

December 2024

Innovating for Everyone

Clinical-stage biopharmaceutical company
focused on next generation therapeutics
meeting unmet patient needs.



 Nasdaq: HOTH

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Our Mission

At Hoth Therapeutics, we strive to develop innovative, impactful, and ground-breaking treatments with a goal to improve patient quality of life. We are a catalyst in early-stage pharmaceutical research and development, elevating promising drugs from the bench to pre-clinical and clinical testing. Utilizing a patient-centric approach, we collaborate and partner with a team of scientists, clinicians, and key opinion leaders to seek out and investigate medications that hold immense potential to create breakthroughs and diversify treatment options. Our mission is to bring value to both our shareholders and our patient populations.



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Key Investment Highlights



Clinical Programs



**Robust Pre-Clinical
Development
Programs**



**Targeting Unmet
Medical Needs to
Address Broad Market**



**Experienced
Management and
Advisory Board**

Pipeline: Multiple Shots on Goal

	PRODUCT	DISEASE	PROOF OF CONCEPT	PRECLINICAL	IND-ENABLING	PHASE 1	PHASE 2	PHASE 3	LAUNCH	
Oncology	HT-KIT	Mast-Cell Derived Cancers	[Progress bar: Proof of Concept to Ind-Enabling]							
Neurology	HT-TBI	Traumatic Brain Injury/Ischemic Stroke	[Progress bar: Proof of Concept to Preclinical]							
	HT-ALZ	Alzheimer's Disease	[Progress bar: Proof of Concept to Preclinical]							
Dermatology	HT-001	Skin Toxicity associated with EGFR Inhibitors	[Progress bar: Proof of Concept to Launch]							
	BioLexa	Atopic Dermatitis	[Progress bar: Proof of Concept to Phase 1]							
	HT-003D	Acne	[Progress bar: Proof of Concept to Preclinical]							
Inflammatory	HT-004	Asthma	[Progress bar: Proof of Concept to Ind-Enabling]							
	HT-003IBD	Inflammatory Bowel Diseases	[Progress bar: Proof of Concept to Preclinical]							

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Primary Development

 HOTH THERAPEUTICS

HT-001 Topical Gel

HT-KIT Injection

HT-ALZ Oral Soluble Film

BioLexa Lotion

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HT-001:

Value Proposition



Market Growth: EGFR Inhibitor Skin Toxicity market predicted to grow from \$52M in 2018 to \$391M by end of 2030*

Mechanism of Action: 12-week study conducted at GW suggests the topical application of HT-001 significantly reduces erlotinib-induced cutaneous toxicities applied preventatively or proactively. It supports that HT-001 may be used as a topical intervention to treat EGFR-inhibitor-induced cutaneous toxicity.**

Addresses Unmet Need: No current approved product on the market that specifically treats EGFR inhibitor cutaneous toxicities, which occur in up to 90% of patients undergoing EGFR inhibitor therapy.***

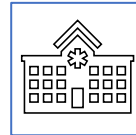
*EGFR Inhibitors-Induced Skin Disorders-Market Insights, Epidemiology, and Market Forecast-2030

**<https://ir.hoththerapeutics.com/ht-001>

***<https://jamanetwork.com/journals/jamadermatology/article-abstract/2767656>

Recent & Upcoming Milestones:

HT-001 Topical Gel



Q1 2023

Initiated Phase 2a Clinical Trial in Open Label Cohort

Q4 2024

All Clinical Sites Active and Enrolling in Open Label and Double-Blind Randomized Cohorts

Q1 2025

Initial Interim Open Label PK Cohort Data

Q3 2025

Full Data Set for Open Label PK Cohort

IND-Opening Trial:

CLEER-001 Phase 2a
Dose Ranging
Study

A Randomized, Placebo-Controlled, Parallel Phase 2a Dose Ranging Study to Investigate the Efficacy, Safety, and Tolerability of Topical HT-001 for the Treatment of Cutaneous Toxicities Associated with EGFR Inhibitors

2 Parts – Parallel Study Design:

- **Part 1:** Open-label treatment with HT-001 2% for 6 weeks (PK cohort)
- **Part 2:** Randomized double-blind treatment with HT-001 0.5%, 1%, 2% or placebo

Part 1

Open-Label PK Cohort

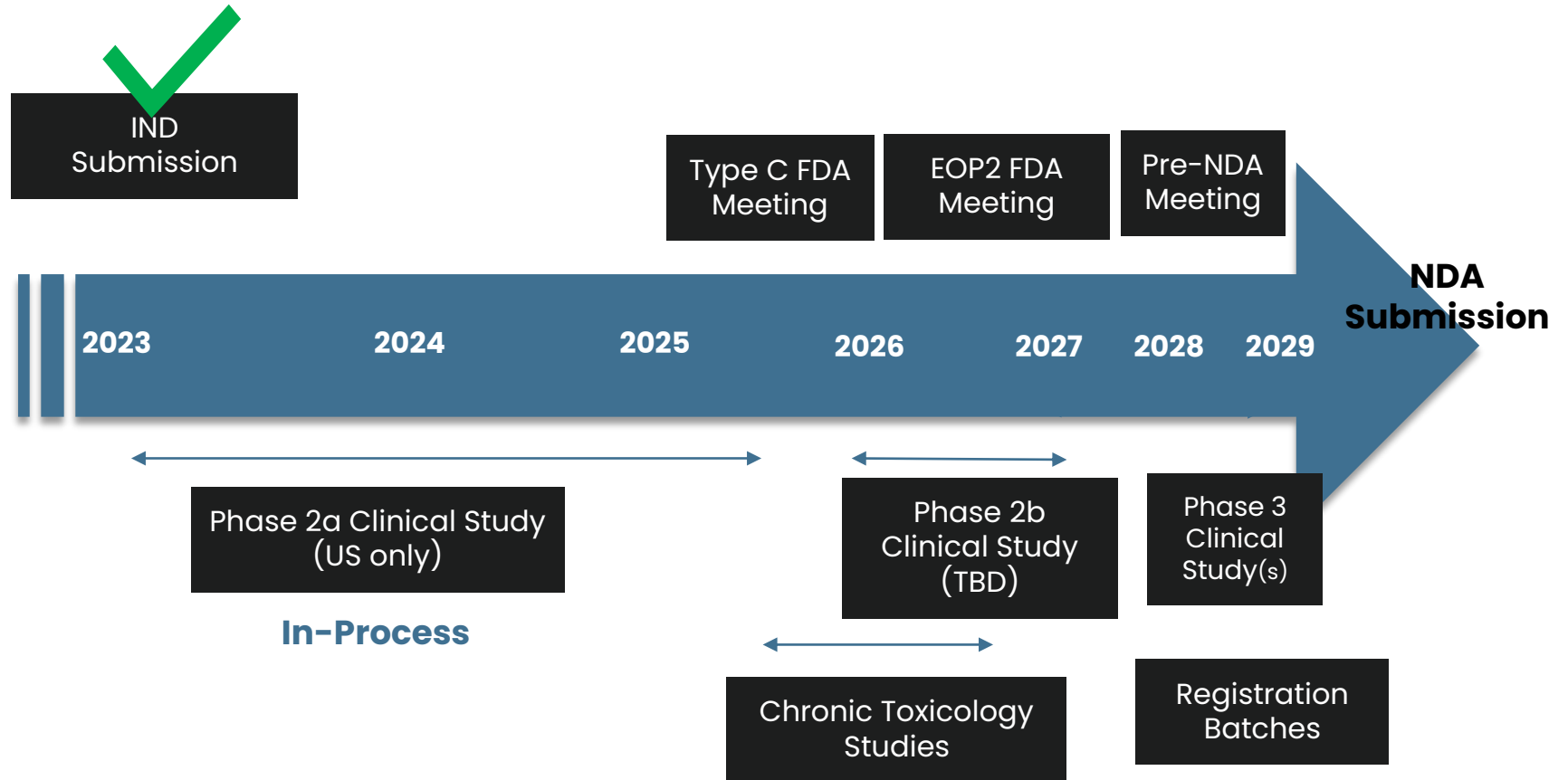
(6 weeks treatment
+ 2 weeks follow-up)
N = 12 patients

Part 2

Randomized, Double Blind Period

(6 weeks treatment
+ 2 week treatment follow-up)
N = 140 patients

HT-001 505(b)(2) Development Pathway



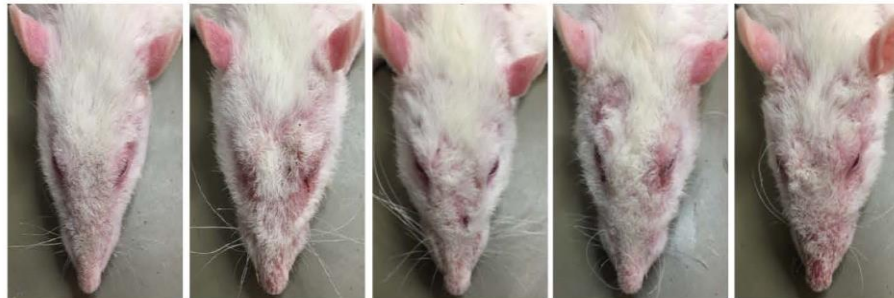
Current estimated dates; pending FDA meetings for phase 2b/phase 3 clinical studies

Proactive Topical HT-001 Significantly Reduces EGFR Inhibitor- Induced Cutaneous Toxicity

Erlotinib (noVeh C) – Week 12



Erlotinib + Topical HT-001 Initiated Week 1 – Week 12



Erlotinib + Topical HT-001 Initiated Week 6 – Week 12



Group	Change Compared to Erlotinib Only Group: Facial Skin Lesions at 12 weeks	Change Compared to Erlotinib Only Group: Hair Loss at 12 weeks
Preventative Topical HT-001 + Erlotinib	58.5% Reduction (p<0.001 vs Erl and p<0.01 vs control)	56.2% reduction in hair loss (p<0.001 vs Erl and p<0.001 vs control)
Proactive (week 6) Topical HT-001 + Erlotinib	47.8% reduction (p<0.001 vs Erl and p<0.001 vs control)	44.4% reduction in hair loss (p<0.001 vs Erl and p<0.001 vs control)

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HT-KIT:

Value Proposition

Market Growth: Global systemic mastocytosis treatment revenue is \$128M and projected to grow at 5.8% CAGR through 2031*

Mechanism of Action: HT-KIT is an antisense oligonucleotide that results in non-functional cKIT via mRNA frameshift.**

Addresses Unmet Need: KIT D816V mutation found in >80% of adult systemic mastocytosis cases results in conformational changes that make some tyrosine kinase inhibitor drugs ineffective.**

cKIT is also implicated in gastrointestinal stromal tumors, acute myeloid leukemia, and other rare cancers



*Global Systemic Mastocytosis Treatment Market Research Report, January 2022, Market.US

**Snider et al., Targeting KIT by frameshifting mRNA transcripts as a therapeutic strategy for aggressive mast cell neoplasms, Molecular Therapy (2021), <https://doi.org/10.1016/j.ymthe.2021.08.009>

Recent & Upcoming Milestones: HT-KIT Injection



Q4 2023

Pre-IND Meeting with FDA and strategy confirmed



Q1 2024

IND-enabling animal toxicology studies initiated



Q1 2025

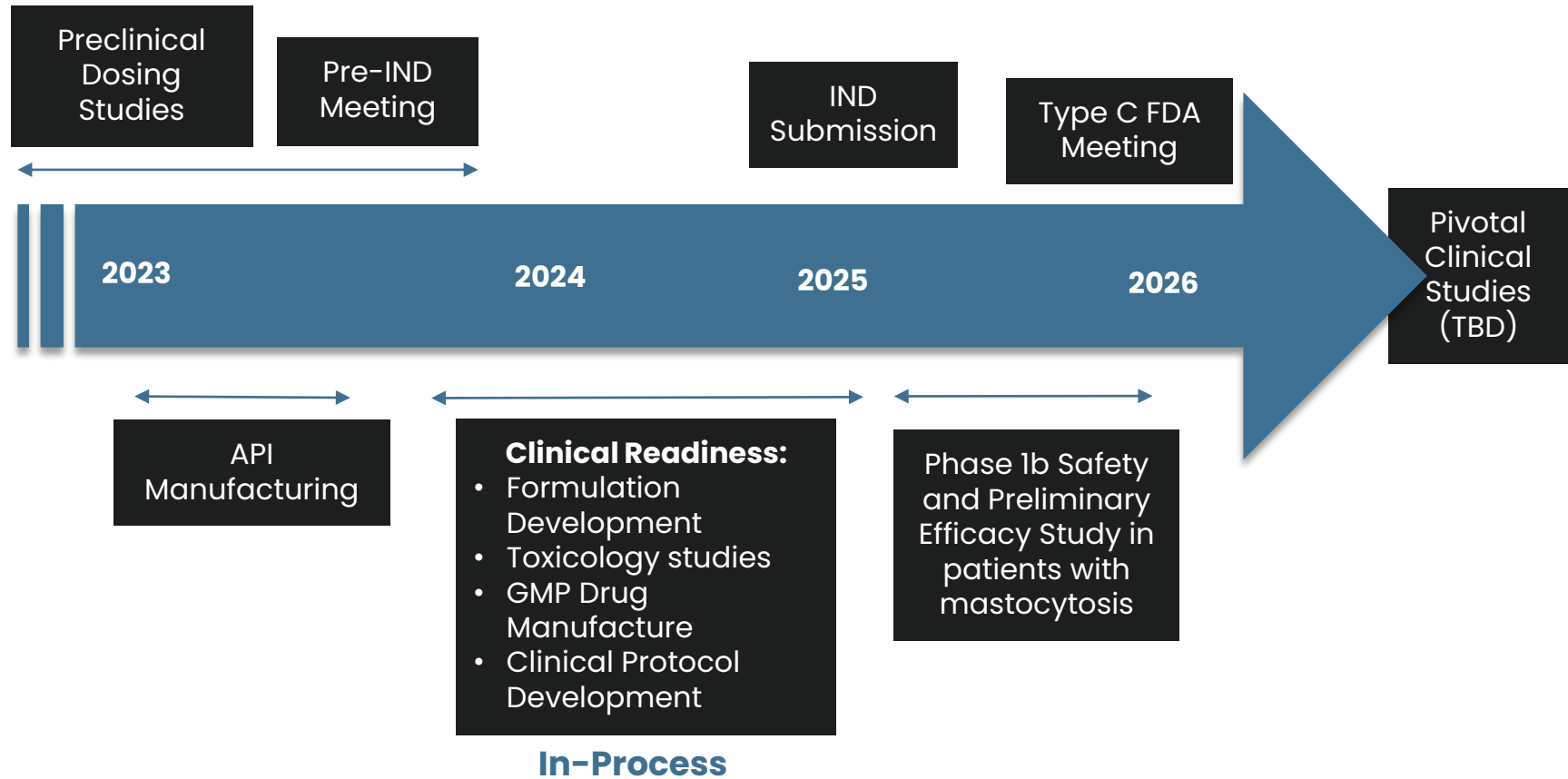
GLP animal studies and GMP API manufacturing initiation target



Q4 2025

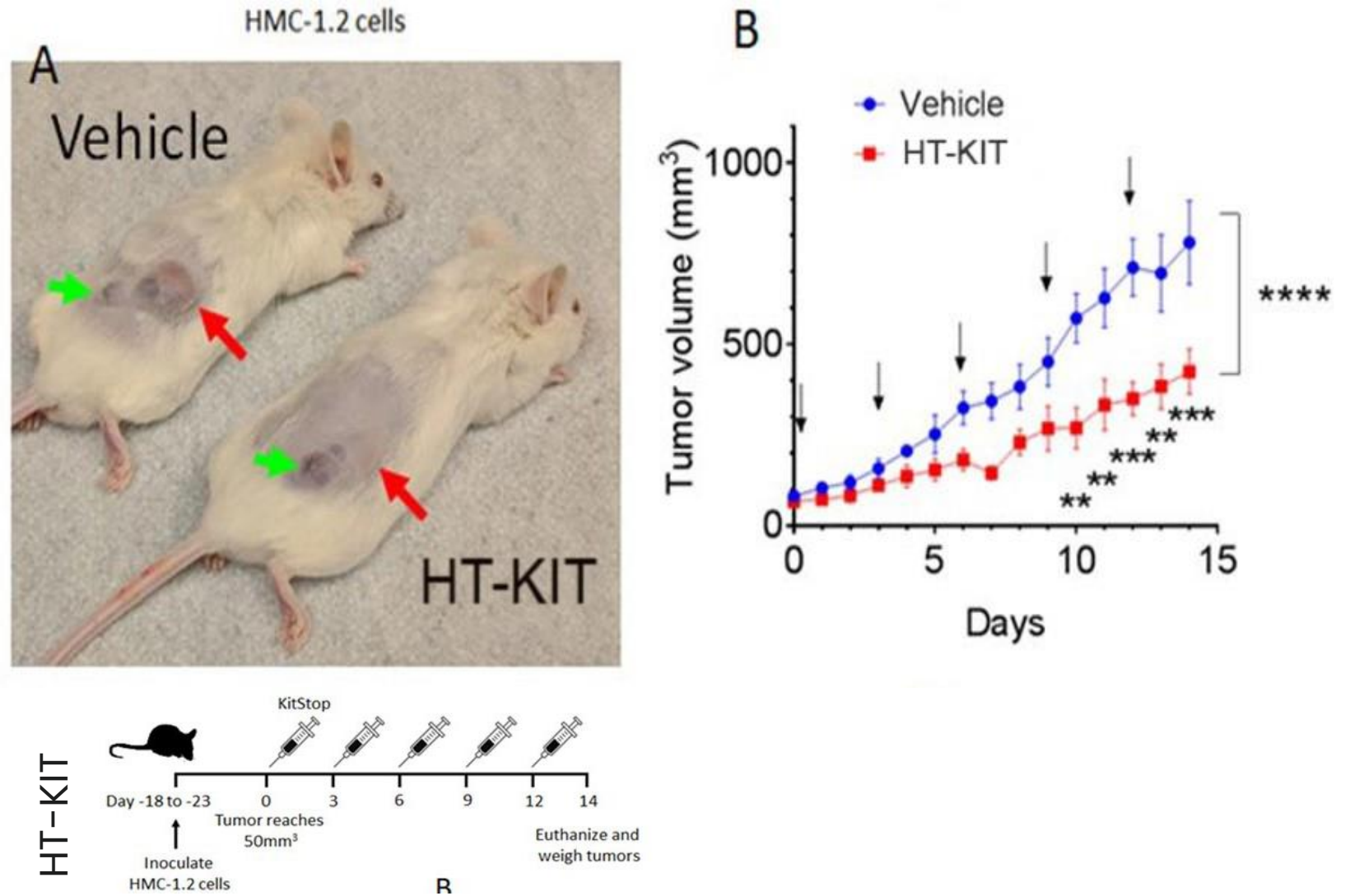
IND Submission target

HT-KIT Orphan Drug Development Pathway



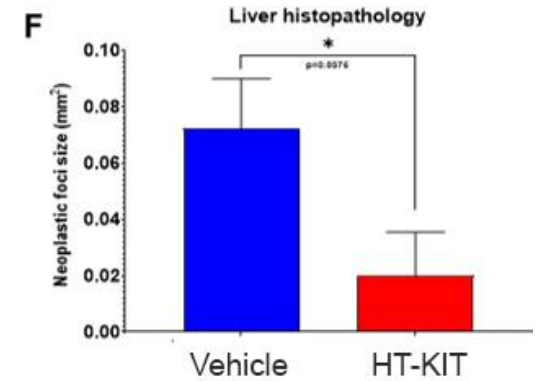
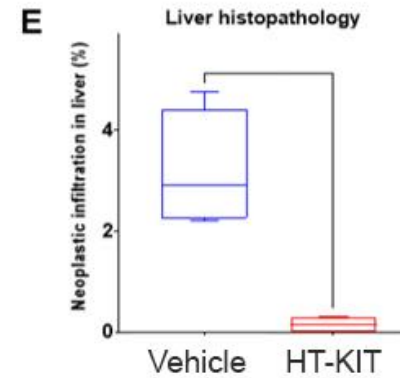
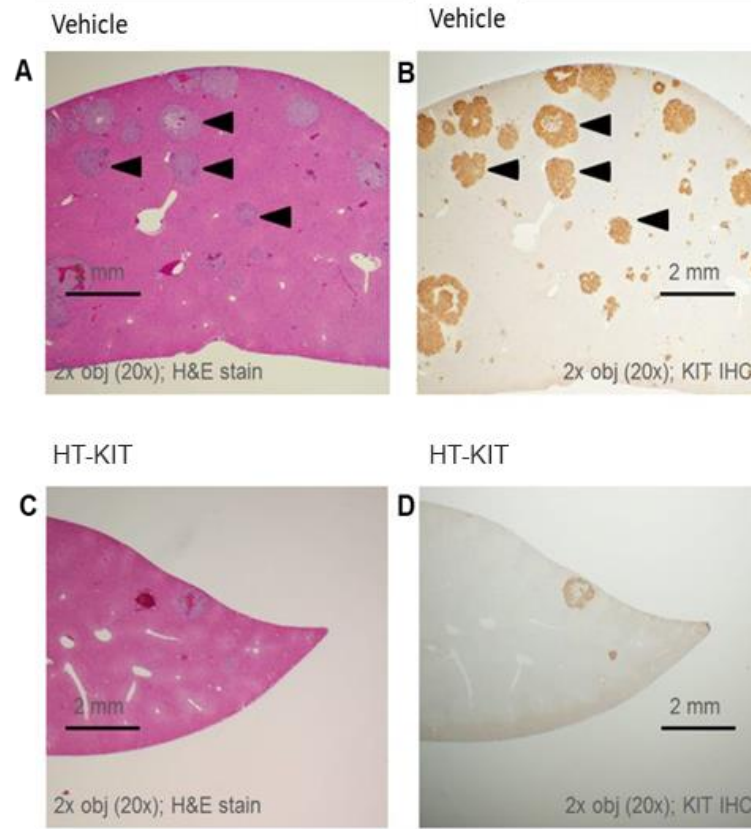
Current estimated dates; pending FDA meetings for clinical studies.

Systemic delivery of human HT-KIT inhibits tumor growth in a humanized xenograft mast cell neoplasia model



Figures from Douglas B. Snider¹, Greer K. Arthur¹, Guido H. Falduto², Ana Olivera², Lauren C. Ehrhardt-Humbert¹, Emmaline Smith¹, Cierra Smith¹, Dean D. Metcalfe² and Glenn Cruse¹ (1Department of Molecular Biomedical Sciences, CVM, NC State University 2Laboratory of Allergic Diseases, NIAID, NIH). Targeting KIT by frameshifting mRNA transcripts as a therapeutic strategy for aggressive mast cell neoplasms. Poster presentation at ASCO June 2021.

HT-KIT Reduces Liver Infiltration of Neoplastic Mast Cells in a Humanized Xenograft Model of Mast Cell Neoplasia



Figures from Douglas B. Snider¹, Greer K. Arthur¹, Guido H. Falduto², Ana Olivera², Lauren C. Ehrhardt-Humbert¹, Emmaline Smith¹, Cierra Smith¹, Dean D. Metcalfe² and Glenn Cruse¹ (1Department of Molecular Biomedical Sciences, CVM, NC State University 2Laboratory of Allergic Diseases, NIAID, NIH). Targeting KIT by frameshifting mRNA transcripts as a therapeutic strategy for aggressive mast cell neoplasms. Poster presentation at ASCO June 2021.

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HT-ALZ:

Value Proposition

Market Growth: The Global Alzheimer's Disease Treatment Market is expected to grow at a CAGR of around 12.8% from 2020 to 2027 and reach the market value of over \$5.2B by 2027.*

Mechanism of Action: HT-ALZ targets the Substance P/Neurokinin-1 Receptor pathway** in the brain, which has both negative (inflammatory) and positive (anti-amyloidogenic, memory, neuroprotective) roles in Alzheimer's disease.

Addresses Unmet Need: : There are currently no drugs approved that are considered disease modifying and demonstrate cognitive improvement. Preclinical data with HT-ALZ indicates HT-ALZ may provide reduced neuroinflammation and significant improvements in cognitive functions such as memory and learning.

*<https://www.acumenresearchandconsulting.com/alzheimers-disease-treatment-market>

**Martinez AN, Philipp MT. Substance P and Antagonists of the Neurokinin-1 Receptor in Neuroinflammation Associated with Infectious and Neurodegenerative Diseases of the Central Nervous System. J Neurol Neuromedicine. 2016;1(2):29-36. doi:10.29245/2572.942x/2016/2.1020

**Severini C, Petrella C, Calissano P. Substance P and Alzheimer's Disease: Emerging Novel Roles. Curr Alzheimer Res. 2016;13(9):964-72. doi:10.2174/1567205013666160401114039. PMID: 27033058.

Recent & Upcoming Milestones: HT-ALZ Oral Soluble Film



Q2 2024

HT-ALZ Formulation Work initiated



Q3 2024

US Patent Office Awarded HT-ALZ Patent



Q3 2024

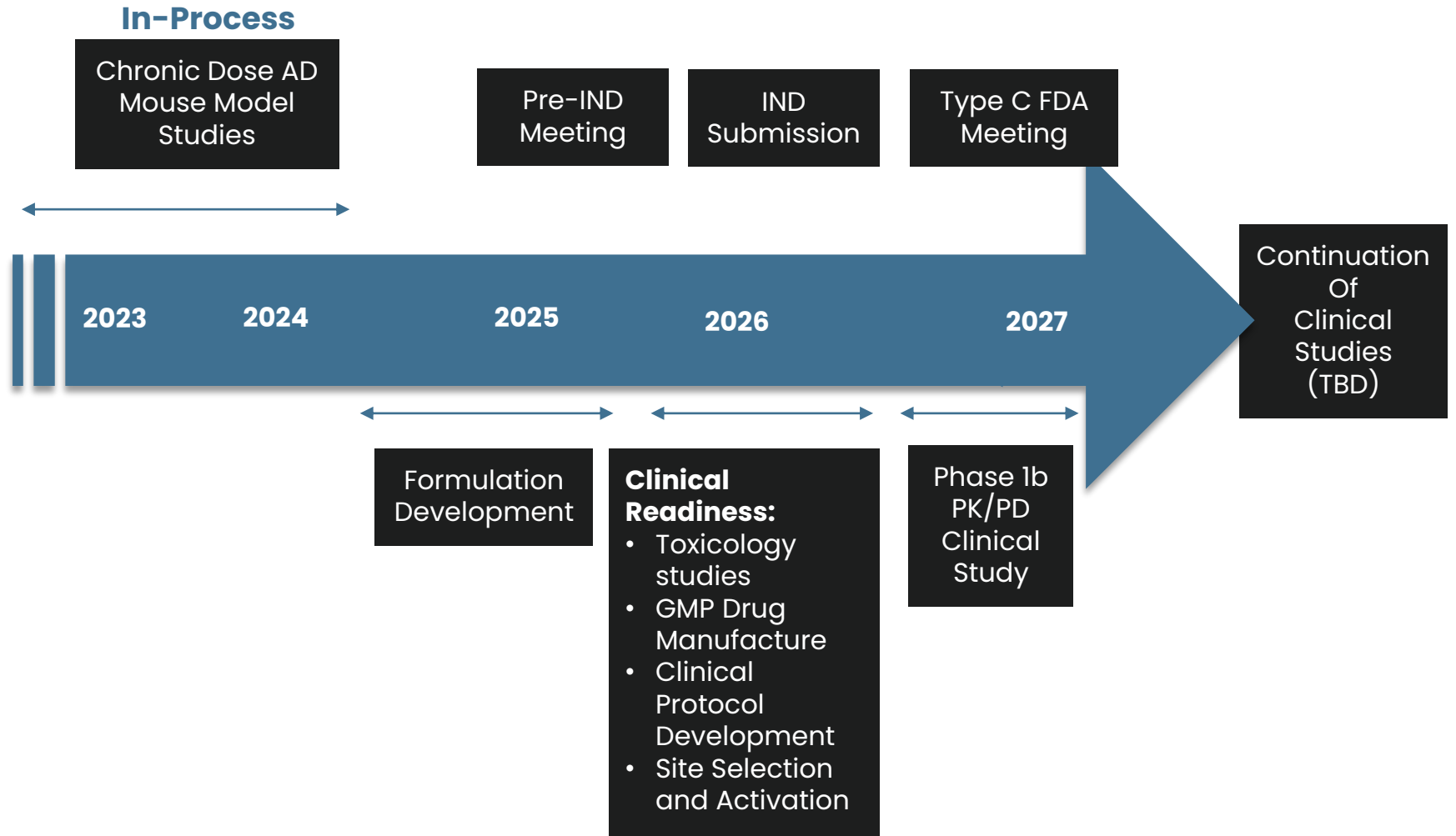
Preclinical Studies completed at WashU



2025

Pre-IND Meeting Submission

HT-ALZ 505(b)(2) Development Pathway



Current estimated dates; pending FDA meetings for clinical studies.

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Biolexa:

Value Proposition

Market Growth: Atopic dermatitis market predicted to grow from \$6.4B in 2017 to \$18.3B by end of 2027*

Mechanism of Action: Novel mixture of two previously approved compounds targeting the underlying Staphylococcus aureus infection hypothesize to potentiate Atopic Dermatitis (AD) or eczema flares – First compound prevents biofilm formation, which protects the underlying infection, allowing the second, an antibiotic, to more effectively treat the underlying infection.

Addresses Unmet Need: Non-corticosteroid treatment targeted for treatment of both pediatric and adult mild to moderate AD populations

*Atopic Dermatitis Market – Global Industry Analysis, Size and Forecast, 2017-2027

 HOTH THERAPEUTICS

Recent & Upcoming Milestones: BioLexa Lotion



2021

Phase 1b Cohort 1 with
healthy subjects
completed



Dec 2021

Phase 1b cohort in
patients with mild to
moderate atopic
dermatitis initiated



Sep 2022

Open Label dosing
portion of Phase 1b Study
is completed

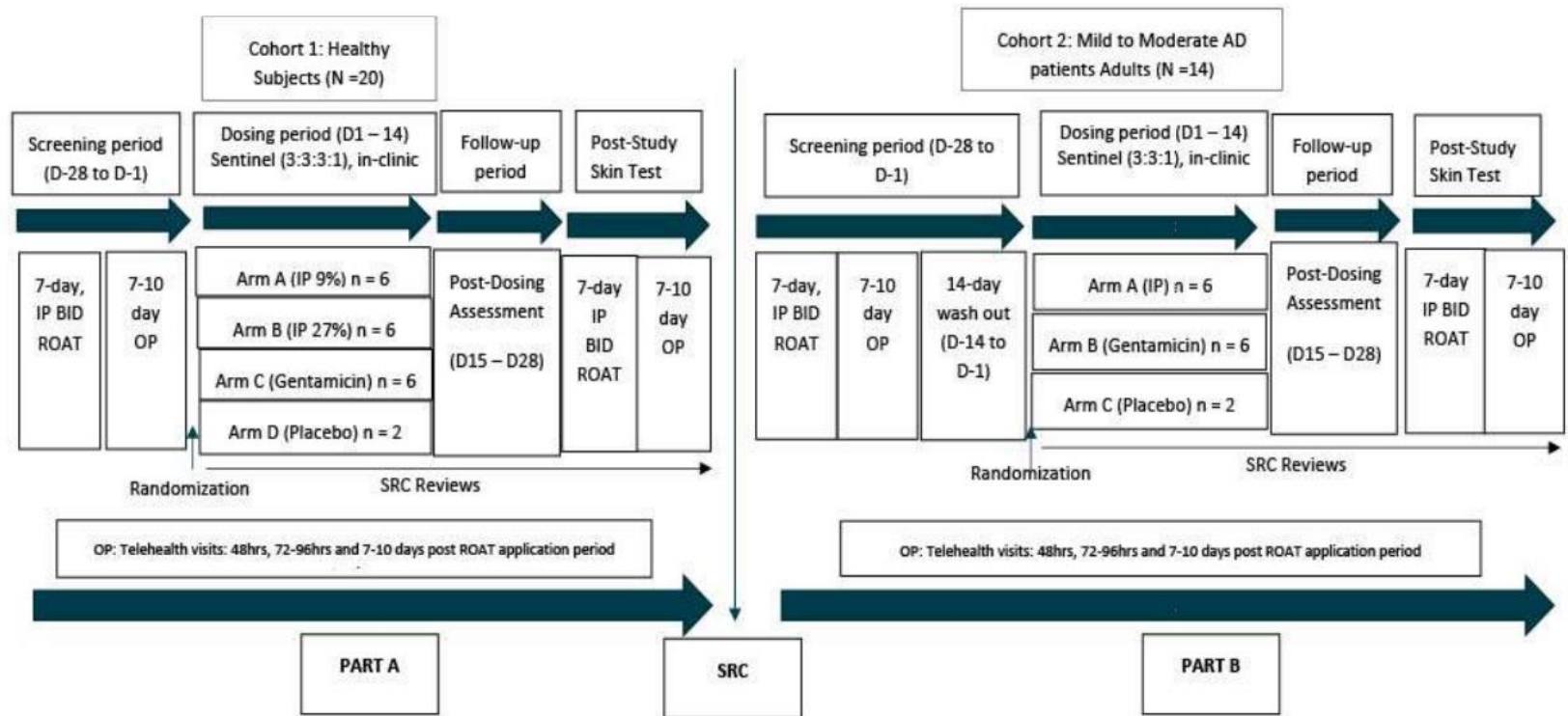


2023

Data Readout from Phase
1b Clinical Study

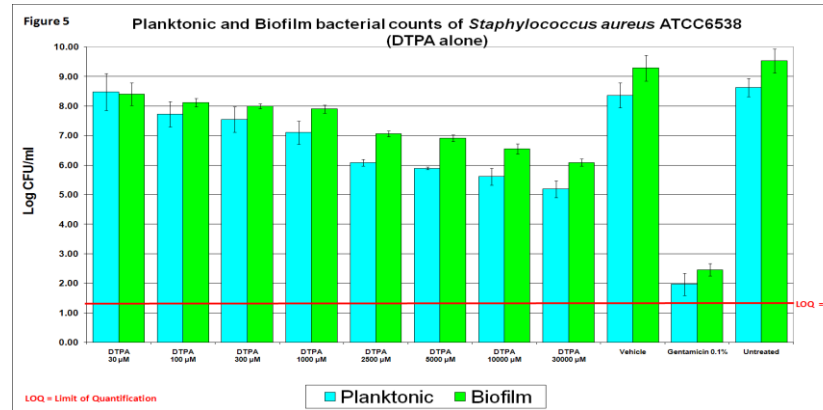
BioLexa Phase 1b Clinical Study Design

A Randomised, Double-Blind, Vehicle Controlled, Sequential Group Study to Determine the Safety, Tolerability, Pharmacokinetics and Efficacy of Twice Daily Application of Topical BioLexa™ in Adult Healthy Subjects and Patients with Mild to Moderate Atopic Dermatitis

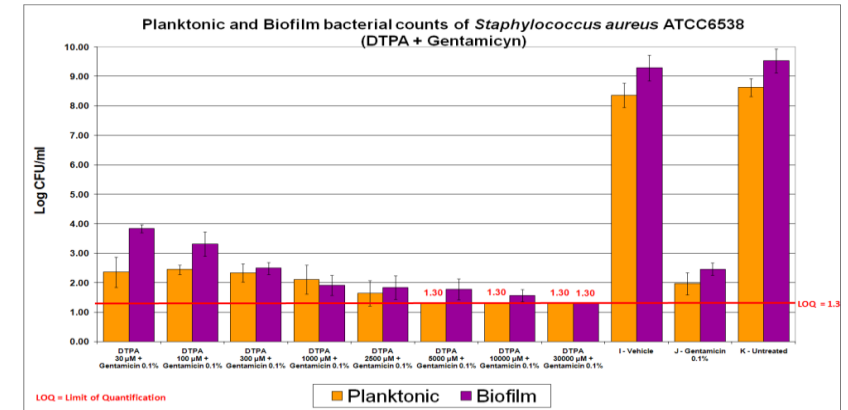


BioLexa: Proof-of- Concept Results

This study concluded that the combination of gentamicin and Ca-DTPA is more effective to reduce bacteria growth and inhibit the formation of biofilms than each compound individually.



← DTPA Alone → Gentamicin Alone ↑



↑ Combination Reduced Bacteria Below LOQ

Miller School of Medicine, of the University of Miami and University of Cincinnati - Determination of the effects of a novel antimicrobial agent used in conjunction with Gentamicin on *Staphylococcus aureus* using a porcine model: preliminary evaluations Jose Valdes, Joel Gil, Andrew Herr, Andrew Harding and Stephen Davis

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Preclinical Development

 HOTH THERAPEUTICS

HT-003

HT-004

HT-TBI

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HT-003:

Value Proposition



Market Growth: The global acne treatment market size was valued at \$5.46 Bn in 2019 & is projected to reach \$7.19 Bn by 2027, with a CAGR of 4.6% during forecast period.* IBD Treatment market was valued at USD 15.87 billion by 2019, growing with 4.1% CAGR during the forecast period, 2020-2026**

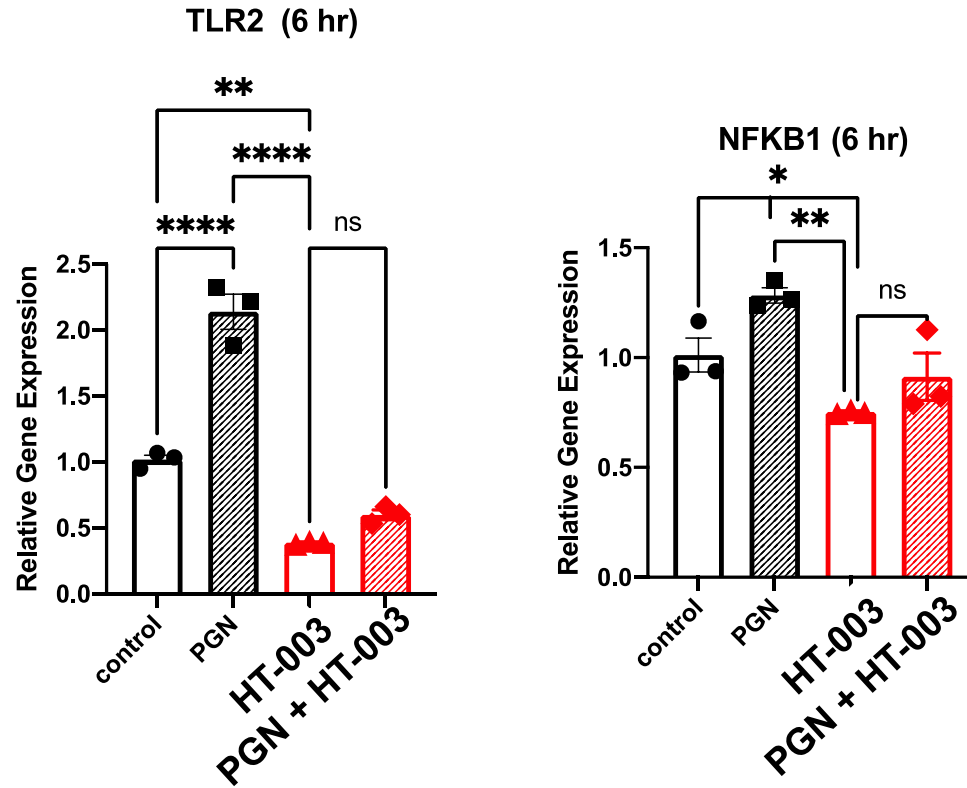
Mechanism of Action: Group of novel inhibitors of retinoic acid metabolism (collectively called RAMBAs), which prolong the presence of retinoic acid. Retinoids play key role in the regulation of immune cells and inflammation and are also important for differentiation of the skin.

Addresses Unmet Need: Focuses on restoring immune system rather than inducing immune suppression (current therapies)

*<https://www.fortunebusinessinsights.com/acne-treatment-market-103361>

**<https://www.marketwatch.com/press-release/inflammatory-bowel-disease-ibd-treatment-market-analysis-share-trends-size-forecast-from-2020---2030-2021-11-01?tesla=y>

HT-003D: Dermal Preclinical Study Results



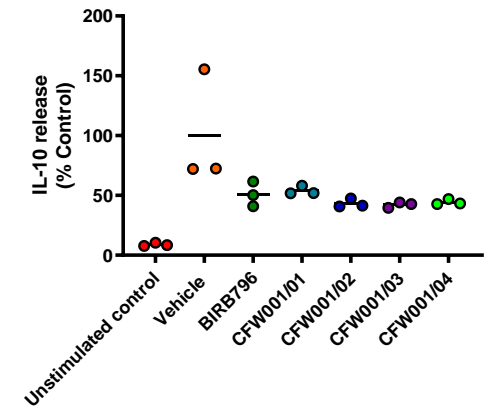
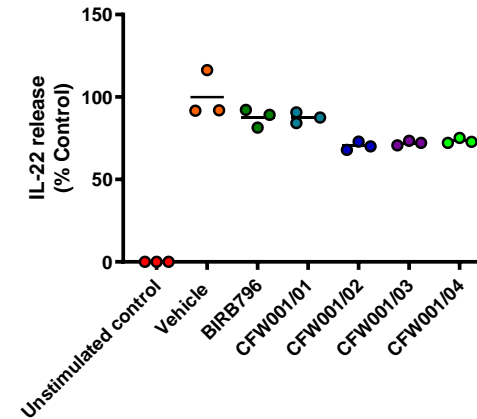
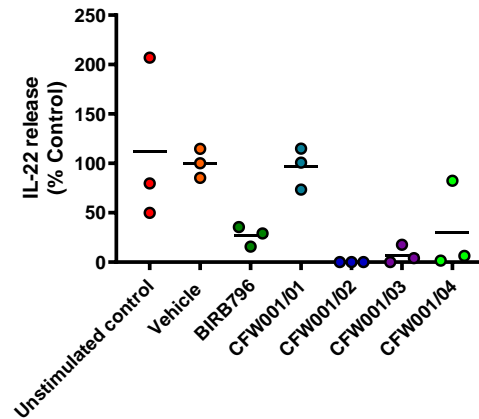
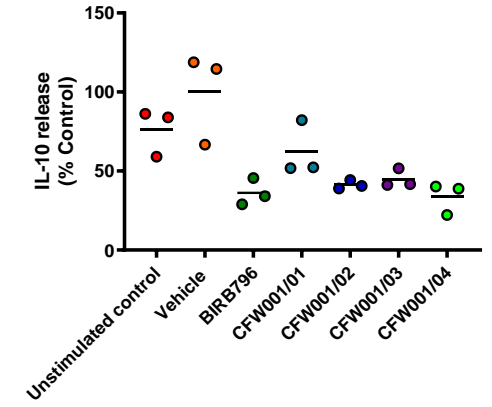
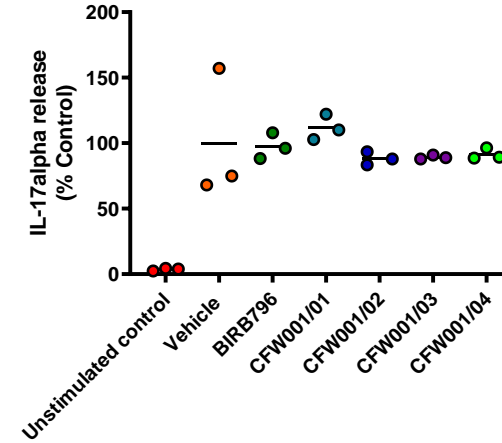
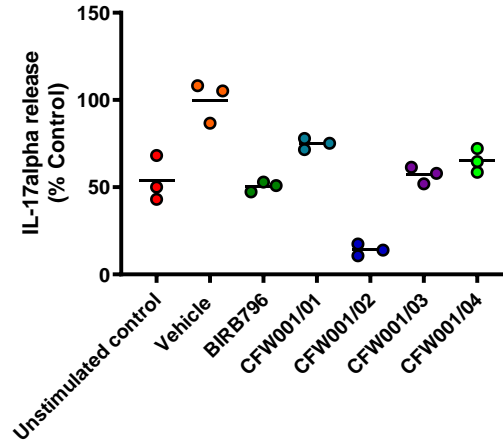
TLR2 is one of the most critical genes for acne pathophysiology



Data shows that HT-003 significantly downregulates TLR2 expression after challenge with PGN (TLR2 agonist) in an in vitro human keratinocyte model

HT-003IBD: Preclinical Study Results

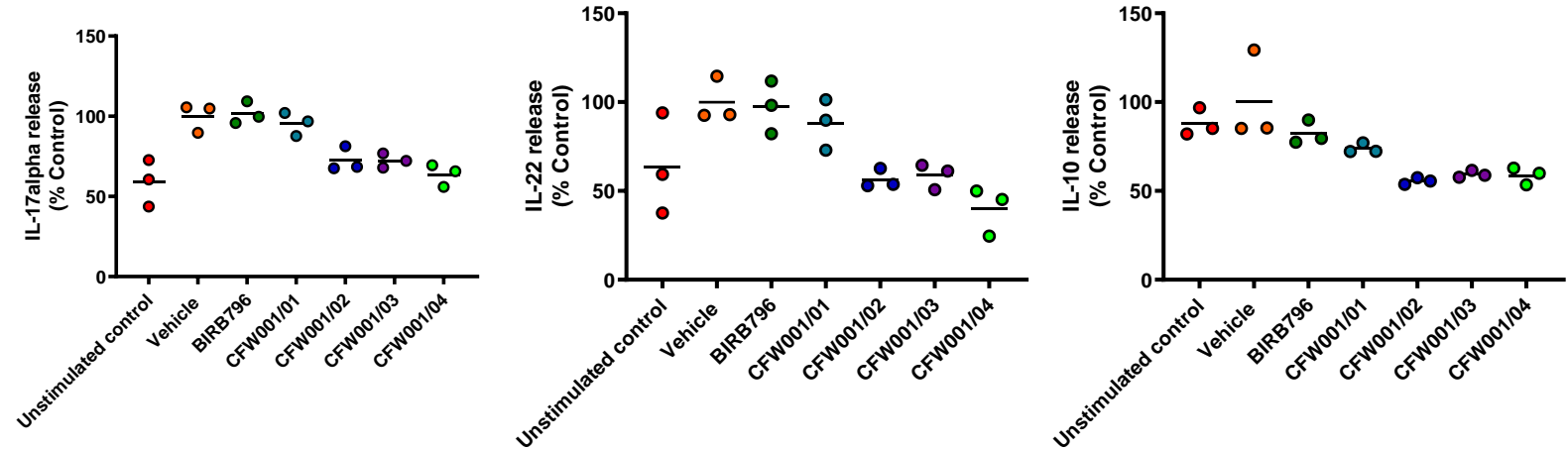
Ulcerative Colitis
Ex Vivo Tissue
(n = 2 donors)



HT-003 molecules reduce inflammatory cytokines associated with IBD and promotes intestinal homeostasis

HT-003IBD: Preclinical Study Results

Crohn's Ex Vivo
Tissue
(n = 1 donor)



HT-003 molecules reduce inflammatory cytokines associated with IBD and promotes intestinal homeostasis

CFW = HT-003 molecules 1 – 4 unique entities | BIRB796 = positive therapeutic control

HT-004: Value Proposition

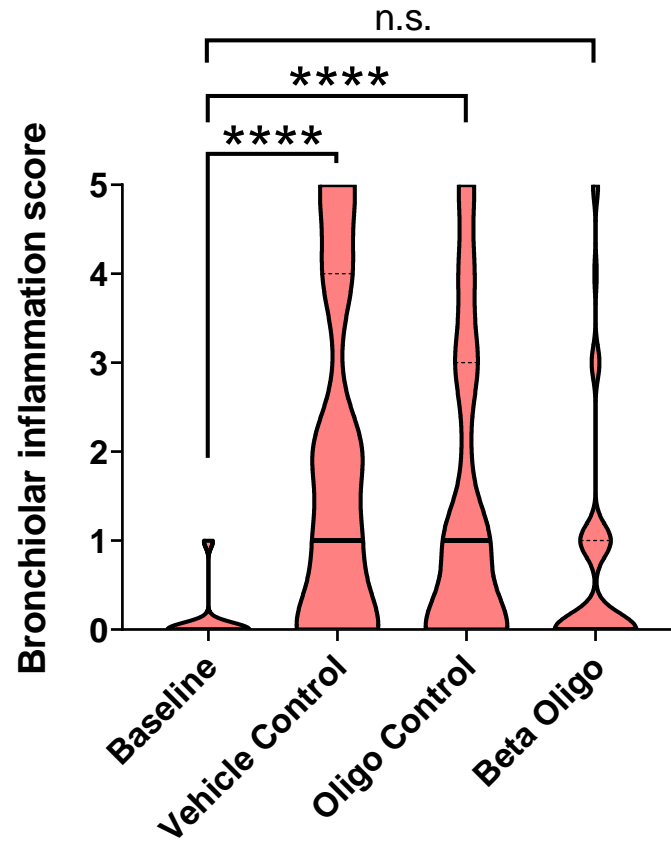
Market Growth: The global asthma therapeutics market reached a value of \$17.6B in 2020. The market is expected to reach a value of \$19.13B by 2026, expanding at a CAGR of 1.60% during 2021-2026.*

Mechanism of Action: Target IgE receptor trafficking to prevent downstream inflammatory pathways

Addresses Unmet Need: New class of drug for maintenance treatment of asthma with potential for a better safety profile

*Asthma Therapeutics Market: Global Industry Trends, Share, Size, Growth, Opportunity and Forecast 2021-2026, imarc

HT-004: Asthma & Allergic Inflammation



- Peribronchiolar Inflammation was reduced by inhalation of HT-004 that targets FcER1-beta alternative exon splicing.
- Ovalbumin inhalation induced airway-centric recruitment of inflammatory cells predominated by eosinophils admixed with lymphocytes, macrophages, and fewer mast cells.
- Inflammatory cell recruitment was minimal in lungs of mice lacking the ovalbumin-induced allergic airway disease and administered only PBS vehicle control.
- Inflammatory cell recruitment was moderate to marked resulting in expansion of peribronchiolar connective tissues by several cells thick in some areas for mice in control treatment groups with ovalbumin-induced allergic airway disease (vehicle control and oligo (non-target) control).
- Despite ovalbumin-induced allergic airway induction, lungs from mice receiving inhalation of HT-004 had reduced inflammatory cell recruitment around bronchioles.

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HT-TBI:

Value Proposition



Market Growth: The global stroke management market size was valued at \$31.7B in 2020, and is projected to reach \$67.7B by 2030, registering a CAGR of 7.8% from 2021 to 2030.*

The traumatic brain injuries treatment market to account \$201.1B by 2029 by growing at a CAGR of 5.00% in the forecast period of 2022-2029.**

Mechanism of Action: Target neurokinin-1/substance P to prevent downstream inflammatory pathways leading to secondary brain injury (edema, inflammation)

Addresses Unmet Need: : There is insufficient clinical evidence to support the use of the current hyperosmotic therapy methods (eg, mannitol) for lowering intracranial pressure per the Guidelines for the Management of Severe Traumatic Brain Injury; hyperosmotic therapy can also be associated with risk to patient morbidity and mortality.***

*Stroke Management Market Statistics 2030, Allied Market Research

**Global Traumatic Brain Injuries Treatment Market – Industry Trends and Forecast to 2029, Data Bridge Market Research

***Guidelines for the Management of Severe Traumatic Brain Injury 4th Edition, Brain Trauma Foundation

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Investment Highlights

 HOTH THERAPEUTICS

Programs in Clinical Stage of Development

- Addressing multi-billion-dollar unmet market opportunities across indications
- HT-001 – no approved product/competitor currently on the market, clinical trial currently enrolling
- HT-KIT – Pre-IND Meeting with FDA successful and IND-enabling tox studies and development planned for 2025

Diverse and Robust Pipeline of Pre-Clinical Candidates

- Offers strong intellectual property portfolio, including exclusive licenses to patents and trademarks
- Multiple shots on goal with diversified portfolio and market
- Multiple assets have platform technology possibilities

Clean Financials

- 7.7 million shares outstanding (as of November 29, 2024)
- Cash on hand is sufficient to take company through the clinical and pre-clinical programs currently in development

Experienced Management, Board and Scientific Advisors

- Experienced management team, board of directors and scientific advisors with proven financial, capital markets and drug development experience

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**Thank
You.**



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