Company Overview Presentation

Making Fresh Tracks in Medicine®
Forward-Looking Statements

Any statements made in this presentation relating to future financial, business, and/or research and development, investigational, preclinical or clinical performance and potential, conditions, plans, prospects, impacts, shifts, trends, progress, or strategies and other such matters, including without limitation, Fresh Tracks Therapeutics Inc.’s (“FRTX”) strategy; future operations; future potential; future financial position; future liquidity; future revenue; territorial focus; projected expenses; results of operations; the anticipated timing, scope, design, results, possible impact of, and/or reporting of data of ongoing and future nonclinical and clinical trials involving FRTX-02 and any other products; intellectual property rights, including the acquisition, validity, term, and enforceability of such; the expected timing and/or results of regulatory submissions and approvals; and prospects for treatment of patients and commercializing (and competing with) any product candidates for any disease by FRTX or third parties, or research and/or licensing collaborations with, or actions of, its partners, including in the United States, Japan, South Korea, or any other country, are forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995. In addition, when or if used in this presentation, the words “may,” “could,” “should,” “might,” “show,” “topline,” “positive,” “announce,” “anticipate,” “advance,” “reflect,” “believe,” “estimate,” “expect,” “intend,” “plan,” “predict,” “potential,” “will,” “evaluate,” “advance,” “excited,” “aim,” “strive,” “help,” “progress,” “meet,” “support,” “select,” “initiate,” “look forward,” “promise,” “provide,” “commit,” “best-in-class,” “first-in-class,” “standard-of-care,” “on track,” “opportunity,” “disrupt,” “reduce,” “restore,” “demonstrate,” “suggest,” “attenuate,” “reinforce,” “imply,” “induce,” “attain,” “regulate,” “dampen,” “inhibit,” “target,” “shift,” and similar expressions and their variants, as they relate to FRTX or any of FRTX’s investigational products, partners, or third parties, may identify forward-looking statements. FRTX cautions that these forward-looking statements are subject to numerous assumptions, risks, and uncertainties, which change over time, often quickly, and in unanticipated ways. Important factors that may cause actual results to differ materially from the results discussed in the forward-looking statements or historical experience include risks and uncertainties, including without limitation, research results and data that do not meet targets; study limitations, including small sample sizes and the enrollment of only healthy patients; data variability; expectations or regulatory approval requirements; ability to obtain adequate financing for (i) product development, (ii) clinical trials, (iii) regulatory submission(s), and (iv) any future commercialization; ability to acquire, maintain, and enforce global intellectual property rights; potential delays or alterations in (i) product development, (ii) trials of any type, and (iii) regulatory submission and reviews; changes in law or policy; litigation; regulatory agency actions; feedback, or requests; supply chain disruptions; unanticipated demands on cash resources; interruptions, disruption, or inability by FRTX, its partners, or third parties to obtain or supply (i) research material, (ii) raw materials, and/or (iii) product anywhere, or secure essential services, in the world; the outcome of and reaction to FRTX’s current and planned preclinical and clinical trials across its portfolio of assets and for the SAD/MAD portion of this Phase 1 study on FRTX-02; the inability of third parties to achieve the regulatory and sales-based events under FRTX’s agreements with them, or their lack of funds, resulting in FRTX not receiving additional or full payments due from them, especially related to the sale and assignment of FRTX’s ownership of sofipironium bromide; and other risks associated with (i) developing and obtaining regulatory approval for, and commercializing, product candidates, (ii) raising additional capital, and (iii) maintaining compliance with Nasdaq listing requirements.

Further information on the factors and risks that could cause actual results to differ from any forward-looking statements are contained in FRTX’s filings with the United States Securities and Exchange Commission, which are available at https://www.sec.gov (or at https://www.frtx.com). The forward-looking statements represent the estimates of FRTX as of the date hereof only. FRTX specifically disclaims any duty or obligation to update forward-looking statements.
Fresh Tracks Therapeutics, Inc.

Clinical-stage pharmaceutical company developing innovative and groundbreaking prescription therapeutics for the treatment of autoimmune, inflammatory and other debilitating diseases

**Potential First-in-Class DYRK1A Inhibitor**
- Reported positive SAD/MAD topline results from FRTX-02 Phase 1 study in March 2023
- FRTX-02 is the first oral DYRK1A inhibitor tested in the clinic for autoimmune diseases
- Broad therapeutic potential for debilitating autoimmune and inflammatory diseases

**Potential First-in-Class STING inhibitor**
- FRTX-10 preclinical development underway
- Demonstrated strong proof-of-mechanism & promising profile in initial preclinical studies
- Potential to treat a wide array of autoinflammatory disorders and rare interferonopathies

**Cutting-Edge Kinase Inhibitors**
- Extensive library of small molecule next-generation kinase inhibitors targeting DYRK1, LRRK2, TTK, and CLK
- Opportunity to explore various autoimmune, inflammatory, neurodegenerative, and oncology diseases

**Experienced Leadership Team**
- Experienced leadership team with proven track record developing and launching several novel products that achieved first-in-class and/or iconic status
- Developed sofpironium bromide (first topical NCE for hyperhidrosis) from preclinical through Phase 3; Asset sold in May ’22 & future payments sold in July ’23

© 2023 Fresh Tracks Therapeutics, Inc. All rights reserved
# Pipeline of NCEs with First-in-Class Potential

<table>
<thead>
<tr>
<th>PROGRAM</th>
<th>DISCOVERY</th>
<th>PRECLINICAL</th>
<th>PHASE 1</th>
<th>PHASE 2</th>
<th>PHASE 3</th>
<th>NEXT MILESTONE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FRTX-02</strong>&lt;br&gt;Oral DYRK1A Inhibitor</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Phase 1 Part 2 Initiation (Atopic Dermatitis Patients)</strong></td>
</tr>
<tr>
<td>AUTOIMMUNE DISEASES: Atopic Dermatitis</td>
<td>Rheumatoid Arthritis</td>
<td>Type 1 Diabetes</td>
<td>Others</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>FRTX-10</strong>&lt;br&gt;Oral STING Inhibitor</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Preclinical Development</strong></td>
</tr>
<tr>
<td>AUTOINFLAMMATORY DISEASES: Systemic Lupus Erythematosus</td>
<td>Dermatomyositis</td>
<td>NASH</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Next-Generation Kinase Inhibitors</strong>&lt;br&gt;Oral DYRK1, LRRK2, TTK &amp; CLK Inhibitors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Preclinical Characterization</strong></td>
</tr>
<tr>
<td>AUTOIMMUNE, NEUROINFLAMMATORY, AND OTHER DISEASES</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>FRTX-03</strong>&lt;br&gt;Topical DYRK1A Inhibitor</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Formulation Development</strong></td>
</tr>
<tr>
<td>AUTOIMMUNE DERMATOLOGY: Atopic Dermatitis</td>
<td>Psoriasis</td>
<td>Others</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Executing Strategy with an Experienced Leadership Team

Our executives have developed and/or supported launches for several novel products achieving first-in-class and/or iconic status.

CO-FOUNDER & CHIEF EXECUTIVE OFFICER
Andy Sklawer
- BrickellBio
- Verid
- Concordia Pharmaceuticals

CHIEF R&D & CHIEF OPERATING OFFICER
Deepak Chadha
- BrickellBio
- Inamed
- Kythera
- Allergan

CHIEF FINANCIAL OFFICER
Albert Marchio II
- BrickellBio
- CytoMX
- Three Fields Capital

GENERAL COUNSEL & CCO
David McAvoy
- BrickellBio
- Endocyte
- Novartis
FRTX-02

Shifting the Balance Through DYRK1A Inhibition
FRTX-02 is a potent, highly selective, and orally bioavailable potential first-in-class DYRK1A inhibitor with strong preclinical validation and broad potential to treat debilitating autoimmune and inflammatory diseases.

**Novel Autoimmunity Target**
- Dual mechanism potentially restoring immune homeostasis through enhanced regulatory T-cell differentiation and concomitant inhibition of pro-inflammatory pathways
- Emerging field with recent significant investor & pharma interest

**Strong Preclinical Validation**
- Proof-of-mechanism established by thorough characterization
- Preclinical proof-of-concept in 10+ animal models of autoimmune disorders
- Promising efficacy profile vs. established therapies

**Significant Market Opportunity**
- Robust potential across multiple different autoimmune diseases
- Oral & topical formulations under development
- Strong IP position (CoM) in U.S. & other key countries through 2038+

**Phase 1 Trial Ongoing**
- Reported positive SAD/MAD topline results from FRTX-02 Phase 1 study in March 2023
- Results support advancement of FRTX-02 as potential first-in-class treatment for autoimmune diseases
- FRTX-02 is first oral DYRK1A inhibitor tested in the clinic for autoimmune diseases

DYRK1A = Dual-specificity tyrosine phosphorylation regulated kinase 1A; CoM = composition of matter
Broad Autoimmune & Inflammatory Disease Potential

DYRK1A inhibitors offer broad potential to treat autoimmune, inflammatory, and other debilitating diseases.

**AUTOIMMUNE DERMATOLOGY**
- Atopic Dermatitis
- Hidradenitis Suppurativa
- Psoriasis

**AUTOIMMUNE AND INFLAMMATORY**
- Rheumatoid Arthritis
- Type 1 Diabetes
- Inflammatory Bowel Disease
- Systemic Lupus Erythematosus
- Osteoarthritis

**NEUROINFLAMMATORY**
- Alzheimer’s Disease & Others Tauopathies
- Down’s Syndrome

**NEXT-GENERATION KINASE INHIBITORS**

---

Immune Imbalance

The immune system is a tightly regulated network that maintains a balance, however this equilibrium becomes disrupted in patients with autoimmune disease and chronic inflammation.

**IMPAIRED T-CELL HOMEOSTASIS**
- Functional and quantitative deficiency of regulatory T cells
- Overactivation/proliferation of pro-inflammatory T cells

**TLR & IL-1R OVERACTIVATION**
- MyD88L induces inflammatory signalling cascade
- Chronic inflammation due to lack of anti-inflammatory MyD88S

Dual Mode of Action

FRTX-02 has a dual mode of action targeting both adaptive and innate immune responses, resulting in the restoration of T-cell homeostasis and inhibition of MyD88/IRAK4 signaling.

Restoring T-Cell Homeostasis

FRTX-02 shifts the T-cell balance, yielding significant decrease in pro-inflammatory cytokines

FRTX-02 increases T\textsubscript{reg} cells & concomitantly decreases pro-inflammatory T\textsubscript{h}17 cells

Serum IL-17
(Rheumatoid Arthritis \textit{in vivo} model)

Serum TNF\alpha
(Rheumatoid Arthritis \textit{in vivo} model)

*\textit{p}<0.05, **\textit{p}<0.01, ***\textit{p}<0.001, ****\textit{p}<0.0001 vs. DMSO or vehicle control

FRTX-02

Innate Immune Response

FRTX-02 induces alternative splicing of MyD88, thereby blocking the IRAK4 pathway and yielding greater inhibition compared to a clinical-stage IRAK4 inhibitor.

FRTX-02 favors MyD88S, resulting in reduced IRAK4 phosphorylation

Significant decrease in IL-6 release

FRTX-02 shows 30-fold higher TLR signalling inhibition vs. IRAK4 inhibitor

*** p<0.001 vs. control; Kim, S. et al. J. Transl. Autoimmun. (2023).

© 2023 Fresh Tracks Therapeutics, Inc. All rights reserved
Preclinical Efficacy in Atopic Dermatitis

FRTX-02 results in strong reduction of atopic dermatitis disease severity and pro-inflammatory cytokines in the skin, with a promising profile as compared to established therapies.

Oral treatment of atopic dermatitis shows competitive effect vs. Upadacitinib (Rinvoq®)

Oral treatment resulted in significant reduction of cytokines & chemokines in the skin


Disease only and vehicle group N=4; treatment groups N=7 per group; Left: *p<0.05 (Dunnett’s test) vs. vehicle control; Right: **p<0.01, ***p<0.001, ****p<0.0001 (unpaired, two-tailed t-test)

Dermatitis Severity Score based on composite score of erythema, scarring, edema, erosion; skin tissue samples taken on Day 14 (last day of treatment) from the back of each animal.
Preclinical Efficacy in Rheumatoid Arthritis

FRTX-02 has successfully demonstrated competitive efficacy to JAK or TNFα inhibition in a rheumatoid arthritis model, where DYRK1A is upregulated.

1. Guo, X. et al. Tissue Cell (2018), RA = rheumatoid arthritis, Con = healthy controls; N=9 per group, 2. Internal data: Collagen-induced arthritis (CIA) mouse model; Clinical score combines severity of lesions, Mankin scores, necrosis and synovial inflammation and hyperplasia (N=10 per group); *p<0.05 (Dunnett’s test) vs. vehicle, PO = peroral, SC = subcutaneous. Based on Evaluate Pharma: Baricitinib (Olumiant®; Eli Lilly) WW Sales Forecast in RA (2026): US$924M; Filgotinib (Jyseleca®, Galapagos) WW Sales Forecast in RA (2026): US$ 356Mn
FRTX-03 results in rapid and strong reduction of disease severity of established atopic dermatitis, which was confirmed in a model of IMQ-induced psoriasis.

1. Kim, S. et al. J. Transl. Autoimmun. (2023). TC/Nga mice; 3-week induction with house dust mite cream prior to treatment initiation (Treatment start: Day 1); N=5 per group; *p<0.05 (Dunnett’s test) vs. vehicle.

# Long-acting, potent steroids such as dexamethasone are broadly immunosuppressive and long-term include skin thinning, telangiectasias, folliculitis, and contact dermatitis.

2. Internal data: BALB/c mice; Disease induction with topical 5% Imiquimod (IMQ) cream on the right ear of animals applied once daily from day 1 to day 9; Treatment start on Day 1 for 9 consecutive days; net ear thickness was defined as the Δ of thickness of the disease-induced right ear vs. healthy left ear control; N=8 per group; *p<0.05 (Dunnett’s test) vs. vehicle.

Once-daily, topical treatment of atopic dermatitis results in rapid, significant decrease of disease burden\(^1\)

Significantly reduced ear thickness was also observed in an IMQ-induced psoriasis\(^2\)

After 9 days of treatment
Nonclinical and CMC Overview

Completed nonclinical studies & CMC activities for FRTX-02 support a 4-week first-in-human trial

OVERVIEW OF COMPLETED NON-CLINICAL STUDIES

**Toxicology**
- Mouse 7-day dose range finding (DRF) study
- Dog 7-day DRF study
- Mouse 4-week repeat dose
- Dog 4-week repeat dose
- Mouse 13-week repeat dose

**ADME**
- Plasma & metabolic stability, PPB, Met. ID
- Predicted human metabolism (liver & kidney)
- CYP & transporter inhibition, CYP induction
- Metabolite identification

**Safety Pharmacology**
- Irwin test (mouse)
- Respiratory (dog)
- Cardiovascular telemetry (dog)
- Human ventricular trabeculae/SA node
- Ion channel assay

**Genotoxicity**
- Ames test
- In vitro micronucleus test
- In vivo micronucleus test

**Reproductive & Development**
- Seg 1 (rat; customized)

OVERVIEW OF CMC

- **GMP process development**: completed drug substance and product scale-up
- **Formulation**: oral immediate release hard capsule (multiple capsule strengths)
- **Stability**: studies of up to 36 & 24 months completed for drug substance and product
- **Phase 1 clinical trial materials**: manufacturing completed, stability testing ongoing
FRTX-02

Phase 1 SAD/MAD Topline Results
Key Highlights from Part 1 (SAD/MAD)

Topline results from Part 1 (SAD/MAD) of the Phase 1 study support the continued development of FRTX-02 as a potential first-in-class, once-daily oral treatment for atopic dermatitis and/or other autoimmune diseases.

- FRTX-02 was generally safe and well tolerated within the potential therapeutic dose range.
- Plasma concentrations within the potential therapeutic dose range were consistent with efficacious exposure levels established in nonclinical disease models.
- Pharmacokinetic (PK) data support once-daily oral dosing with FRTX-02 and steady state concentrations were attained before Day 14.
- Reduction in disease-relevant cytokines was observed in exploratory ex-vivo lipopolysaccharide (LPS)-stimulated whole blood pharmacodynamic (PD) assays.
Phase 1 Clinical Study Design Overview

FRTX-02-101 is a two-part, randomized, double-blinded, placebo-controlled study evaluating the safety, tolerability, PK and PD of oral FRTX-02 in healthy adult subjects (Part 1) and atopic dermatitis patients (Part 2)

**PART 1: SINGLE ASCENDING DOSE (SAD) PHASE**

56 healthy subjects (8 per cohort) randomized 6:2 to once daily doses of FRTX-02 or placebo

Endpoints: safety, tolerability, PK

- **COHORT 1**: 10 mg
- **COHORT 2**: 30 mg
- **COHORT 3**: 75 mg
- **COHORT 4**: 150 mg
- **COHORT 5**: 300 mg
- **COHORT 6**: 450 mg
- **COHORT 7**: 600 mg
- **COHORT 4 (FED)**: 150 mg

**PART 1: MULTIPLE ASCENDING DOSE (MAD) PHASE**

33 healthy subjects (11 per cohort) randomized 9:2 to either 14 once daily doses of FRTX-02 or placebo

Endpoints: safety, tolerability, PK, exploratory PD

- **COHORT 8**: 150 mg QD
- **COHORT 9**: 300 mg QD
- **COHORT 10***: 75 mg QD

*75 mg QD dose was selected for Cohort 10 based on 150 mg QD (Cohort 8) PK exposures exceeding FRTX-02 concentrations at the mouse efficacious dose (30 mg/kg BID) and safety findings from 300 mg QD (Cohort 9).

**PART 2: ATOPIC DERMATITIS**

30-40 patients receiving 28 once-daily doses of FRTX-02 or placebo

Endpoints: safety, tolerability, PK, PD, exploratory efficacy
FRTX-02 was generally safe and well tolerated in all seven SAD cohorts (10 mg - 600 mg)

- No Serious Adverse Events (SAEs) and no discontinuations due to Treatment-Emergent Adverse Events (TEAEs)
- No dose-dependent trend in frequency or severity of TEAEs was observed
- All but one TEAE were mild (single count of moderate back pain unlikely related to treatment in 450 mg cohort)
- Most TEAEs were not related or unlikely related to study treatment
- No ECG or lab findings of clinical relevance

### POSSIBLY RELATED TREATMENT-EMERGENT AEs* (>1 SUBJECT)

<table>
<thead>
<tr>
<th>AE TERM</th>
<th># SUBJECTS</th>
<th>SEVERITY</th>
<th>COHORT</th>
</tr>
</thead>
<tbody>
<tr>
<td>HEADACHE</td>
<td>5</td>
<td>Mild (x5)</td>
<td>75 mg, 150 mg (FAST &amp; FED), 600 mg</td>
</tr>
<tr>
<td>NAUSEA</td>
<td>2</td>
<td>Mild (x2)</td>
<td>75 mg, 600 mg</td>
</tr>
</tbody>
</table>

* Per investigator assessment.
SAD: FRTX-02 PK Summary

FRTX-02 was well absorbed for all SAD doses and reached peak plasma concentrations between 2 to 4.5 hours post dose.

**SAD PK PARAMETERS**

<table>
<thead>
<tr>
<th>PK PARAMETER</th>
<th>10 MG (N=6)</th>
<th>30 MG (N=6)</th>
<th>75 MG (N=6)</th>
<th>150 MG (N=6)</th>
<th>300 MG (N=6)</th>
<th>450 MG (N=6)</th>
<th>600 MG (N=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$C_{\text{MAX}}$ (NG/ML)</td>
<td>156.54 (44.1)</td>
<td>530.98 (40.9)</td>
<td>928.27 (47.6)</td>
<td>2145.52 (48.1)</td>
<td>3052.29 (46.0)</td>
<td>4089.87 (43.7)</td>
<td>5137.33 (11.7)</td>
</tr>
<tr>
<td>$AUC_{0-24}$ (H*NG/ML)</td>
<td>1176.69 (49.3)</td>
<td>4618.56 (55.7)</td>
<td>9895.73 (51.2)</td>
<td>35194.37 (47.7)</td>
<td>45059.69 (50.8)</td>
<td>65041.61 (50.0)</td>
<td>93518.36 (18.2)</td>
</tr>
<tr>
<td>$T_{\text{MAX}}$ (HR)</td>
<td>1.82 (34.7)</td>
<td>2.62 (53.7)</td>
<td>2.50 (25.7)</td>
<td>6.26 (31.9)</td>
<td>3.80 (31.6)</td>
<td>3.81 (50.0)</td>
<td>4.31 (11.9)</td>
</tr>
<tr>
<td>$T_{1/2}$ (HR)</td>
<td>6.98 (33.6)</td>
<td>10.11 (55.2)</td>
<td>15.00 (65.0)</td>
<td>15.56 (33.7)</td>
<td>16.79 (47.9)</td>
<td>30.18 (49.9)</td>
<td>21.99 (52.6)</td>
</tr>
</tbody>
</table>

*Geometric Mean (%CV) reported for all parameters.
SAD: Minimal FRTX-02 Food Effect

Minimal effect of food was observed on PK of a single 150 mg oral dose of FRTX-02.

**150 MG FRTX-02 MEAN PLASMA CONCENTRATIONS OVER TIME**

**SAD PK PARAMETERS***

<table>
<thead>
<tr>
<th>PK PARAMETER</th>
<th>150 MG FAST (N=6)</th>
<th>150 MG FED (N=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$C_{\text{MAX}}$ (NG/ML)</td>
<td>2145.52 (48.1)</td>
<td>2316.81 (25.5)</td>
</tr>
<tr>
<td>AUC$_{0-24}$ (H*NG/ML)</td>
<td>35194.37 (47.7)</td>
<td>33867.79 (30.8)</td>
</tr>
<tr>
<td>$T_{\text{MAX}}$ (HR)</td>
<td>6.26 (31.9)</td>
<td>3.36 (30.0)</td>
</tr>
<tr>
<td>$T_{\frac{1}{2}}$ (HR)</td>
<td>15.56 (33.7)</td>
<td>14.96 (39.0)</td>
</tr>
</tbody>
</table>

*Geometric Mean (%CV) reported for all parameters.
FRTX-02-101

MAD: Blinded Safety Summary

FRTX-02 was safe and generally well tolerated at 75 mg and 150 mg over 14 days of oral QD dosing

- No SAEs
- Majority of TEAEs were mild (single count of moderate headache possibly related to treatment in 300 mg cohort)
- No dose-dependent trend in TEAE frequency or severity observed
- No lab findings of clinical relevance
- QTc prolongation observed in two subjects in 300 mg cohort
  - Both subjects were asymptomatic, their QTc intervals returned to baseline levels and remained in the normal range after dosing cessation, and all study assessments were completed
  - Exposures where QTc prolongation was observed are 2 to 4-fold above exposures within the potential therapeutic dose range (75 mg – 150 mg)

### POSSIBLY RELATED TREATMENT-EMERGENT AE s* (>1 SUBJECT)

<table>
<thead>
<tr>
<th>AE TERM</th>
<th># SUBJECTS</th>
<th>SEVERITY</th>
<th>COHORT</th>
</tr>
</thead>
<tbody>
<tr>
<td>CONSTIPICATION</td>
<td>3</td>
<td>Mild (x3)</td>
<td>75 mg, 150 mg, 300 mg</td>
</tr>
<tr>
<td>HEADACHE</td>
<td>3</td>
<td>Mild (x2)</td>
<td>75 mg, 300 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Moderate (x1)</td>
<td>300 mg</td>
</tr>
<tr>
<td>NAUSEA</td>
<td>2</td>
<td>Mild (x2)</td>
<td>75 mg, 300 mg</td>
</tr>
<tr>
<td>ECG QT PROLONGED</td>
<td>2</td>
<td>Mild (x2)</td>
<td>300 mg</td>
</tr>
</tbody>
</table>

* Per investigator assessment.
MAD: FRTX-02 PK Summary

MAD PK data support once-daily dosing with FRTX-02 and steady state was attained before Day 14.

FRTX-02 MEAN PLASMA CONCENTRATIONS OVER TIME

MAD (DAY 14) PK PARAMETERS*

<table>
<thead>
<tr>
<th>PK PARAMETER</th>
<th>75 MG QD (N=9)</th>
<th>150 MG QD (N=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C&lt;sub&gt;MAX&lt;/sub&gt; (NG/ML)</td>
<td>2450.68 (37.3)</td>
<td>5417.64 (46.6)</td>
</tr>
<tr>
<td>AUC&lt;sub&gt;0-24&lt;/sub&gt; (H*NG/ML)</td>
<td>37898.58 (46.2)</td>
<td>102394.70 (50.3)</td>
</tr>
<tr>
<td>T&lt;sub&gt;MAX&lt;/sub&gt; (HR)</td>
<td>2.68 (49.4)</td>
<td>3.25 (32.8)</td>
</tr>
<tr>
<td>T&lt;sub&gt;1/2&lt;/sub&gt; (HR)</td>
<td>15.97 (37.6)</td>
<td>28.26 (82.46)</td>
</tr>
<tr>
<td>C&lt;sub&gt;TROUGH&lt;/sub&gt; (NG/ML)</td>
<td>1355.53 (888.22)</td>
<td>4266.56 (2239.21)</td>
</tr>
<tr>
<td>DAY 14/1 RATIO&lt;sub&gt;CMAX&lt;/sub&gt;</td>
<td>1.85</td>
<td>2.85</td>
</tr>
<tr>
<td>DAY 14/1 RATIO&lt;sub&gt;AUC&lt;/sub&gt;</td>
<td>2.80</td>
<td>4.20</td>
</tr>
</tbody>
</table>

*Geometric Mean (%CV) reported for all parameters, except for C<sub>TROUGH</sub> where Mean (±SD) concentration is reported.

[1] 1 subject received 8, 1 subject received 9, and the remaining 7 subjects received 10 daily doses of FRTX-02. Dosing was halted (as per pre-defined protocol stopping rules) due to QTc prolongation observed in two subjects.
MAD: Therapeutic Dose Summary

Plasma concentrations within the potential FRTX-02 therapeutic dose range (75 mg and 150 mg) were consistent with efficacious exposure levels established in nonclinical disease models.

- After once-daily dosing with 150 mg FRTX-02 over 14 days:
  - \(C_{\text{max}}\) and AUC\(_{0-24}\) concentrations are above estimated exposures at mouse efficacious dose of 30 mg/kg BID.

- After once-daily dosing with 75 mg FRTX-02 over 14 days:
  - \(C_{\text{max}}\) and AUC\(_{0-24}\) concentrations are consistent with estimated exposures at mouse dose of 20 mg/kg BID.

- If mouse PD effects translate to a human autoimmune patient population (next clinical study), the FRTX-02 therapeutic dose range is expected to be between 75 mg and 150 mg.

MAD: PD Biomarker Sampling Methodology

**Dual Mode of Action**

- **T cell homeostasis**
  - Regulatory T cells
  - Pro-inflammatory T cells
  - FRTX-02

- **TLR/IL-1R signaling**
  - TLR
  - IL-1R
  - MyD88
  - IRAK1/4
  - FRTX-02
  - Pro-inflammatory cytokines

**PD biomarker assay in stimulated PBMCs from healthy subjects**

**PBMC COLLECTION & STIMULATION**

- Patient blood was drawn into TruCulture® tubes coated with LPS to stimulate cytokine release

**SAMPLE PROCESSING**

- Overnight Whole blood stimulation
- Plasma was separated from blood cells within the TruCulture® tube
- Freezing

**CYTOKINE MEASUREMENTS**

- Cytokines in supernatant were measured by a multiplex assay
- IL-6
- IFN-γ
- TNF
- IL-23
- IL-10
- 37 °C
MAD: FRTX-02 PD Summary

Reduction in disease-relevant cytokines was observed in exploratory _ex-vivo_ LPS-stimulated whole blood pharmacodynamic assays

- Exploratory PD activity was measured by impact on cytokine secretion following _ex vivo_ LPS stimulation of peripheral blood mononuclear cells (PBMCs) derived from the MAD cohorts.
- Cytokines were selected for assessment based on those observed to be reduced by FRTX-02 in various nonclinical disease models.
- FRTX-02 demonstrated a reduction in disease-relevant proinflammatory cytokines, suggesting initial support for the FRTX-02 mechanism of action.
- Mean percent cytokine reduction from baseline after 14 days of once-daily 75 mg or 150 mg FRTX-02 treatment versus placebo were in the range of approximately 66% to 20% for IFNγ, IL-23, IL-10, IL-6, and TNFα.
- Maximum individual subject cytokine reductions from baseline were shown to be >90% for IFNγ, >50% for IL-23, IL-10 and TNFα, and approximately 40% for IL-6.
FRTX-10

A First-in-Class Approach to Treating Inflammation
Potential First-in-Class Oral STING Inhibitor

FRTX-10 is a novel, potent, and orally bioavailable covalent STING inhibitor with demonstrated proof-of-mechanism and broad potential to treat autoinflammatory and rare monogenic diseases.

**Strong Scientific Rationale & Interest**
- Overactivation of cGAS-STING is well documented as a key pathway in inflammatory conditions.
- Several large pharma companies have invested in this target, given its broad potential.

**Lead FRTX-10 with Proof-of-Mechanism**
- Highly selective, novel, orally available STING inhibitor with low nanomolar potency.
- Preclinical in vitro and in vivo PoM established demonstrating dose-dependent cytokine reduction.
- Initial in vitro and in vivo DMPK and TK studies completed and additional studies ongoing.

**Broad Therapeutic Opportunity**
- Potential to address high unmet need diseases, ranging from broad autoinflammatory diseases to rare genetic interferonopathies.
- Strong biomarker hypothesis may allow for targeted clinical development approach.

**Exclusive Global Rights & Compound Library**
- Acquired exclusive global rights for all uses from Carna Bio in February 2022.
- Compound library of 300+ small molecule NCEs provides potential for strong IP protection, with CoM patents filed in 2021.

STING = Stimulator of Interferon Genes; PoM = proof of mechanism; CoM = composition of matter.
Broad Potential in Inflammatory Diseases

STING inhibitors have the potential to treat inflammatory diseases ranging from broad autoimmune and aging-related conditions to rare genetic interferonopathies.

**RARE GENETIC DISORDERS**
- Aicardi–Goutières syndrome (AGS)¹²
- STING-associated vasculopathy with onset in infancy (SAVI)¹²

**AUTOIMMUNE/INFLAMMATORY WITH BIOMARKER HYPOTHESIS**
- Systemic Lupus Erythematosus³⁵
- Rheumatoid Arthritis⁴

**OTHER INFLAMMATORY**
- Age-related macular degeneration⁶
- Non-alcoholic steatohepatitis (NASH)⁷

**TARGETED THERAPY**

**NOVEL THERAPEUTIC APPROACH**

---

*Elevated cGAS expression was found in notable clinical subpopulations of SLE and RA.*³⁴

Mechanism of Action

FRTX-10 covalently inhibits STING activation, resulting in reduction of proinflammatory cytokines such as IL-6 and Interferon (IFN)-β.

Decout, A et al. (2021) Nature Reviews Immunology
Competitive Advantage Against Other STING Inhibitors

FRTX-10 inhibits STING palmitoylation, which may present a more effective way to treat inflammation caused by aberrant STING signaling.

<table>
<thead>
<tr>
<th>Competitive Inhibitor</th>
<th>FRTX-10</th>
</tr>
</thead>
<tbody>
<tr>
<td>MECHANISM</td>
<td>FRTX-10</td>
</tr>
<tr>
<td>Dependent on endogenous cGAMP levels</td>
<td>Independent of cGAMP levels</td>
</tr>
<tr>
<td>STING VARIANTS</td>
<td>FRTX-10</td>
</tr>
<tr>
<td>Potency on inhibition could vary between variants</td>
<td>Inhibits all four major variants of human STING</td>
</tr>
<tr>
<td>STING MUTANTS</td>
<td>FRTX-10</td>
</tr>
<tr>
<td>Always active regardless of cGAMP binding</td>
<td>Inhibits pathologic STING mutants</td>
</tr>
</tbody>
</table>

FRTX-10 is a highly selective STING inhibitor that exhibits potent inhibition of human and murine STING compared to other covalent inhibitors.

Preclinical Proof-of-Mechanism

FRTX-10 demonstrated proof-of-mechanism on relevant pathways in vitro, resulting in significant reduction of key cytokines IL-6 and IFNβ after single and multiple dose oral treatment in vivo.

FRTX-10 inhibits the phosphorylation of key proteins in the STING pathway

<table>
<thead>
<tr>
<th></th>
<th>cGAMP (+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>H-151</td>
<td>1 0.1 0.01</td>
</tr>
<tr>
<td>FRTX-10</td>
<td>1 0.1 0.01</td>
</tr>
</tbody>
</table>

- pSTING (S366)
- STING
- pTBKI (S172)
- TBKI
- pIRF3 (S396)
- IRF3
- β-actin

Once-daily oral FRTX-10 treatment resulted in significant reduction of cytokines in a CMA-stimulated mouse model

- IL-6 (plasma)
- IFNβ (plasma)

2. C57BL/6N mice treated with FRTX-10 QD, single or repeated (5 days). Mice were stimulated with 224 mg/kg CMA i.p. and blood samples were taken 2 hours after CMA stimulation. Serum levels of IL-6 and IFNβ were measured by ELISA. *p<0.05 **p<0.01 (unpaired, Welch’s two-tailed t-test).
Next-Generation Kinase Inhibitors

Platform Overview
Platform of Next-Generation Kinase Inhibitors

Our platform of next-generation kinase inhibitors include small molecules that inhibit DYRK1, LRRK2, TTK and CLK with various potency and selectivity profiles.

**Patented Next-Gen Kinase Inhibitors**
Includes kinase inhibitors for DYRK1, LRRK2, LRRK2(G2019S), TTK and CLK

**Initial Characterization**
Completed for various molecules

**Lead Optimization and Preclinical Studies**
- **BRAIN-Penetrating**
  - Neuroinflammatory diseases
- **Non-BRAIN-Penetrating**
  - Autoimmune, inflammatory & other diseases

**Lead Selections**
Thank You!

Making Fresh Tracks in Medicine®

ir@frtx.com

August 2023