Celldex therapeutics

CDX-0159 Phase 1b Study Results in Cold Contact Urticaria and Symptomatic Dermographism

EAACI 2021
July 12, 2021

Safe Harbor Statement

This communication contains "forward-looking" statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements other than statements of historical fact are statements that could be forward-looking statements. You can identify these forward-looking statements through our use of words such as “may,” “will,” “can,” “anticipate,” “assume,” “should,” “indicate,” “would,” “believe,” “contemplate,” “expect,” “seek,” “estimate,” “continue,” “plan,” “point to,” “project,” “predict,” “could,” “intend,” “target,” “potential” and other similar words and expressions of the future. These forward-looking statements are subject to risks and uncertainties that may cause actual future experience and results to differ materially from those discussed in these forward-looking statements. Important factors that might cause such a difference include, but are not limited to, the timing, cost and uncertainty of obtaining regulatory approvals for product candidates; our ability to develop and commercialize products before competitors that are superior to the alternatives developed by such competitors; the validity of our patents and our ability to avoid intellectual property litigation, which can be costly and divert management time and attention; and the other factors listed under “Risk Factors” in our filings with the SEC, including Forms 10-K, 10-Q and 8-K. Celldex does not undertake any obligation to release publicly any revisions to such forward-looking statement to reflect events or circumstances after the date hereof or to reflect the occurrence of unanticipated events.

Phase 1b Single Dose of CDX-0159 in Chronic Inducible Urticaria

95% Complete Response Rate, Rapid Onset and Sustained Durability

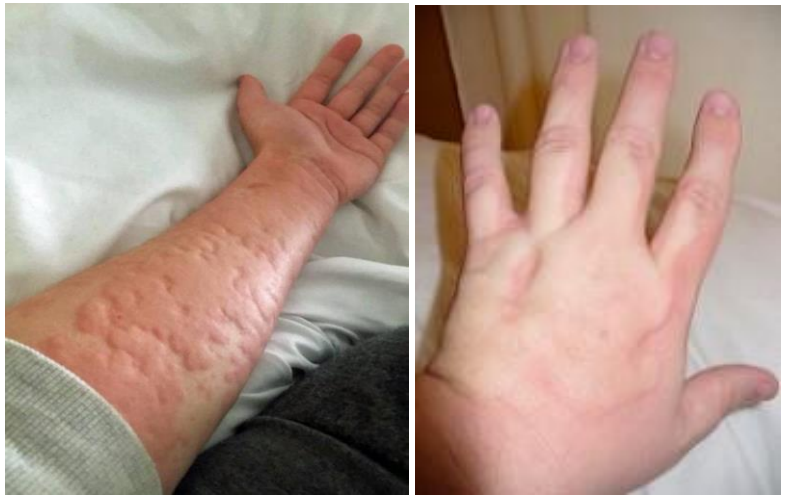
- Rapid, profound and durable responses offer patients opportunity for quick, lasting, meaningful relief
- Median duration of response 77+ days in Cold Urticaria and 57+ days in Symptomatic Dermographism
- Serum tryptase and skin mast cell depletion mirror clinical activity
- Novel mechanism safely depletes mast cells indicating potential to impact other diseases with mast cell involvement
- Favorable safety profile

Chronic Inducible Urticaria can be a Severe, Debilitating Disease with a Significant Impact on Quality of Life

- Significant medical need with limited or no treatment options

- Patients suffer both physically and psychologically with impaired quality of life.
  - Extensive impacts on social life, work and school

Cold Urticaria (ColdU)
Occurs when the skin comes in contact with temperatures below skin temperature - symptoms like itching, burning wheals (hives) and/or angioedema and, in some cases, anaphylaxis will occur



Symptomatic Dermographism (SD)
Development of itching/burning skin and wheals in response to shearing forces on the skin including rubbing, scratching or scrubbing

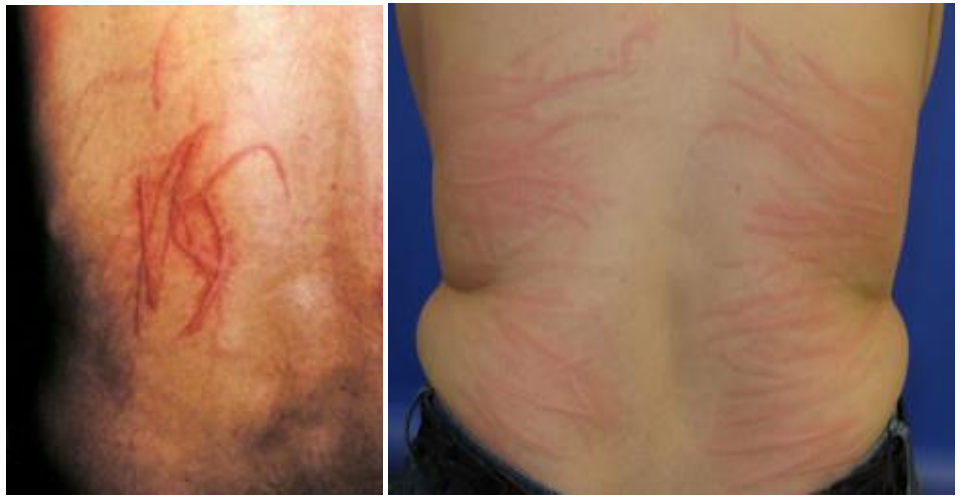
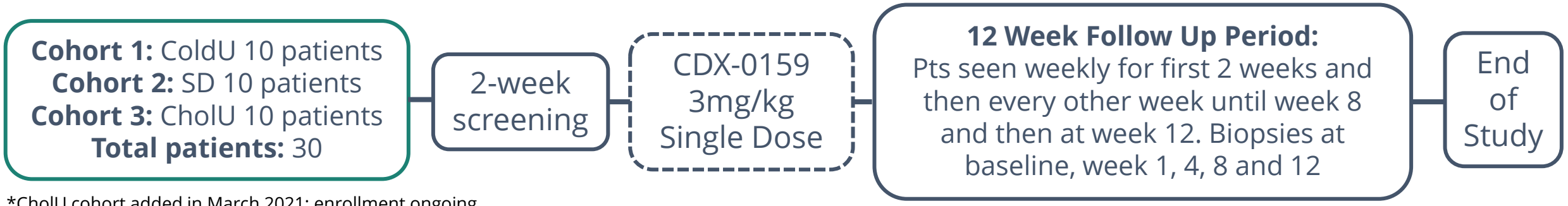


Image Sources:
https://dermnetnz.org/topics/dermographism/
https://www.bbc.co.uk/bbcthree/article/d7ae42f3-b3ae-47ae-9464-eb8c328fe3dc

Phase 1b Single Dose of CDX-0159 in Chronic Inducible Urticaria (CIndU) Trial Design



*CholU cohort added in March 2021; enrollment ongoing

Population: Cold Urticaria (ColdU), Symptomatic Dermographism (SD), Cholinergic Urticaria (CholU)
- Patients refractory to antihistamines

Design: Single dose with 12 week follow up

Primary Endpoint: Safety and Tolerability

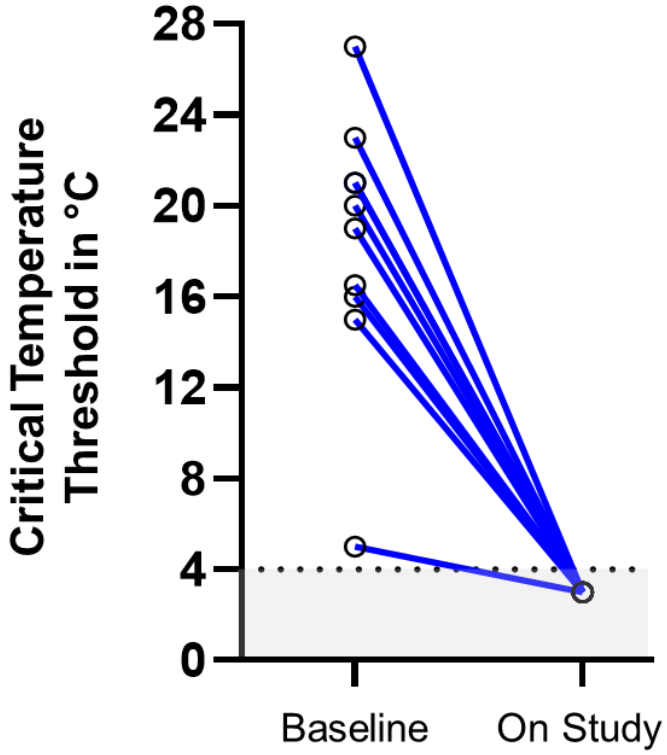
Secondary Endpoints: Activity, PK, PD

Study being conducted by Dr. Marcus Maurer, Professor of Dermatology and Allergy at Charité - Universitätsmedizin in Berlin

95% Complete Response Rate in Patients with Inducible Urticaria

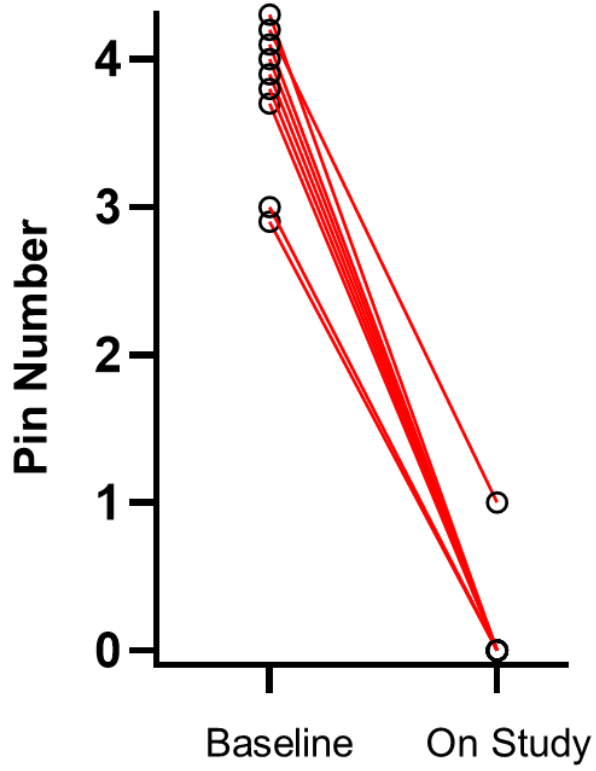
Cold Urticaria

10/10 Complete Responses



Symptomatic Dermographism

8/9 Complete Responses; 1/9 Partial Responses



- Compete responses observed in all 3 patients (1 cold contact; 2 symptomatic dermographism) with prior Xolair® (omalizumab) experience, including two who were Xolair refractory

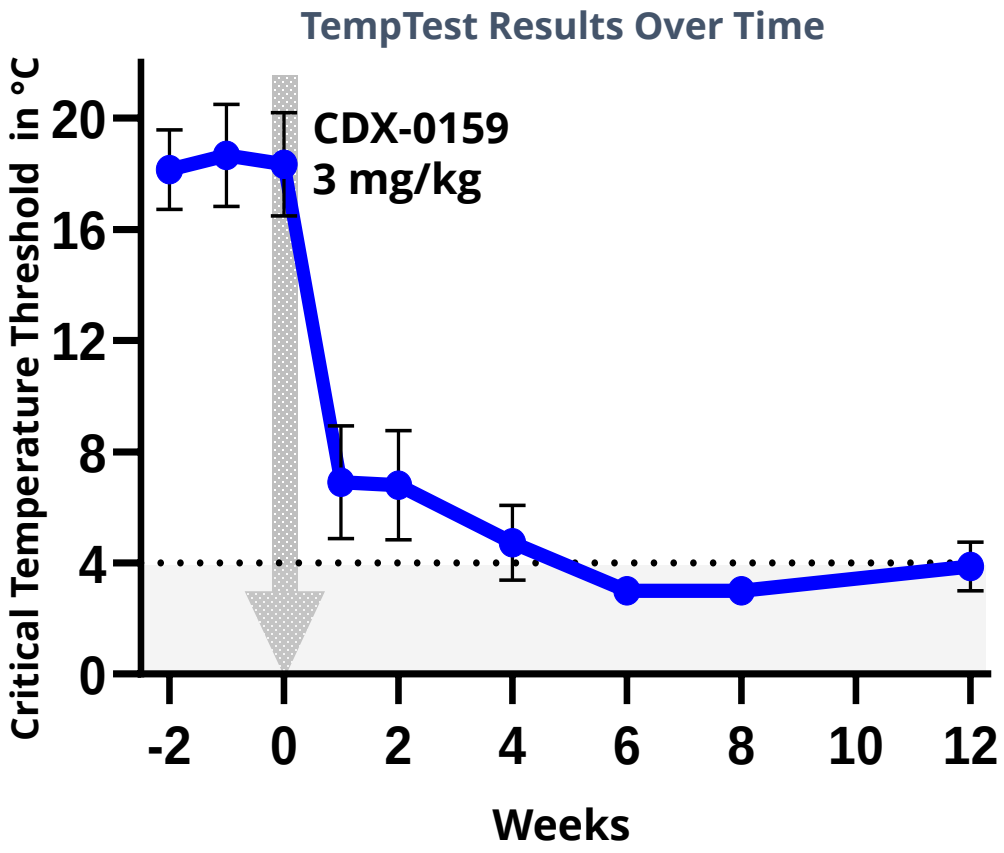
Complete Response=negative provocation test at ≤4°C or 0 pins; Partial Response=improvement by 4°C or ≥2 pins; Maximum response for each patient is shown

Responses were Rapid, Profound and Durable After Single Dose

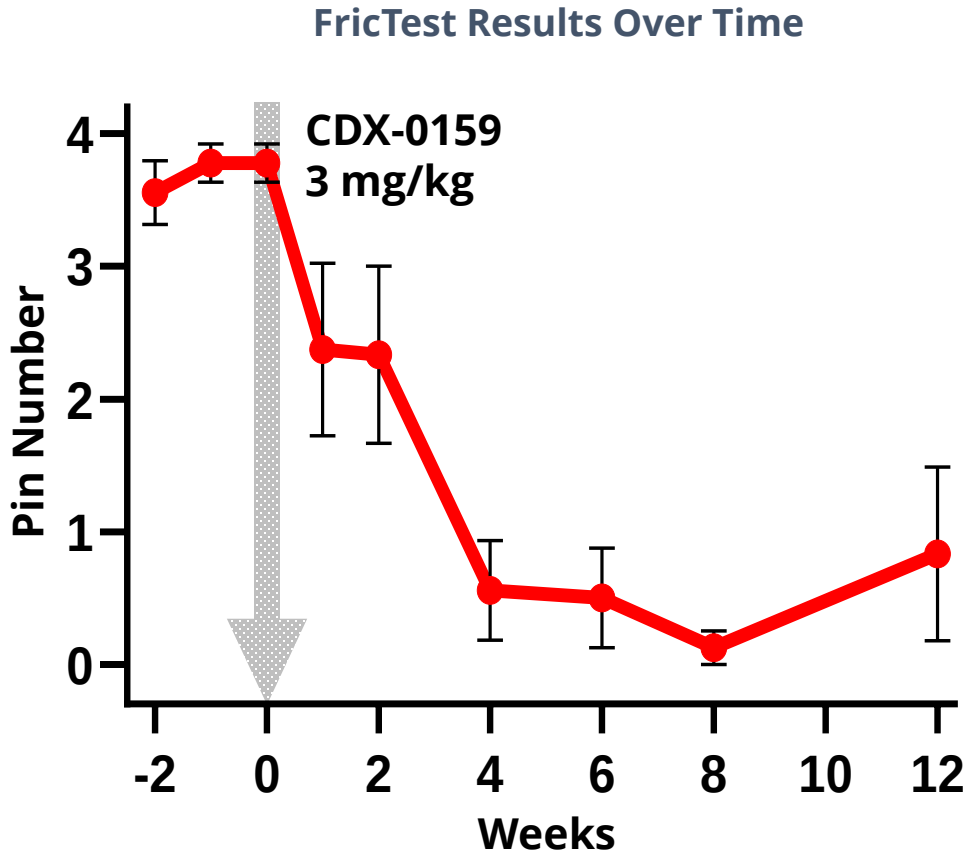
- Complete Responses were experienced by 7/10 ColdU patients at week 1 and 7/8 SD patients at week 4

- Median duration of response was 77+ days for ColdU and 57+ days for SD

Cold Urticaria



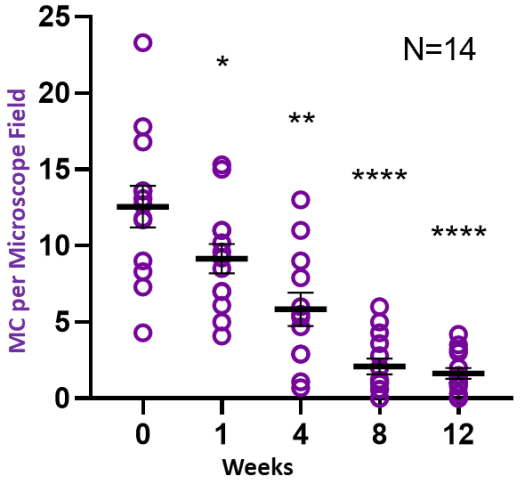
Symptomatic Dermographism



Rapid, Marked and Durable Depletion of Skin Mast Cells Reflected by Drop in Serum Tryptase

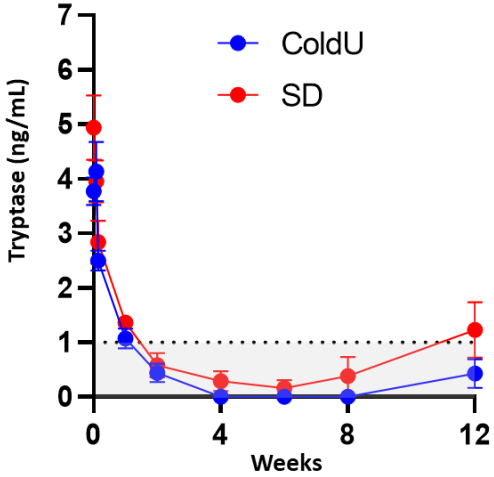
- CDX-0159 treatment markedly depletes skin mast cells and serum tryptase
- Mast cell depletion demonstrate potential of CDX-0159 to investigate role of mast cells across many disease settings

87% Reduction of Skin Mast Cell Numbers



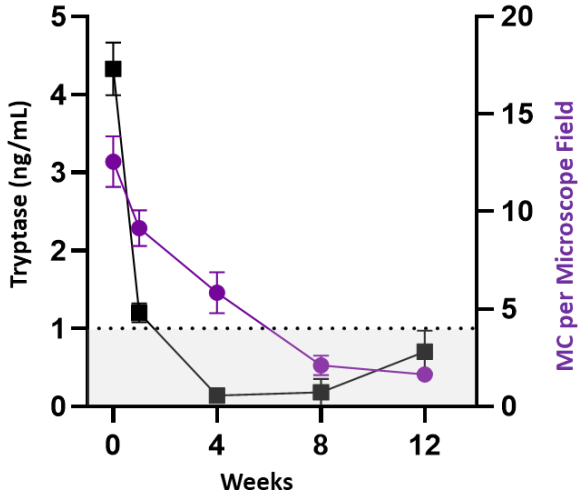
*p<0.05, **p<0.01, ***p<0.001, ****p<0.0001

Reduction of Serum Tryptase Below Detection in All Patients

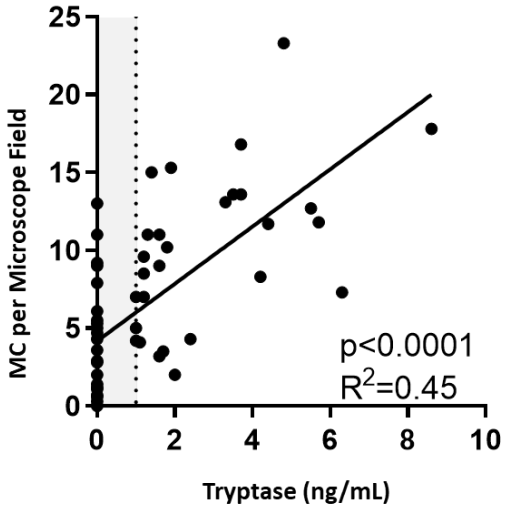


- Tryptase values below assay limit of quantitation (LLoQ = 1 ng/mL) normalized to 0

Mast Cell and Tryptase Kinetics



Skin Mast Cell Numbers Correlate with Serum Tryptase Levels

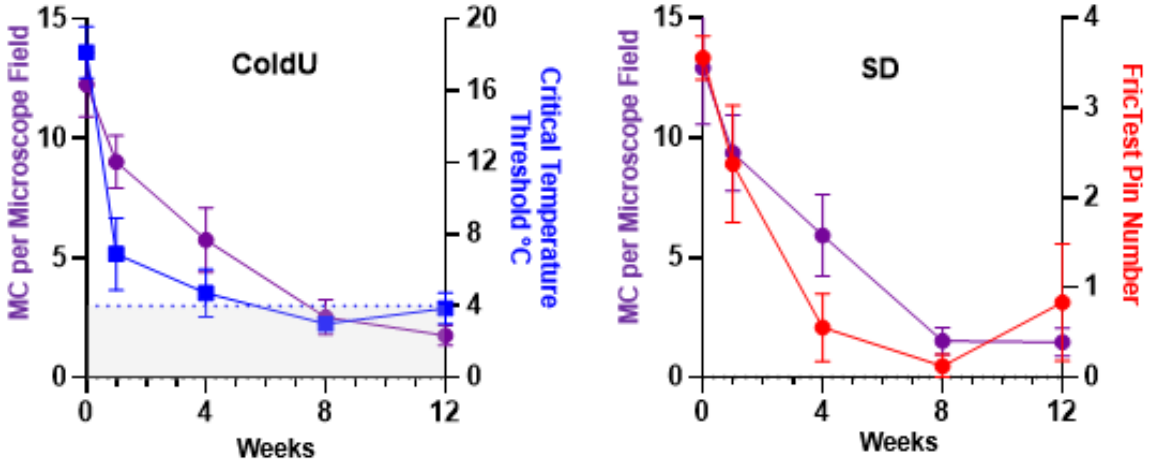


- Tryptase values below LLoQ normalized to 0.
- Critical temperature threshold values below 4°C (negative test) assigned a value of 3°C

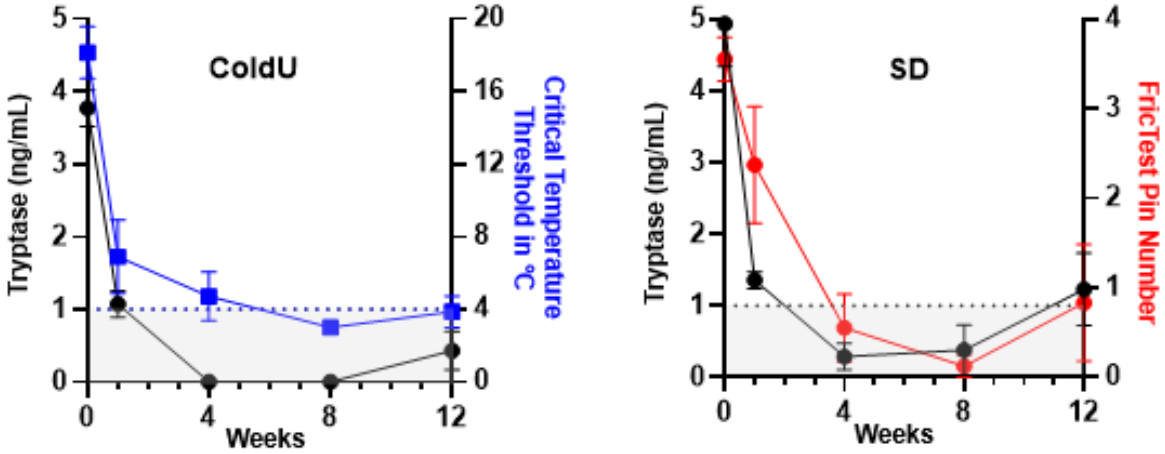
Kinetics for Skin Mast Cell and Tryptase Depletion Mirror Decreases in Provocation Thresholds

- The kinetics of skin mast cell and serum tryptase depletion mirror clinical activity
- Serum tryptase level is a robust pharmacodynamic biomarker for assessing MC burden and clinical activity in patients with CIndU and potentially other diseases

Mast Cells



Tryptase



- Tryptase values below LLoQ normalized to 0.
- Critical temperature threshold values below 4°C (negative test) assigned a value of 3°C

Favorable Safety Profile

- CDX-0159 continues to be generally well tolerated

- Most common adverse events:
  - Hair color changes (generally small areas of hair lightening)
  - Infusion reactions
  - Transient changes in taste perception (generally partial changes of ability to taste salt)

- Hair color changes and taste disorders are **consistent with inhibiting KIT signaling** in other cell types and are **expected to be fully reversible**

- As previously reported, single severe infusion reaction of loss of consciousness in a patient with a history of fainting was observed. Patient rapidly recovered. **Importantly, no mast cell activation was observed** based on tryptase monitoring

- **No evidence of clinically significant decreases** in hematology parameters

Leading Medical Expert: Prof. Dr. Marcus Maurer, MD

Professor of Dermatology and Allergology; Head of Dermatological Allergology at the Allergie-Centrum-Charité; Head of the Specialty Clinics for Urticaria, Mastocytosis, MCAS, Pruritus, Autoinflammatory Syndromes and Angioedema and the Dermatological Allergology Lab at Charité – Universitätsmedizin Berlin, Germany

Conducting Phase 1b CIndU and CSU Trials with Celldex

Prof Maurer is a Dermatologist and Allergologist, and he also trained in experimental pathology at the Beth Israel Deaconess Hospital and Harvard Medical School in Boston (1995-1998)

Coordinator of the Global Allergy and Asthma European Networks of urticaria and angioedema centers of reference and excellence, UCARE and ACARE

Areas of clinical interest include angioedema, urticaria, mastocytosis, pruritus, skin infections, and allergic diseases. Research is focused on the biology of mast cells, neuroimmunology, inflammation, innate immunity and tolerance

Has supervised more than 60 clinical trials, Phase 1 through 4. Contributed to more than 600 publications in peer-reviewed journals (>25.000 citations, H Index 79) and 40 books and book chapters

CDX-0159 Planned Development Timeline

2H 2021	1H 2022	2H 2022
Initiate SubQ HV Study – Q3	SubQ will be used to initiate Phase 2 Studies	
Initiate Ph 1 PN Study – Q4	Ongoing PN Study	
Ongoing Ph 1b CIndU Study	**Ph 1b Cholinergic Data – Q1**	
Ongoing Ph 1b CSU Study	**Ph 1b CSU Data**	Ongoing Follow Up Ph 1b CSU
	Initiate RCT Ph 2 in CIndU	Ongoing Ph 2 CIndU
	Initiate RCT Ph 2 in CSU	Ongoing Ph 2 CSU
		Initiate Additional Indications

IV Formulation

SubQ Formulation

HV – healthy volunteer; RCT – randomized controlled trial

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Questions