QUINCE THERAPEUTICS

Overview of Prior eDSP Studies

Ataxia-Telangiectasia
Ulcerative Colitis
Chronic Obstructive Pulmonary Disease
Cystic fibrosis

eDSP — Encapsulated dexamethasone sodium phosphate

One of the first drugs Quince encapsulated in autologous red blood cells was dexamethasone sodium Phosphate, or DSP.

DSP is a corticosteroid well-described for its anti-inflammatory properties but is also coupled with serious adverse events, including adrenal suppression. eDSP is designed to maintain the well-described efficacy of DSP while reducing or eliminating the significant adverse events that accompany chronic corticosteroid treatment. The altered biodistribution, pharmacokinetics, and pharmacodynamics of eDSP enabled by autologous red blood cells may, therefore, improve the safety profile while maintaining and/or improving the desired therapeutic effects of DSP.

eDSP was previously evaluated in multiple early-stage investigator-initiated trials and clinical trials to evaluate safety and efficacy across a number of disease indications, including the company's lead indication ***Ataxia-Telangiectasia (A-T)***, as well as inflammatory bowel disease, including ***Crohn's disease (CD)*** and ***ulcerative colitis (UC)***, ***chronic obstructive pulmonary disease (COPD)***, and ***cystic fibrosis (CF)***. These previous clinical studies provide a robust set of efficacy and safety data upon which Quince's development pipeline is informed.

Phase 2 study of eDSP in Ataxia-Telangiectasia (A-T)

Quince completed an open-label, single-arm, multicenter Phase 2 clinical trial in 2012 evaluating the efficacy and safety of eDSP on neurological symptoms and adaptive behavior in patients with A-T (NCT01255358). The study included 22 patients with A-T (mean age: 11.2 years) with confirmed diagnoses and partially supported or autonomous gait treated with monthly infusions of eDSP for six months and a 19-month extension for some participants. The primary endpoint utilized the rating scale ICARS to measure ataxia symptoms.

The study results found a significant reduction in ICARS scores (mean reduction: 4 points for the intention-to-treat group and 5.2 points for the per-protocol group). A subgroup undergoing extended treatment showed a slower progression of the disease compared to untreated controls. eDSP was also well-tolerated with most adverse events being mild and unrelated to the treatment. No typical long-term corticosteroid side effects, such as weight gain or metabolic disruptions, were observed. The study concluded that eDSP significantly improved neurological symptoms and adaptive behavior in patients with A-T without well-described steroid-related side effects. These findings provided the basis for advancing eDSP into a Phase 3 study in A-T.

Reference: Chessa et al. Intra-erythrocyte infusion of dexamethasone reduces neurological symptoms in ataxia telangiectasia patients: results of a phase 2 trial. Orphanet J Rare Dis. 2014 Jan 9;9:5. doi: 10.1186/1750-1172-9-5. PMID: 24405665; PMCID: PMC3904207.

Phase 2 study of eDSP in ulcerative colitis (UC)

Quince completed a double-blind, randomized, placebo-controlled Phase 2 clinical trial in 2012 evaluating the efficacy and safety of eDSP in enabling oral corticosteroid withdrawal while maintaining remission in steroid-dependent patients with UC (NCT01171807). The study included 37 patients with corticosteroid-dependent UC randomized in two cohorts to receive eDSP (n=19) or placebo infusions (n=18) for six months with the primary endpoint measuring the proportion of patients with UC who discontinued oral corticosteroids while maintaining remission. Secondary endpoints included reduction in corticosteroid-related adverse events and mucosal healing.

Study results included: 1) efficacy measured by 68.4% of eDSP treated patients with UC successfully discontinuing oral corticosteroids while maintaining disease remission compared to 22.2% in the placebo group (p-value = 0.008), and 2) safety demonstrated by corticosteroid-related adverse events decreasing significantly in the treatment group to 26.3% versus 72.2% in placebo controls (p-value = 0.008). Relapse occurred shortly after eDSP treatment cessation, highlighting the need for ongoing therapy for long-term benefits. The study concluded that eDSP enabled effective corticosteroid withdrawal and reduced adverse events in patients with UC, presenting a promising alternative for managing corticosteroid dependency.

Reference: Bossa et al. Erythrocytes-mediated delivery of dexamethasone 21-phosphate in steroid-dependent ulcerative colitis: a randomized, double-blind Sham-controlled study. Inflamm Bowel Dis. 2013 Aug;19(9):1872-9. doi: 10.1097/MIB.0b013e3182874065. PMID: 23714676.

Phase 2 study of eDSP in UC (cont.)

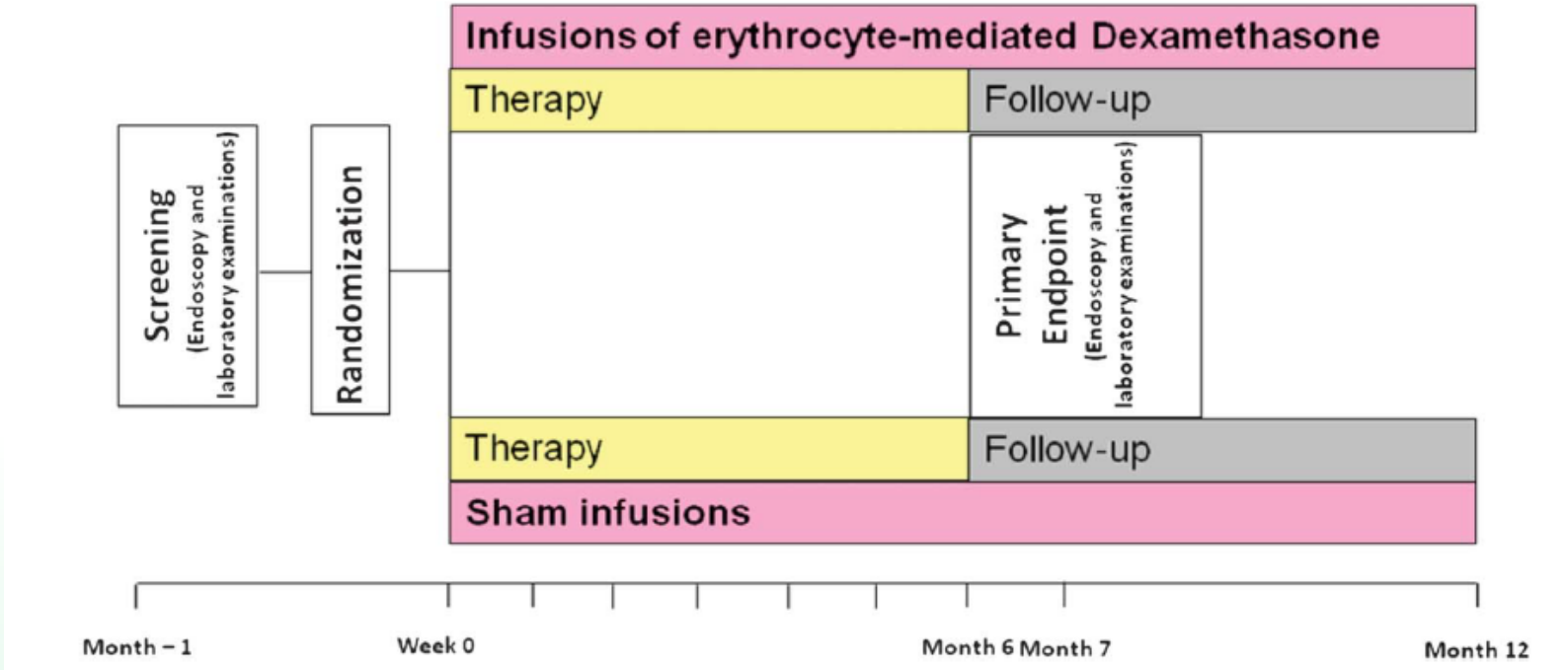

FIGURE 1. Study protocol. During the screening period (duration 1 month), the enrolled patients underwent clinical, endoscopic, and biochemical evaluations. The treatment period lasted 6 months during which the patients received monthly infusions of Dex 21-P or placebo. At each visit, the Powell-Tuck score and complete biochemical values were rechecked. All patients underwent sigmoidoscopy 1 month after stopping the infusions.

Reference: Bossa et al. Erythrocytes-mediated delivery of dexamethasone 21-phosphate in steroid-dependent ulcerative colitis: a randomized, double-blind Sham-controlled study. Inflamm Bowel Dis. 2013 Aug;19(9):1872-9. doi: 10.1097/MIB.0b013e3182874065. PMID: 23714676.

Phase 2 study of eDSP in UC (cont.)

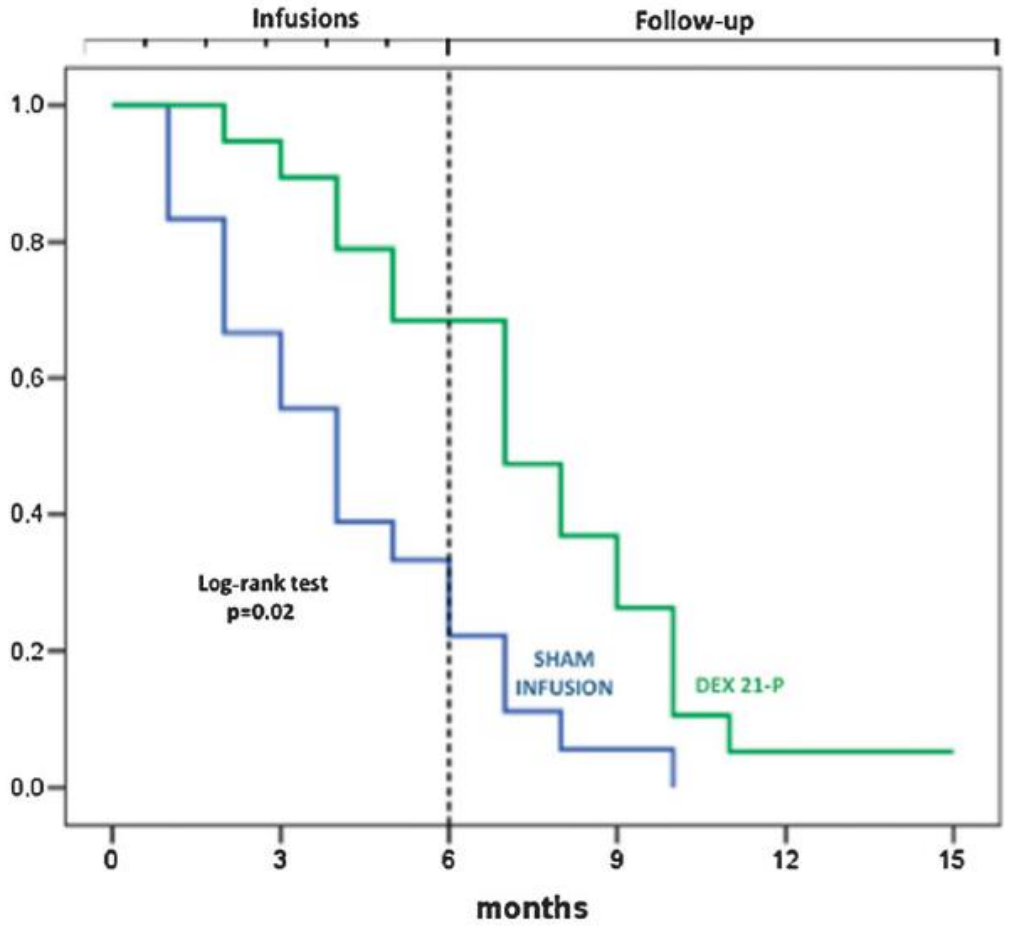

FIGURE 5. Probability over time to relapse during and following treatment with dexamethasone 21-phosphate loaded into autologous red blood cells.

Reference: Bossa et al. Erythrocytes-mediated delivery of dexamethasone 21-phosphate in steroid-dependent ulcerative colitis: a randomized, double-blind Sham-controlled study. Inflamm Bowel Dis. 2013 Aug;19(9):1872-9. doi: 10.1097/MIB.0b013e3182874065. PMID: 23714676.

Phase 2 study of eDSP in UC (cont.)

TABLE 3. Steroid-related Adverse Events Recorded at Study Inclusion and at the End of the Infusion Time

	Dex 21-P Infusions		Sham Infusions	
	Baseline	At End of Infusion	Baseline	At End of Infusion
Weight gain	8	3	9	9
Acne	5	1	5	5
Hirsutism	2	1	None	None
Amenorrhea	1	0	None	None
Insomnia	2	0	3	3
Moon face	6	3	6	6
Hyperglycemia	2	0	1	1

Reference: Bossa et al. Erythrocytes-mediated delivery of dexamethasone 21-phosphate in steroid-dependent ulcerative colitis: a randomized, double-blind Sham-controlled study. Inflamm Bowel Dis. 2013 Aug;19(9):1872-9. doi: 10.1097/MIB.0b013e3182874065. PMID: 23714676.

Phase 1b/2a study of eDSP in chronic obstructive pulmonary disease (COPD)

Quince completed a Phase 1b/2a clinical trial in 2000 evaluating the efficacy and safety of eDSP in enabling a slow, prolonged release of corticosteroids as a novel approach managing COPD while potentially reducing well-described side effects and improving compliance. The study included 10 patients with severe COPD, all of whom were previously treated with systemic or inhaled corticosteroids and β2-agonists. Participants were randomized in three cohorts to receive eDSP as follows: 1) group A (n=5): single administration with varying doses, 2) group B (n=3): two infusions at 15-day intervals, and 3) group C (n=2): single infusion of eDSP monitored for pharmacokinetics. Following the administration of eDSP, all patients with COPD suspended previous systemic or inhaled corticosteroids and β2-agonists therapies and were requested to record the time at which they felt the need to take these drugs. The primary endpoint was measured by clinical improvement (e.g., reduced symptoms, decreased need for other medications) and pharmacokinetics of dexamethasone.

Study results included: 1) efficacy as measured by significant clinical improvements in breathing, coughing, bronchospasm, and bronchostenosis, patient ability to avoid corticosteroids and β2-agonists for up to 30 days after infusions, and reduced symptoms of dyspnea and bronchial obstruction; 2) safety demonstrated by no significant side effects observed and lower doses of dexamethasone used (25–50 times less than conventional doses) thereby minimizing exposure and potential toxicity. The study concluded that eDSP provided a promising alternative for managing COPD, reducing drug burden and side effects while maintaining efficacy.

Reference: Rossi et al. Erythrocyte-mediated delivery of dexamethasone in patients with chronic obstructive pulmonary disease. Biotechnol Appl Biochem. 2001 Apr;33(2):85-9. doi: 10.1042/ba20000087. PMID: 11277860.

Phase 1b/2a study of eDSP in cystic fibrosis (CF)

Quince completed a Phase 1b/2a clinical trial in 2004 evaluating the efficacy and safety of eDSP in patients with CF. The study included 17 patients with CF are homozygous for the ΔF508 mutation.

Study results found that the procedure for loading red blood cells with DSP was safe and reproducible with no significant adverse effects observed, in addition to eDSP providing slow and prolonged release of DSP in the bloodstream, detectable for up to 28 days after infusion. Patients with CF treated with eDSP showed significant improvement in lung function (FEV1), significant reduction in infective relapses due to Pseudomonas aeruginosa, no significant changes in BMI, and a decrease in plasma levels of the inflammatory cytokine IL-8. The study concluded that eDSP offered a promising approach for reducing pulmonary inflammation and improving lung function in CF without the adverse effects commonly associated with conventional corticosteroid therapy.

Reference: Rossi et al. Low doses of dexamethasone constantly delivered by autologous erythrocytes slow the progression of lung disease in cystic fibrosis patients. Blood Cells Mol Dis. 2004 Jul-Aug;33(1):57-63. doi: 10.1016/j.bcmd.2004.04.004. PMID: 15223012.

Phase 1b/2a study of eDSP in CF (cont.)

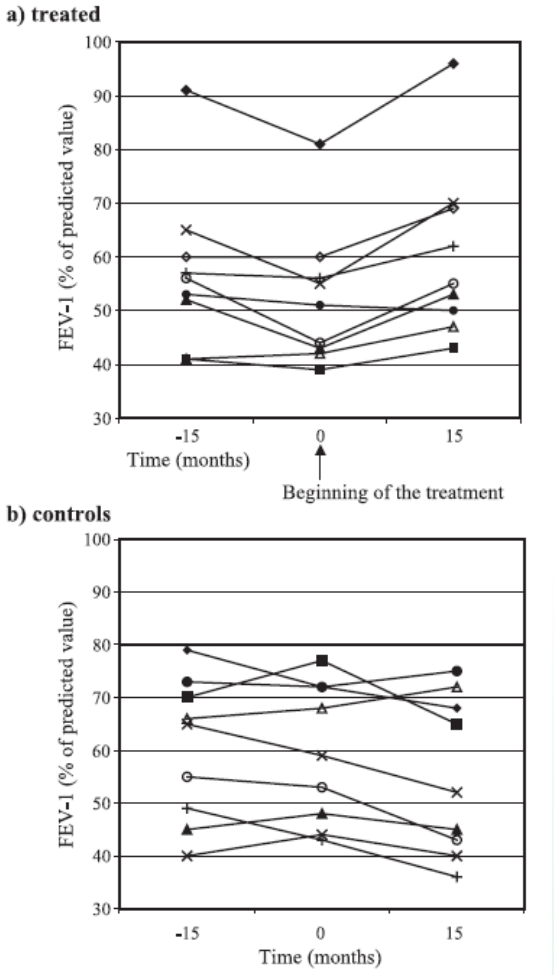

Fig. 2. Effect of treatment on pulmonary expiratory function. (a) Forced expiratory volume in 1 s (FEV_1) in nine CF patients that received erythrocytes loaded on the average with 8.9 ± 3.8 mg of Dex 21-P at 1-month intervals. Values were registered both during the treatment and in the preceding 15 months ($P = 0.01$; Friedman's test). (b) Forced expiratory volume in 1 s (FEV_1) in nine control CF patients submitted to usual therapeutic protocols. Values were registered in a 30-month period ($P = 0.0002$; Mann–Whitney U test on deltas, posttreatment minus pretreatment, between the two groups).

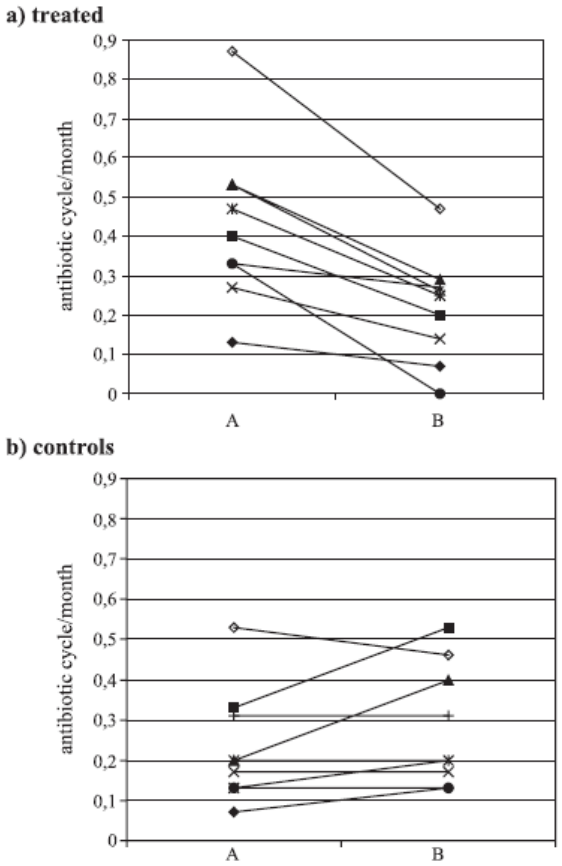

Fig. 3. Effect of treatment on infective relapses by *P. aeruginosa*. (a) Plot of antibiotic cycles per month in nine CF patients in the 15 months preceding treatment with Dex 21-P-loaded erythrocytes (A) and in the 15 months following Dex 21-P-loaded erythrocyte administrations (B). (b) Plot of antibiotic cycles per month in nine control CF patients in a 30-month period. First 15 months (A) and second 15 months (B). The delta's (posttreatment minus pretreatment) were compared: $P = 0.0002$ Mann–Whitney U test. Infective relapses by *P. aeruginosa* were monitored by registering the frequency of antibiotic therapy cycles per month.

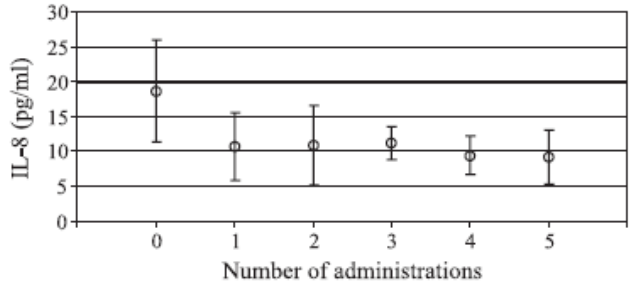

Fig. 4. Plasma level of IL-8. Mean IL-8 values in plasma samples of three CF patients (nos. 10, 12, and 13) during a 5-month period of treatment with Dex 21-P-loaded erythrocytes at 1-month intervals. IL-8 was evaluated immediately before starting therapy (time 0) and about 1 week post each infusion. IL-8 normal values = 0–8.1 pg/ml.

Reference: Rossi et al. Low doses of dexamethasone constantly delivered by autologous erythrocytes slow the progression of lung disease in cystic fibrosis patients. Blood Cells Mol Dis. 2004 Jul-Aug;33(1):57-63. doi: 10.1016/j.bcmd.2004.04.004. PMID: 15223012.

Selecting A-T as lead indication for eDSP

While each of these potential indications showed promising clinical study results, it was determined to advance eDSP for further evaluation of its efficacy and safety for the treatment of A-T primarily due to:

- ***Unmet need with no approved therapeutics for patients with A-T***
- ***Previous literature showing a positive response to corticosteroids in the disease***
- ***Development path allowing for comparison to placebo control***
- ***Favorable competitive landscape***
- ***Significant commercial opportunity***