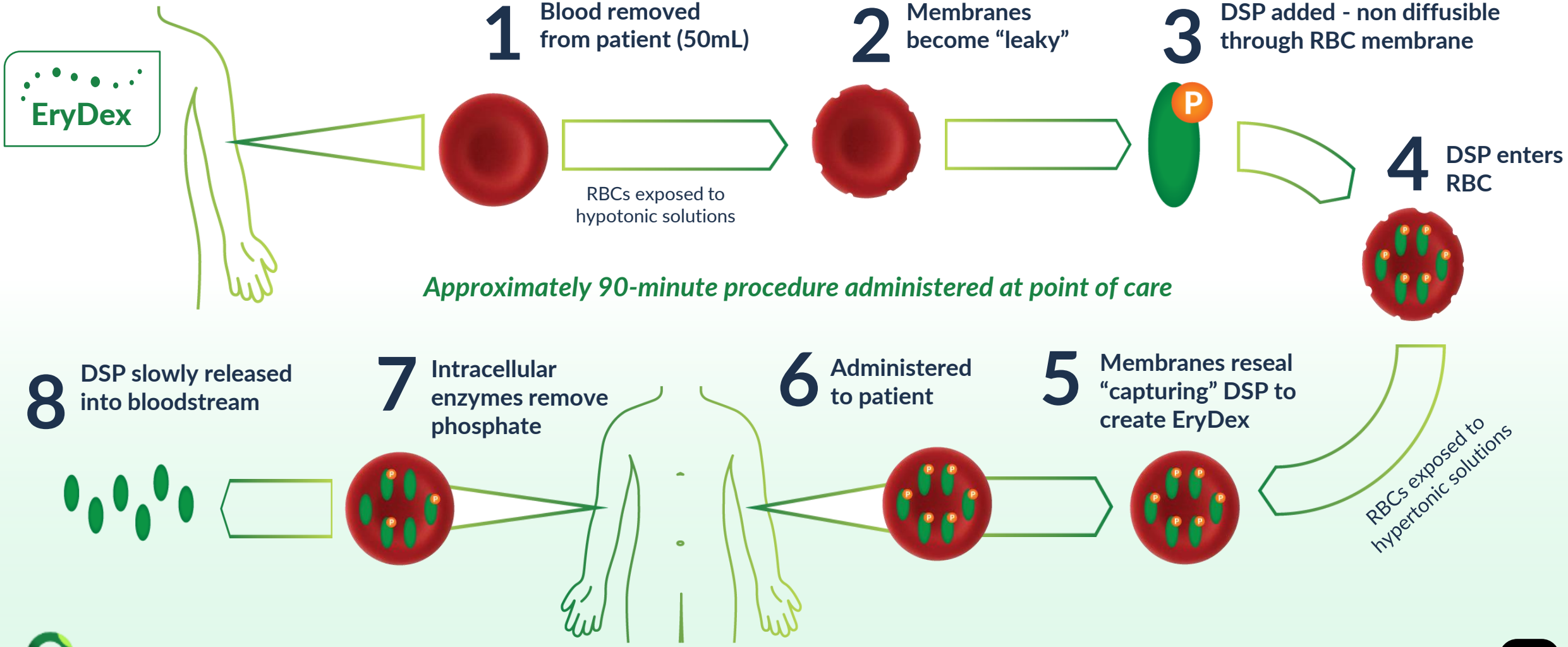
- √ **Improved biodistribution** that may enable slow release of drug while circulating through tissues, organs, and capillary beds where therapeutic effect is desired
- √ **Altered pharmacokinetics and pharmacodynamics**, including long circulating half-life, and altered or improved tissue distribution, 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

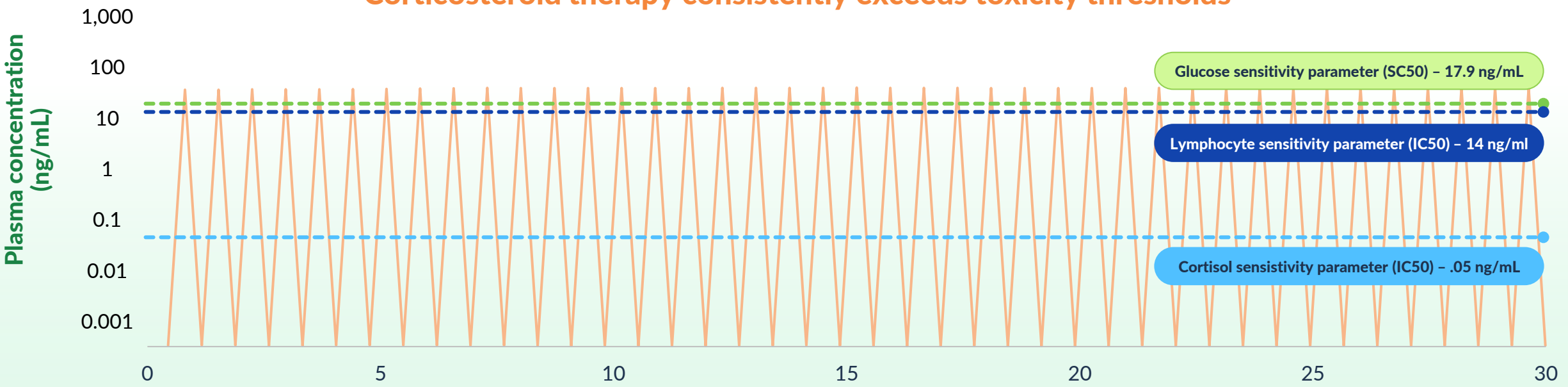
Adrenal suppression

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

Elevated glucose resulting in hyperglycemia and diabetes

Immunosuppression resulting in infections

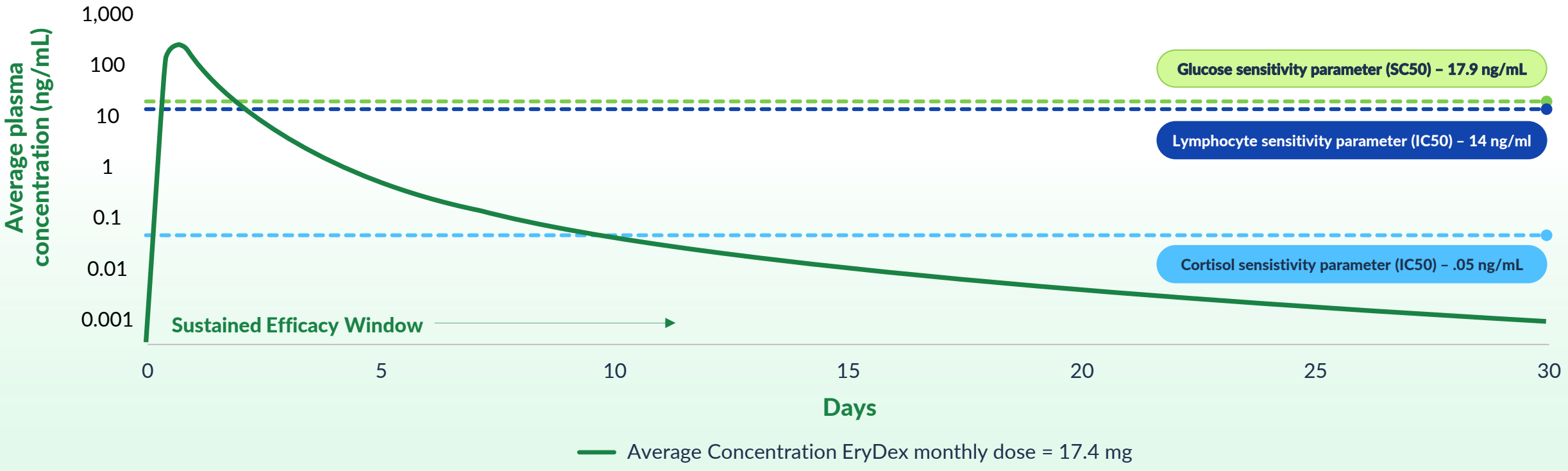
Pharmacokinetics of daily IV dexamethasone (6 mg)
Corticosteroid therapy consistently exceeds toxicity thresholds



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



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.

How can potential efficacy be maintained without toxicity?

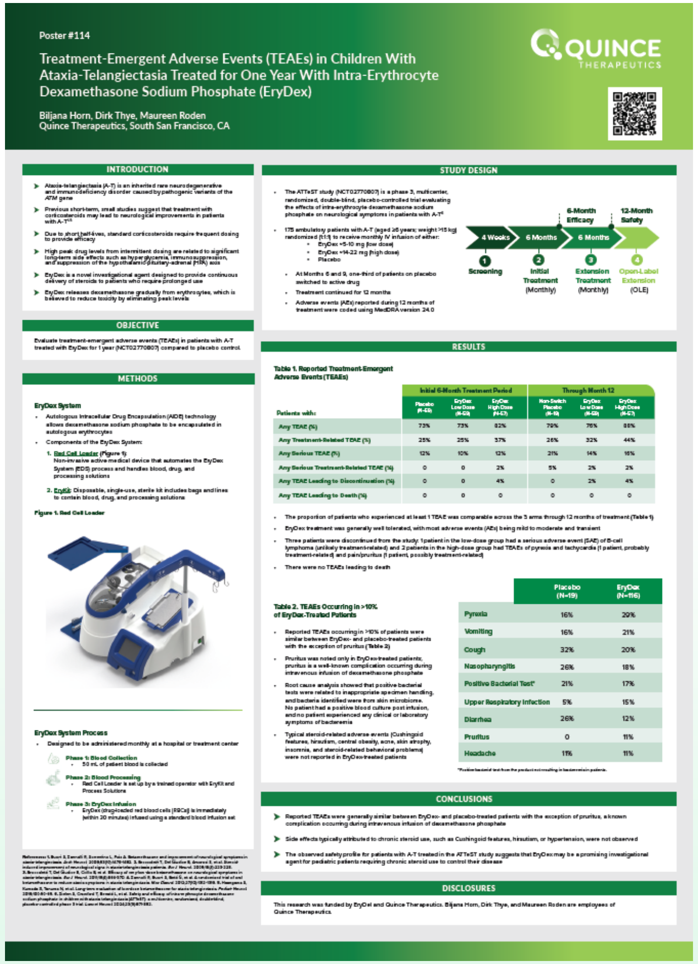
Principles of corticosteroid delivery resulting in optimal efficacy

Clinical efficacy depends on the *magnitude* and *duration* of *exposure of glucocorticoid receptors* (GRs) to glucocorticoid (GC)

- **Optimal results achieved by initial bolus dose to achieve GR saturation**
- **Followed by continuous exposure to maintain GC binding to GR**
- **Then dose-tapering to achieve gradual recovery of suppressed HPA axis**

References: 1. Meduri GU, et al. *Intensive Care Med*. 2020;46(12):2284-2296.

Child Neurology Society 2024



Treatment-Emergent Adverse Events (TEAEs) in Children With Ataxia-Telangiectasia Treated for One Year With Intra-Erythrocyte Dexamethasone Sodium Phosphate (EryDex)

- EryDex treatment generally well tolerated with most TEAEs mild to moderate and transient, and generally similar between EryDex- and placebo-treated patients
- Side effects typically attributed to chronic steroid use, such as Cushingoid features, hyperglycemia, hirsutism, or hypertension, were not observed
- No TEAEs leading to death

Source: Company data analysis from prior Phase 3 ATTeST clinical trial as presented in posters at the 53rd Child Neurology Society (CNS) Annual Meeting in November 2024.

International Congress for Ataxia Research 2024

Growth and Bone Mineral Density (BMD) in Children with Ataxia-Telangiectasia (A-T) Treated with Intra-Erythrocyte Dexamethasone (EryDex) for 24 months

- 24 months of EryDex treatment did not adversely affect growth and bone mineral density of patients with A-T
- Results compare favorably to natural history of patients with A-T who experience height and weight faltering, in addition to abnormal bone mineral density
- No weight gain, adverse growth, or bone health typically associated with the use of corticosteroids in children were observed


Growth and Bone Mineral Density (BMD) in Children With Ataxia-Telangiectasia (A-T) Treated With Intra-Erythrocyte Dexamethasone (EryDex) for 24 months

QUINCE THERAPEUTICS

Dirk Thye, Biljana Horn, Maureen Roden

Quince Therapeutics, South San Francisco, CA

ABSTRACT

RESULTS

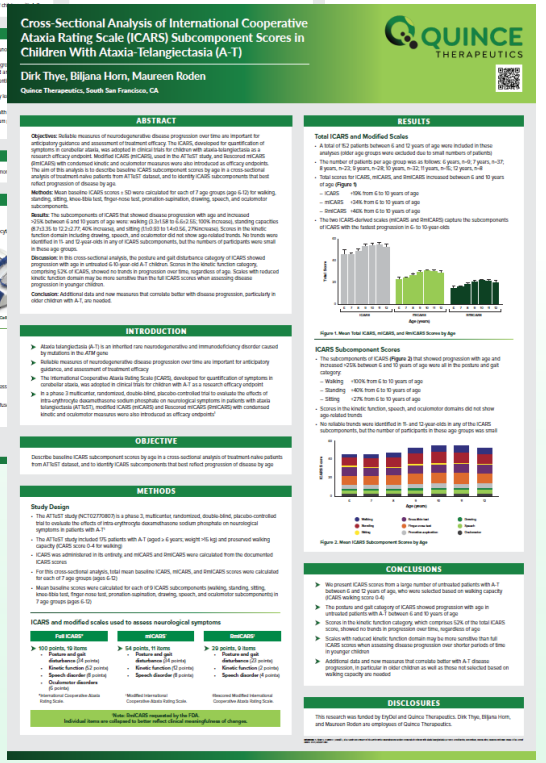
INTRODUCTION

OBJECTIVE

METHODS

Cross-sectional Analysis of International Cooperative Ataxia Rating Scale (ICARS) Subcomponent Scores in Children with Ataxia-Telangiectasia (A-T)

- ICARS subcomponents mICARS and RmICARS analyses capture fastest neurological symptom progression in patients with A-T between ages of six to 10 year olds ambulatory at baseline
- Posture and gait measures showed progression with age in untreated patients with A-T between the ages of six and 10 years old
- Scales with reduced kinetic function domain may be more sensitive than full ICARS scores over shorter periods of time in younger children
- mICARS and RmICARS measures focus on assessment posture and gait as opposed to kinetic function and speech
- mICARS and RmICARS best reflect disease progression by age and capture fastest neurological symptom progression 6 to 10 year olds


Cross-Sectional Analysis of International Cooperative Ataxia Rating Scale (ICARS) Subcomponent Scores in Children With Ataxia-Telangiectasia (A-T)

QUINCE THERAPEUTICS

Dirk Thye, Biljana Horn, Maureen Roden

Quince Therapeutics, South San Francisco, CA

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Source: Company data analysis from prior Phase 3 ATTeST clinical trial as presented in posters at the 2024 International Congress for Ataxia Research in November 2024.

Mary Kay Koenig, M.D.

Professor & Associate Vice-Chair for Clinical Research
Endowed Chair of Mitochondrial Medicine
Director, Center for the Treatment of Pediatric Neurodegenerative Disease
Department of Pediatrics, Division of Child and Adolescent Neurology
University of Texas Health, Houston

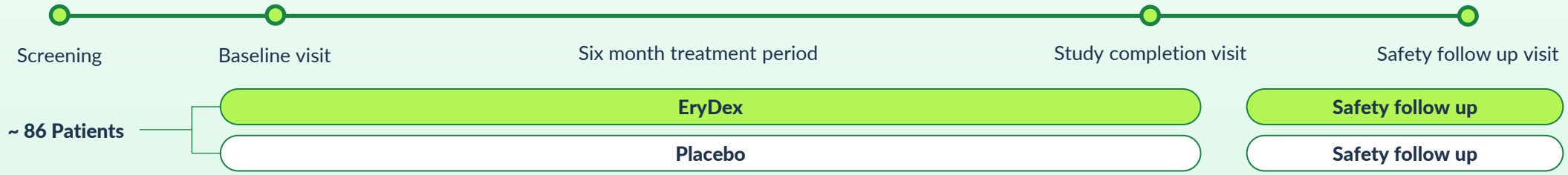
Pivotal Phase 3 NEAT study design

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 quarter of 2025

46 patients with A-T enrolled as of February 7, 2025
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



Note: RmICARS = Rescored Modified International Cooperative Ataxia Rating Scale. Company NEAT clinical trial: ClinicalTrials.gov ID: NCT06193200.

NEAT trial design supports expectation of clear topline results

- Appropriate primary analysis population – focused on 6 to 9 year-olds when rate of neurological decline most severe
- Well-defined primary endpoint – RmICARS recommended by FDA as it best focuses on gait and posture measurements
- Sufficiently powered – based on prior ATTeST study
- Inclusion of patients 10 years and older – recommended by FDA for potentially broader label
- Pivotal study being conducted under SPA agreement with FDA

Anticipated impact of approved EryDex in A-T patient population

Goal to start treatment as early as possible to slow deterioration

Expectation of lifetime administration

- Clinical meaningfulness for patients with A-T would include any slowing – or even lack of – clinical decline
- Observed expanded access program (EAP) patients who stopped treatment return to rapid rate of deterioration – similar to decline observed in natural history of 6 to 9 year olds
- Three EAP patients at UT Houston – all treated since before COVID with no intention to stop
- Majority of patients travel for treatment without issue – easily completed with day trip
- Experienced and trained operators ensure seamless patient experience – ensure availability of back up machine
- Marked first NEAT study patient rolling over into OLE – demonstrating commitment to ongoing treatment

Questions & Answers

QUINCE THERAPEUTICS

Ataxia-Telangiectasia

Unlocking the power of a patient's own biology to address high unmet need for rare neurodegenerative and immunodeficiency disorder

Investor Webinar

February 7, 2025