# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION
**Washington, D.C. 20549**

# FORM 8-K

**CURRENT REPORT**
**Pursuant to Section 13 or 15(d)**
**of the Securities Exchange Act of 1934**

**Date of Report (Date of earliest event reported): August 17, 2021**

# INHIBIKASE THERAPEUTICS, INC.
**(Exact Name of Registrant as Specified in its Charter)**

| **Delaware** | **001-39676** | **26-3407249** |
|---|---|---|
| **(State or Other Jurisdiction of Incorporation)** | **(Commission File Number)** | **(IRS Employer Identification No.)** |

| **3350 Riverwood Parkway SE, Suite 1900 Atlanta, Georgia** | **30339** |
|---|---|
| **(Address of Principal Executive Offices)** | **(Zip Code)** |

**Registrant's Telephone Number, Including Area Code: (678) 392-3419**

**(Former Name or Former Address, if Changed Since Last Report)**

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (*see* General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

| Title of each class | Trading Symbol(s) | Name of each exchange on which registered |
|---|---|---|
| **Common Stock, $0.001 par value** | **IKT** | **The Nasdaq Stock Market LLC** |

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter). Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

**Item 7.01 Regulation FD Disclosure.**

On August 17, 2021, Inhibikase Therapeutics, Inc. (the "Company"), made available on the Company's website at www.inhibikase.com a corporate presentation which may be used in presentations to investors and analysts from time to time in the future. A copy of the Company's corporate presentation is attached hereto as Exhibit 99.1 and is incorporated herein by reference.

The information contained in this Current Report on Form 8-K speaks only as of the date hereof. While the Company may elect to update the information in this Current Report on Form 8-K in the future, the Company disclaims any obligation to do so except to the extent required by applicable law.

The information furnished in this Item 7.01 of this Current Report on Form 8-K and Exhibit 99.1 attached hereto shall not be deemed "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section. The information in this Item 7.01 of this Current Report on Form 8-K is not incorporated by reference into any filings of the Company made under the Securities Act of 1933, as amended, or the Exchange Act, whether made before or after the date of this Current Report on Form 8-K, regardless of any general incorporation language in the filing unless specifically stated so therein.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits.

| Number | Description |
|---|---|
| 99.1 | Corporate Presentation of Inhibikase Therapeutics, Inc. |

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: August 17, 2021

INHIBIKASE THERAPEUTICS, INC.

By: /S/ MILTON H. WERNER
Milton H. Werner, Ph.D.
President and Chief Executive Officer

Exhibit 99.1

Inhibikase Therapeutics

Nasdaq | IKT

# Clinical Development of Therapies Intended to Reverse the Functional Loss in Parkinson's and Related Disorders

**3Q 2021** BUSINESS PRESENTATION

# Disclaimer

This presentation shall not constitute an offer to sell or a solicitation of an offer to buy any securities, nor shall there be any sale of such securities in any state or jurisdiction in which such offer, solicitation, or sale would be unlawful prior to registration or qualification under the securities laws of any such state or jurisdiction.

This presentation contains information that may constitute “forward-looking statements” within the meaning of Section 27A of the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended. Inhibikase Therapeutics, Inc. (the “Company” or “we”) intends for the forward-looking statements to be covered by the safe harbor provisions for forward-looking statements in those sections. Generally, we have identified such forward-looking statements by using the words “believe,” “expect,” “intend,” “estimate,” “anticipate,” “project,” “target,” “forecast,” “aim,” "should," “will,” "may", “continue” and similar expressions. Such statements are subject to a number of assumptions, risks and uncertainties which may cause actual results, performance or achievements to be materially different from those anticipated in these forward-looking statements. You should read statements that contain these words carefully because they discuss future expectations and plans which contain projections of future clinical studies, regulatory approvals, product candidate development, results of operations or financial condition or state other forward-looking information. However, the absence of these words or similar expressions does not mean that a statement is not forward-looking. Forward-looking statements are not historical facts, but instead represent only the Company’s beliefs regarding future events, many of which, by their nature, are inherently uncertain and outside of the Company’s control. It is possible that the Company’s actual results and financial condition may differ, possibly materially, from the anticipated results and financial condition indicated in these forward-looking statements. Management believes that these forward-looking statements are reasonable as of the time made. However, caution should be taken not to place undue reliance on any such forward-looking statements because such statements speak only as of the date when made. The Company undertakes no obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law. In addition, forward-looking statements are subject to certain risks and uncertainties that could cause actual results to differ materially from the Company's historical experience and our present expectations or projections. Important factors that could cause actual results to differ materially from those in the forward-looking statements are set forth in the Company’s filings with the Securities and Exchange Commission, including its registration statement on Form S-1, as amended (File No. 333-240036), including under the caption "Risk Factors.

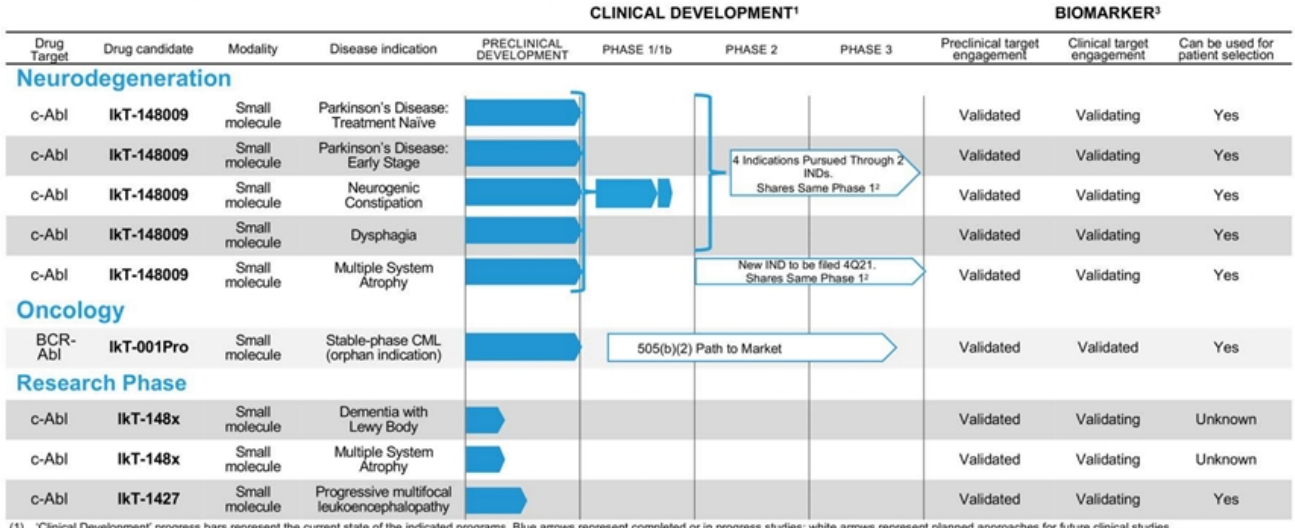
We do not intend our use or display of other entities’ names, trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, any other entity.

COMPANY HIGHLIGHTS

# Driving Functional Reversal of Parkinson's Disease

- Five clinical programs in neurodegeneration and one clinical program in oncology planned by close of 2021
- Multi-therapeutic pipeline with emphasis on neurodegeneration inside and out side of the brain
- Our lead inhibitor of the Abelson Tyrosine Kinase (c-Abl), IkT-148009, halts and reverses functional loss in animal models that recreate progressive human disease
- Phase 1 trial with IkT-148009 reached therapeutic drug exposures seen in animal models at just 25 mg oral dose 1x/day in humans
- Multiple patent families for lead compound with expiration of 2036 and beyond
- $20.4 million in grants and contracts from NIH, DoD, the Michael J. Fox Foundation and the Georgia Research Alliance, all peer-reviewed
- $63 million gross proceeds in investor capital in 2021
- Highly experienced and respected management team, consultants, Board of Directors and nearly all KOLs in the field on Scientific Advisory Board

# Multi-Indication Pipeline in Neurodegeneration, Oncology and Infectious Disease




(1) 'Clinical Development' progress bars represent the current state of the indicated programs. Blue arrows represent completed or in progress studies; white arrows represent planned approaches for future clinical studies.
(2) Four indications will be pursued for IkT-148009 in PD, which will be pursued through two INDs, one focused on treatment in the brain in treatment-naïve or early-stage patients and the second focused on GI complications.
(3) For biomarker status, 'Validated' refers to proof of target engagement in the target tissue which has been performed using rodent tissues and fluids. We are currently developing methods for using clinical samples for validating our ability to confirm target engagement in patients. 'Validating' in this context indicates ongoing efforts to prove target engagement using proprietary sources and methods under development from human tissues and fluids. Target engagement measures if and to what extent a compound occupies its target. 'Can be used for patient selection' refers to our ability to use one or more markers we are currently 'Validating' to screen patients for the presence of that marker as a means of defining the patients most likely to benefit from the proposed treatment.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Parkinson's Disease Market &
Strategy

# Parkinson's Disease in the U.S.[1]

## Large Market, Opportunity For Disease Modification

**Chronic Disease for a Long Time**
1/3 of a Patient's Lifespan = 25 years

**60,000**
NEW CASES / YR

**38,000**
DEATHS / YEAR

**Men twice as likely as women to contract disease**

**700,000 – 1,000,000**
**U.S. Patients**

**60**
AVERAGE AGE OF ONSET

**Other illnesses complicate development**

**47%** ARTHRITIS

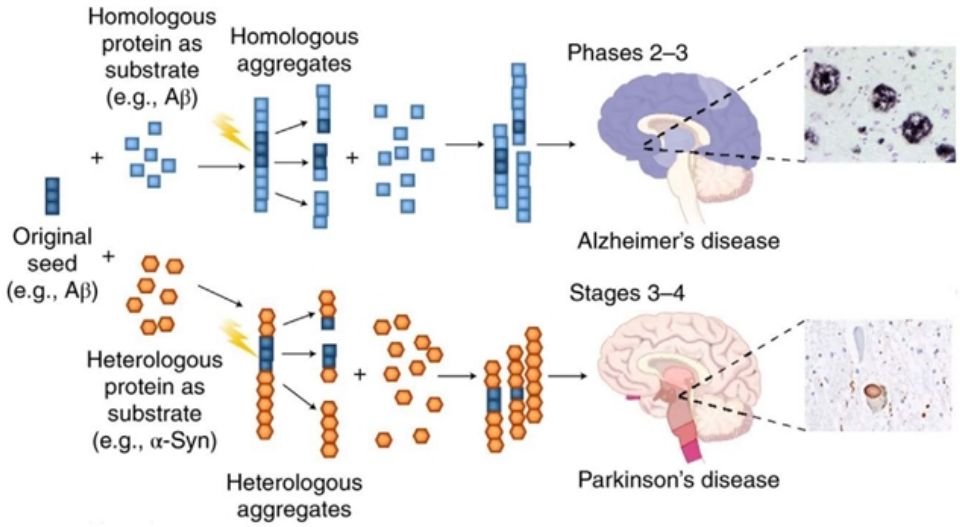
**36%** HEART / CIRCULATORY

**35%** PSYCHOSIS

**30%** DEMENTIA

[1]Parkinson's Disease Foundation Decisions Resources 2016, ParkinsonismRelatDisord . 2012;18:1073-1078, , Neuroepidemiology 2010;34:143–151 , J Neurol Neurosurg Psychiatry. 1997 Jan;62(1):10-5.
[2]

# Causation in Parkinson's and Alzheimer's is closely related[1]




What role does the misfolded protein play?

[1]Nat. Neurosci. 21: 1332-1340 (2018)

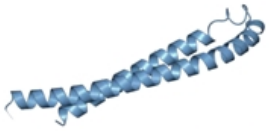
CAUSE OF NEURODEGENERATION

# Evaluation of the Misfolded Protein 'Seed' in Parkinson's Reveals c-Abl as the Primary Culprit, NOT the Misfolded Protein

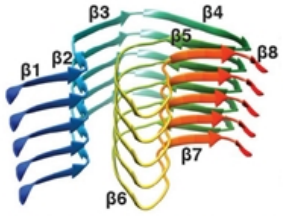
- Parkinson's Disease (PD) is a neurodegenerative disease which limits function of nerve cells throughout the brain and gut following misfolding of non-essential α-Synuclein.

- α-Synuclein, an abundant and non-essential protein
  - Normally, α-Synuclein plays a role in neurotransmission by dopamine.
  - In the disease state, α-Synuclein is remodeled into protein aggregates we call plaques, which have been thought to be the cause of disease.

- The Company and it's collaborators have demonstrated that **plaques of α-synuclein cannot cause disease on their own**.
  - Plaques are internalized and activate c-Abl.
  - c-Abl is actually driving the disease.



**α-Synuclein Is normally in a helix-turn-helix configuration[1]**

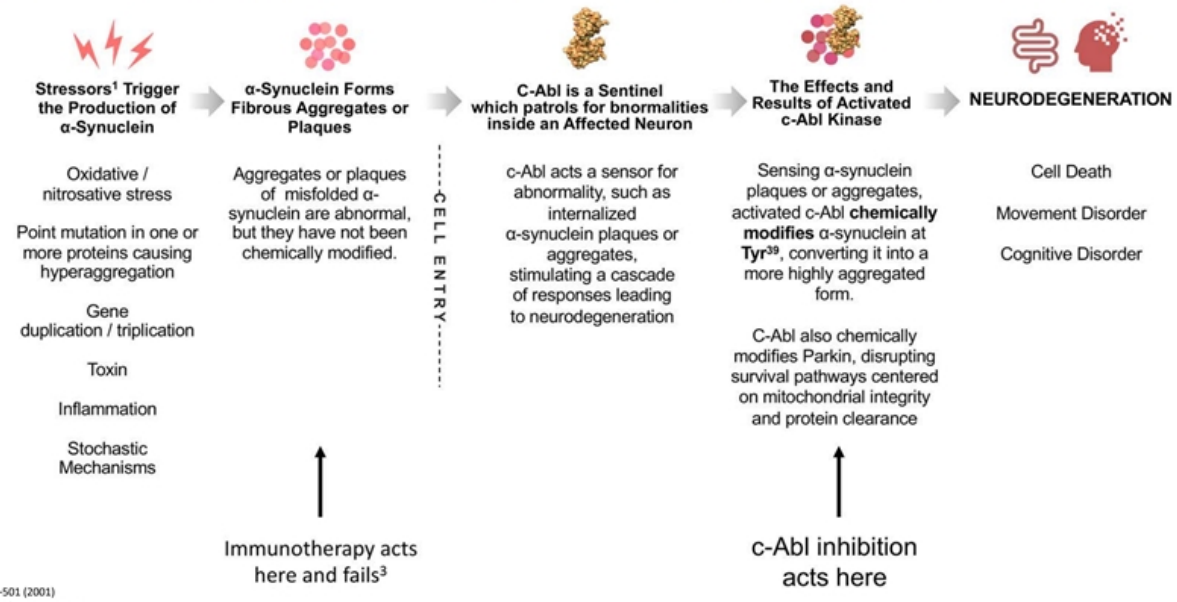



**In the disease state, α-Synuclein reorganizes to form fibrous aggregates ("Plaques")[2]**

[1]Biochim Biophys Acta. 1818:1013-8 (2012)
[2]Pathogens 7:50 (2018)

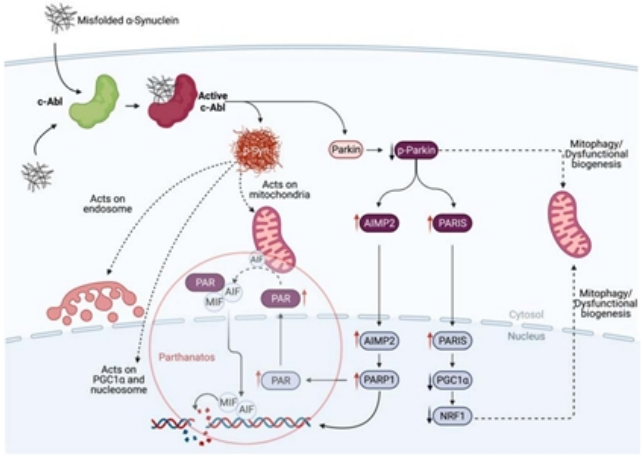
THE PATH TO NEURODEGENERATION

# Stressors Trigger the Production of Misfolded α-Synuclein Which Activates c-Abl to Drive Neurodegeneration[2]

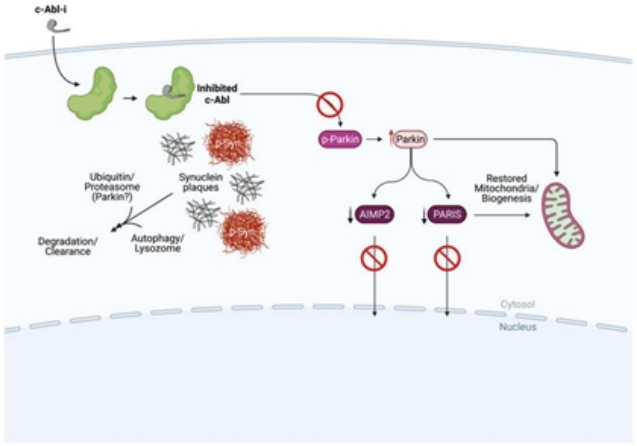



[1] *Nat Rev Neurosci.* **2**, 492–501 (2001)
[2] Werner and Olanow (2021), under review
[3] https://ir.prothena.com/news-releases/news-release-details/update-phase-2-pasadena-study-prasinezumab-prx002rg7935
http://media.biogen.com/node/22876/html

# Biochemistry of Parkinson's Disease Initiation and Progression[1]




Disease process




Treatment effect

[1]Werner and Olanow (2021), under review, J Clin Invest. 2016; 126: 2970-2988 , Brain 2019; 142:2380-2401 , Cell 2011; 144: 689-702 , Nat Neurosci. 2013; 16: 1392-1400 , Adv Neurobiol. 2017; 15:403-425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How Inhibikase Will Modify Disease

IkT-148009 IS A SMALL MOLECULE c-ABL INHIBITOR

# IkT-148009: Low Toxicity, Selective, Brain Penetrant c-Abl Inhibitor in Clinical Development

IkT-148009 Selective Inhibitor of c-Abl and Abl2/Arg bypasses toxicity of cancer drugs

**Table 1: $IC_{50}$ of Commercial c-Abl inhibitors for inhibition of wildtype Abl-family kinases[1] vs. IkT-148009**

| Inhibitor | c-Abl/Abl1 (nM) | Abl2/Arg (nM) | c-Kit (nM) | PDGFRα (nM) | PDGFRβ (nM) |
|---|---|---|---|---|---|
| Imatinib | 828 | 1000 | 31 | 100 | 100 |
| Dasatinib | 0.6 | * | 79 | * | * |
| Nilotinib | 48 | 41 | 279 | * | * |
| Ponatinib | 0.37 | * | * | 1.1 | * |
| IkT-148009 | 33 | 14 | 2975 | 1009 | 881 |

* = not determined

IkT-148009 No organ toxicity High brain penetrance

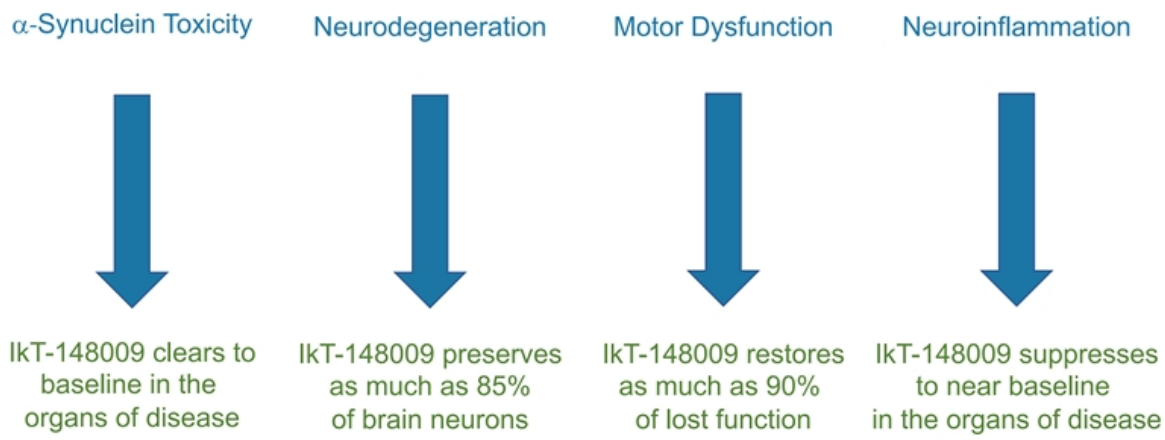
| Toxicology in Rat/Monkey[1] | |
|---|---|
| Human equivalent dose of 600 mg | |
| Cardiovascular | None |
| Renal | None |
| Liver | None |
| Bone marrow | None |
| Sternum | None |
| Blood | None |
| PBMCs | Slight increase in neutrophils within normal limits |
| Cytotoxicity | None in primary or mature cells |
| Sustained brain concentration | > 1 micromolar |

[1]Ongoing chronic toxicology studies in rat and monkey have completed 13 weeks

[1]See SelleckChem.com

IkT-148009 MODIFIES DISEASE

# c-Abl inhibition by IkT-148009 blocks the four pillars of Parkinson's Disease in Validated Animal Models

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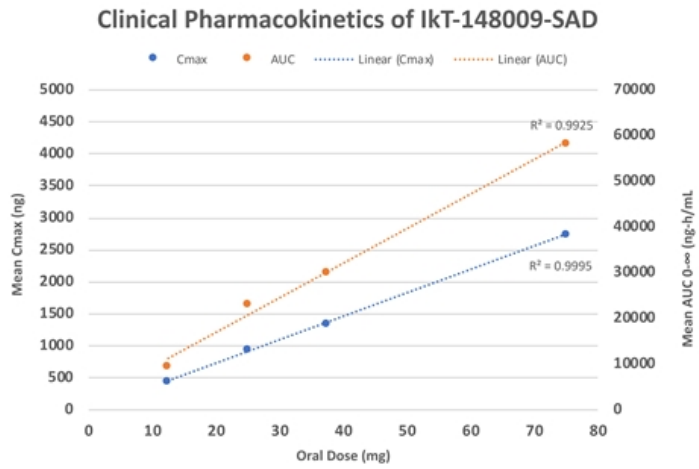
Clinical Development

# Phase 1:Dose Proportional Clinical Pharmacokinetics and No Clinically Significant Adverse Events

| Category | Demographic | Value (% of Total N=42) |
|---|---|---|
| Gender | Female | 12 (28.6) |
| | Male | 30 (71.4) |
| Age | Average (SD) | 56.2 (6.33) |
| | Median | 56.5 |
| | Range | 45, 68 |
| Ethnicity | Hispanic or Latino | 6 (14.3) |
| | Not Hispanic or Latino | 36 (85.7) |
| Race | Black or African American | 28 (66.7) |
| | White | 13 (31.0) |
| | Other - mixed | 1 (2.4) |
| Adverse events | | 1 (2.4), Grade 1, two weeks post-dose |

# Phase 1:Dose Proportional Clinical Pharmacokinetics and No Clinically Significant Adverse Events




**Human safety to date**

- No clinically significant adverse events have been observed across 5 dosing cohorts

**Significance of clinical pharmacokinetics**

- High exposures at low oral dose, linearly dose proportional. Exposures at 75 mg IkT-148009 comparable to 500 mg imatinib[1]

[1]FDA summary data for approval 21-335

# Phase 1: Low Oral Dose in Humans Reaches Therapeutic Exposures of Animal Models

| Clinical Pharmacokinetics IkT-148009 compared to therapeutic dose in animal models of progressive disease | | | | | | |
|---|---|---|---|---|---|---|
| | | | $t_{1/2}$ | $t_{max}$ | $C_{max}$ | $AUC_{0-\infty}$ |
| | | mg/day | (h) | (h) | (ng/mL) | (h*ng/mL) |
| IkT-148009 Clinical N=6 | Mean | **25**[1] | 25.2 | 6 | 945 | 23200 |
| IkT-148009 Efficacy, mouse model N=5 | Mean | **1.25**[1] | 12.7 | 2.2 | 2562 | 19650 |

[1]25 mg/day in humans equivalent to 0.128 mg/day in mouse assuming a 25 g mouse
Oral doses analyzed between 12.5 mg 1x/day to 75 mg 1x/day across 4 cohorts analyzed. 8 patients/cohort, 32 patients total 3:1 randomized against placebo.

**Therapeutic exposures defined**

- Laboratory efficacy studies in mice have an AUC equivalent to clinical exposure at 25 mg/day oral dose.
- Long half-life at low oral dose suggests long-term exposure to drug on a daily basis

# Model studies suggest the gut could be where Parkinson's disease originates in the body and is a critical organ for analysis[1]

**Parkinson's May Begin in the Gut**

Easy access

Can demonstrate disease benefit with quantitative endpoints

Biopsy and Biomarkers

Large effect size

**GI disorders resulting from kinase modification of α-synuclein:**

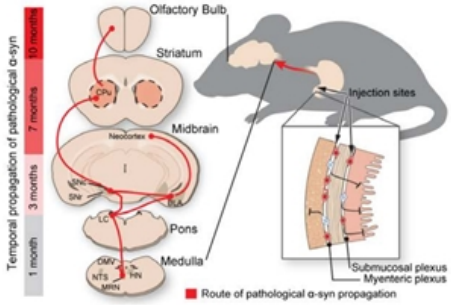
Dysphagia

Unresolvable constipation

Gastroesophageal reflux

Gastroparesis

**The Gut-Brain Connection Enables Innovation in Trial Design**




Introduction of synuclein plaque in the **gut leads to progressive disease in the brain**

[1]Neuron 2019; 103:1–15

IkT 148009 ONGOING TRIALS IN SAFETY AND DOSING

# Updated Phases and Development Intervals for 2021

**Phase 1b ▶**

**Multiple Ascending Dose (MAD): 7-Day**
- 3 dosing cohorts, 3:1 randomized with placebo, doses determined from SAD PK and safety
- 8 patients/dose 7 day dosing 1x/day
- Primary objectives safety, tolerability, pharmacokinetics (PK), urine, plasma spinal fluid concentrations, steady-state
- Exploratory: UPDRS II, III, II+III, MMSE, Whole Gut Transit Time, CSBM, PAGI-SYM, Biomarkers GI and Brain

**Multiple Ascending Dose (MAD): 3 Mos**
- 3 dosing cohorts
- Treatment native/Early state patients (H&Y ≤ 2.0)
- 30 patients/dose 1:1 randomized 13 week dosing 1x/day
- Primary objectives safety, tolerability, pharmacokinetics
- Secondary/Exploratory objectives UPDRS II, III, II+III, MMSE, Whole Gut Transit Time, CSBM, PAGI-SYM, Biomarkers GI and Brain
- **Timing for initiation of 3 month depends on early experience in 7 day dosing and FDA agreement**

IkT 148009 Phase 1b MAD (6-7 Months)

IkT 148009 Phase 1b (Overlapping, Up to 6 months)


IkT 148009 Phase 1 Chronic Toxicology Studies (4 Months to go)

**Comparative Toxicology to Imatinib at Toxic Dose**

RAT: 3 month done and 6-month completing 1 August
- 3-month readout going to FDA by August 26

MONKEY: 3 month done and 9-month completing 15 November
- 3-month readout going to FDA by August 26

# Selected Financial and Stock Data

| Capitalization Table | June 30, 2021 |
|---|---|
| Common Shares Outstanding | 25,133,345 |
| Options (WAEP: $2.47) | 3,624,658 |
| Warrants (WAEP: $5.21) | 1,561,913 |
| **Fully Diluted Shares Outstanding** | **30,319,916** |

$20.4M non-dilutive grant revenue pre-IPO (NIH, DoD, State gov'ts)

| Balance Sheet | June 30, 2021 |
|---|---|
| Current Assets: | |
| Cash | $ 46,836,556 |
| Grants Receivable | $ 586,581 |
| Prepaid research and development | $ 958,779 |
| Prepaid expenses and other current assets | $ 833,963 |
| Total Current Assets | $ 49,215,879 |
| Total Current Liabilities | $ 2,161,527 |
| Working Capital | $ 47,054,352 |
| Active grant funding available in accounts held by the U.S. treasury | $772,420 |
| Total Working Capital | **$ 47,826,772** |

COMPANY HIGHLIGHTS

# Upcoming Milestones

➢Remainder of 3Q21

- 148009
  - ➢ Initiate dosing in Parkinson's patients (H&Y < 2.5), 3:1 randomized, 8 patients/cohort, 7 day dosing. Up to 3 cohorts. Goal is Safety, PK, Exploratory measures in brain and GI for PD
  - ➢ Complete 100mg SAD and 25 mg MAD in healthy subjects with CSF collection in MAD
- 001Pro
  - ➢ Complete IND
- Onboard Clinical Operations expansion, Mfg expansion, Finance expansion

➢4Q21

- 148009
  - ➢ Formulate 148009 into film-coated tablet and assess single dose PK
  - ➢ File 3 month toxicology data with FDA
  - ➢ File MSA IND with Phase 2 protocol

- 001Pro
  - ➢ Clinical bioequivalence of 001Pro to standard of care
  - ➢ Initiate NDA manufacturing planning steps for 001Pro

# Management Team with Deep Experience in Drug Development and Commercialization

## Executive

**Milton Werner, PhD President & CEO**
Previously, Dr. Werner served as Director of Research at Celtaxsys. From September 1996 until June 2007, Dr. Werner was a Head of the Laboratory of Molecular Biophysics at The Rockefeller University in New York City. Throughout his scientific career, Dr. Werner has been an innovator integrating chemistry, physics, and biology into a comprehensive approach to solving problems in medicine. Dr. Werner is the author or co-author of more than 70 research articles, reviews, and book chapters and has given lectures on his research work throughout the world.

**Joseph Frattaroli, CPA Chief Financial Officer**
Mr. Frattaroli is a certified public accountant with more than 15 years of experience in public company filings and compliance for Nasdaq and OTC Markets companies. Previously, he provided chief financial officer and consulting services for several emerging biopharmaceutical and medical device companies, with responsibilities that included capital formation, deal structuring, and assisting private companies in their transition to becoming publicly traded SEC registrants.

**C. Warren Olanow, MD, Interim Chief Medical Officer and Chief Executive Officer of CLINTREX**.
Dr. Olanow is the former Henry P. and Georgette Goldschmidt Professor and Chairman of the Department of Neurology at the Mount Sinai School of Medicine Prior to joining Mount Sinai, he served on the faculties of McGill University, Duke University, and the University of South Florida. He is the former President of the Movement Disorder Society, past President of the International Society of Motor Disturbances, and former Treasurer of the American Neurological Association. He has served on the executive committee of the Michael J. Fox Foundation Scientific Advisory Board, and he is the former Chairman of the Scientific Advisory Board of the Bachmann-Strauss Parkinson Foundation and of the Dystonia Foundation. Dr. Olanow is the former Co-Editor-in-Chief of the journal Movement Disorders. Dr. Olanow received his medical degree from the University of Toronto, performed his neurology training at the New York Neurological Institute at Columbia Presbyterian Medical Center at Columbia University, and undertook postgraduate studies in neuroanatomy at Columbia University and authored more than 600 articles in the field of neurodegeneration.

# Board of Directors

**Mr. Dennis Berman**

- Co-founder, board member, and/or seed investor in many private biotechnology and technology companies, five of which have gone public.
- Currently serves as the President of Molino Ventures, LLC a board advisory and venture capital firm and was co-founder and Executive Vice President of Corporate Development of Tocagen.
- Seed investor, co-founder, and/or board member of Intervu, Kintera, Inc., Gensia, Calabrian

**Dr. Paul Grint, MD**

- 20+ years experience in biologics and small-molecule research and development, including the successful approval and commercialization of products in the infectious diseases, immunology, and oncology therapeutic areas.
- Director of Amplyx Pharmaceuticals and Synedgen.
- Served in senior management roles at Cerexa, Forest Laboratories, Kalypsys, Pfizer, IDEC Pharmaceuticals, and Schering-Plough Corporation.
- Fellow of the Royal College of Pathologists and a medical degree from St. Bartholomew's Hospital College, University of London.

**Dr. Roy Freeman, MD**

- Professor of Neurology at the Harvard Medical School and Director of the Center for Autonomic and Peripheral Nerve Disorders in the Department of Neurology at Beth Israel Deaconess Medical Center
- Former chairman of the World Federation of Neurology research group on the autonomic nervous system, former President of the American Autonomic Society, and former chairman of the Autonomic Section of the American Academy of Neurology.
- Editor-in-Chief of Autonomic Neuroscience: Basic and Clinical and on the editorial boards of The Clinical Journal of Pain, Pain: Clinical Updates, and Clinical Autonomic Research.
- Serial founder of several companies in pain and neurodegenerative disease and is on the scientific advisory boards of many large and small pharmaceutical and biotechnology companies.

**Ms. Elizabeth O'Farrell**

- 25-year career with Eli Lilly and Company, lastly serving as Chief Procurement Officer and Leader, Global Head of Shared Services
- Served in senior management at Lilly including Senior Vice President, Policy and Finance; Senior Vice President, Finance; Chief Financial Officer, Lilly USA; Chief Financial Officer, Lilly Canada; and General Auditor. Before joining Eli Lilly, Ms.
- Director of PDL BioPharma, Geron Corporation and Lensar
- BS in accounting with honors and an MBA in management information systems from Indiana University.

# Industry-Leading Advisors

**Robert Hauser, MD**
Professor of Neurology, University of South Florida College of Medicine - Director USF Parkinson's Disease and Movement Disorders Center

**Jeffrey Kordower, PhD**
Alla V and Solomon Jesmer Professor of Aging & Neurological Sciences Rush University Medical Center

**Dr. Ken Marek**
President and Senior Scientist, Institute of Neurodegenerative Disorders

**Dr. Ted Dawson, MD, PhD**
Neurodegeneration and Stem Cell Programs, Institute for Cell Engineering, Departments of Neurology, Physiology, Pharmacology, and Molecular Sciences - The Johns Hopkins University School of Medicine

**Dr. Valina Dawson, PhD**
Neurodegeneration and Stem Cell Programs, Institute for Cell Engineering, Departments of Neurology and Physiology
The Johns Hopkins University School of Medicine

**Dr. Warren Olanow, MD, FRCPC**
Henry P. and Georgette Goldschmidt Professor and Chairman Emeritus, Mount Sinai School of Medicine Clintrex, Inc.

**Dr. Karl Kieburtz, MD, MPH**
Robert J. Joynt Professor in Neurology, Senior Associate Dean for Clinical Research, Director of the Clinical &Translational Science Institute, Founder Center for Human Experimental Therapeutics (CHET)- University of Rochester Medical Center Clintrex, Inc.

**Dr. Jay Pasricha, MBBS, MD**
Director, Johns Hopkins Center for Neurogastroenterology
Professor of Medicine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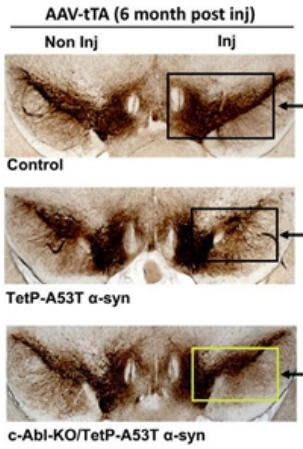
Appendix
Proof of the importance of c-Abl in Disease, Target Engagement and Functional Reversal in the Brain and Gut

# α-Synuclein Plaques Do Not Cause Disease Without c-Abl Modification in Humanized Preclinical Models[1]

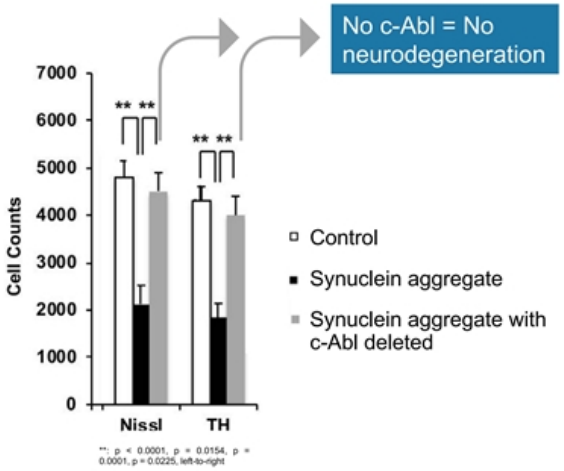
**α-Synuclein plaque in the ABSENCE OF c-Abl CAUSES NO NEURODEGENERATION AFTER 6 MONTHS**




Injection (Inj) of an expression vector for the A53T form of synuclein doesn't degrade neurons until the expression of A53T is turned on

Once turned on, A53T induces 50% neurodegeneration in 6 months. NOTE loss is visible in the dark patches of stained neurons on the right half. The left half was an internal control and is unaffected.

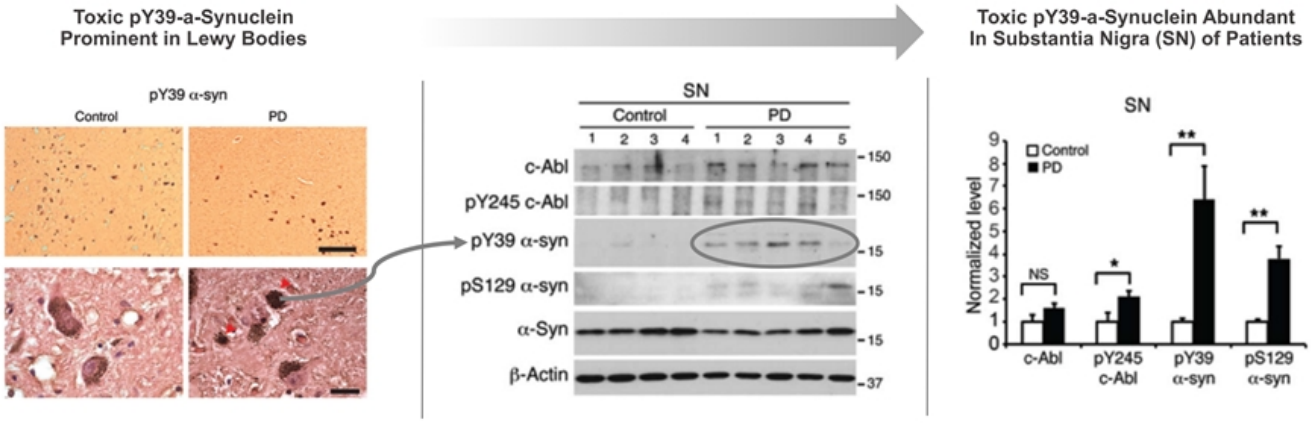
When the expression of A53T is turned on, but c-Abl is genetically deleted from the mouse brain, you don't get any neurodegeneration. Thus, even though the clumps of α-syn are present in the right region of the brain, they don't cause disease until c-Abl acts on them




[1]Brain 142:2380ff (2019)

STUDY

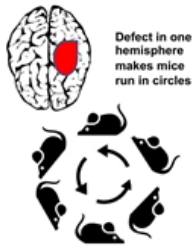
# Pathologic, c-Abl-Modified α-Synuclein (pY39) is Present in Parkinson's Patient Brain[1]




[1]J Clin Invest. **126**, 2970-88 (2016)

# Oral IkT-148009 in Mice Humanized for Parkinson's Disease in Brain Reverses Functional Loss

**Baseline Neuromuscular Coordination Behavioral Marker**

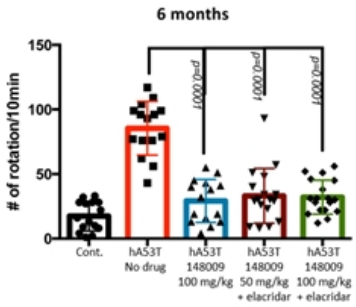



Healthy Mice Run In Circles at the Average Rate of 25 Turns : 10 Min

**Toxic Levels of Synuclein Are Introduced Into One Side of the Mouse Brain**

**Toxicity renders the mice trembling and only able to run in circles**

**Treatment Started 6 Weeks After Onset of Conditions**



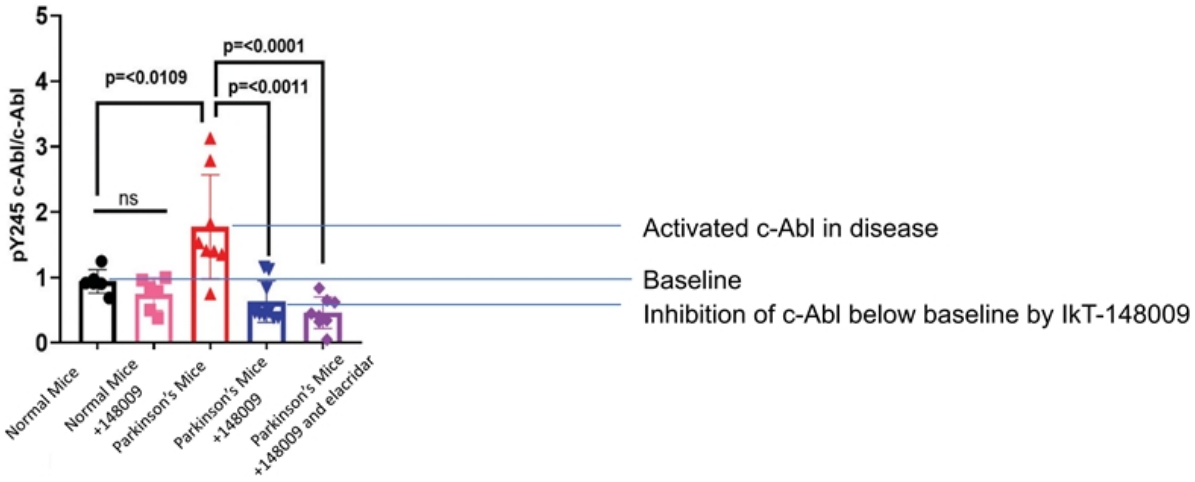

**Near Normal Behavior Returned Following Treatment**

Mice completed 30 turns/10 min when treated a dose of 100 mg/kg dose

**NEARLY COMPLETE RESCUE**

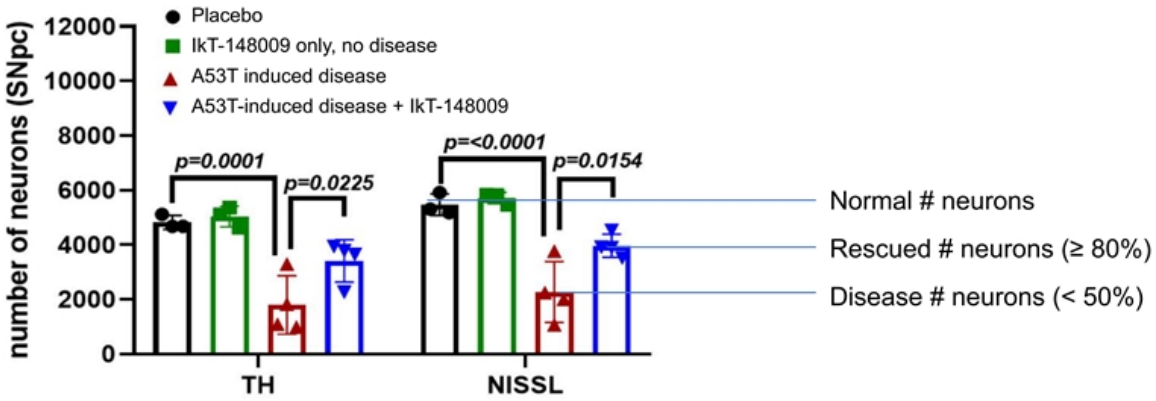
# Oral IkT-148009 Suppresses c-Abl Activation in the Brain that Correlates with Functional Recovery

## IkT-148009 engages the c-Abl target in the brain



# Oral IkT-148009 Preserves Neural Anatomy in the Brain

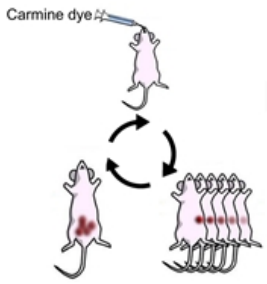
## IkT-148009 stopped loss of neurons, accounting for functional recovery



# Oral IkT-148009 in Mice Humanized for Parkinson's Disease in Gut Reverses Functional Loss

METHOD OF MEASUREMENT

**α-Synuclein Aggregates Introduced Into Gut Slows Gut Transit Time**

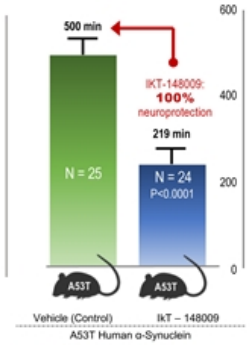


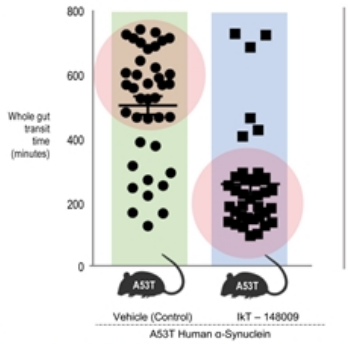

Measure defecation rate

POST TREATMENT RESULTS

**At 3 months defecation slows to 500 min (3x normal); At 6 months defecation slows to 800 min (5x normal); Normal = 165 min**

Neuron count read out by Whole Gut Transit Time - The time it takes for a mouse to defecate



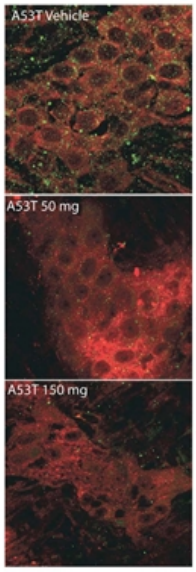




**NOTES**

1. If it weren't for 6 outliers in 96 measures, average would be 170 min, essentially 100% recovery.
2. We find the neuroanatomy is nearly completely restored by measuring the number and distribution of neural ganglia in the tissue.

# Oral IkT-148009 Treatment Clears Toxic α-Synuclein in the brain and gut

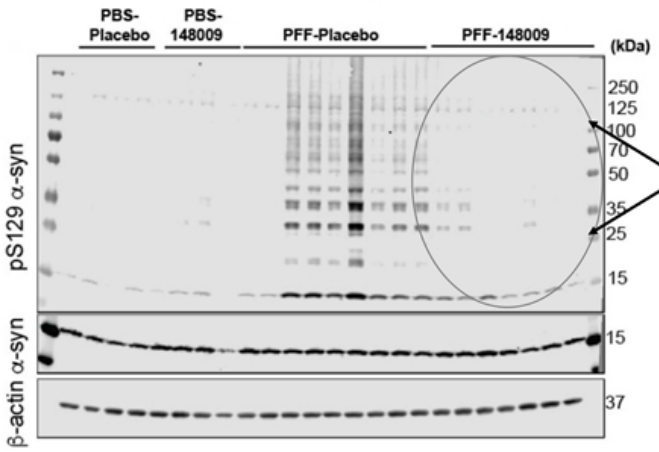
## Clearance of toxicity in the gut



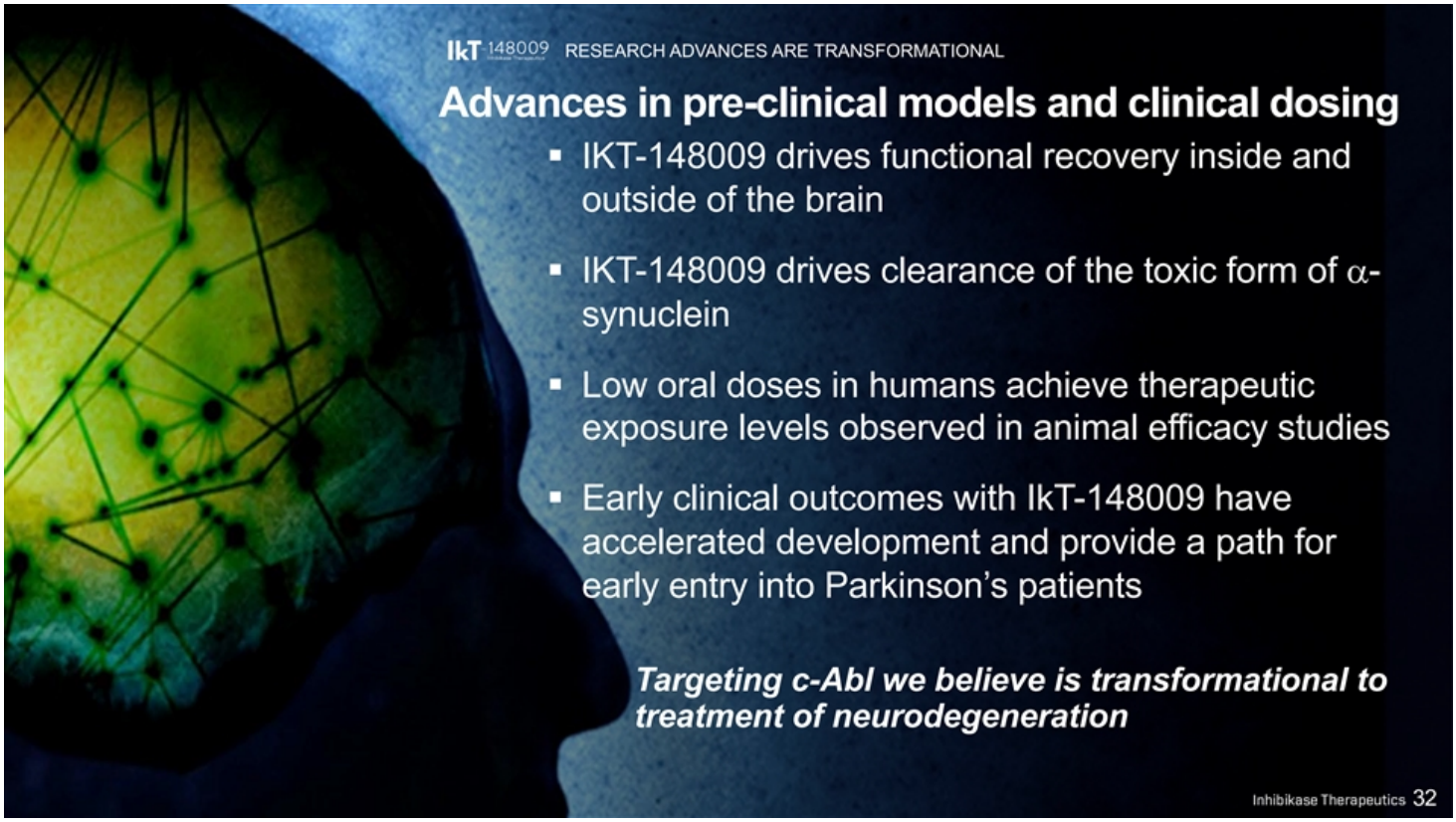

Green: Pathological α-synuclein
Red: Neural ganglia in gut

**IkT-148009 drives clearance of pathological α-synuclein**
(green dots have been cleared)

## Clearance of toxicity in the brain




Aggregates Cleared during treatment with IkT-148009


IkT 148009 RESEARCH ADVANCES ARE TRANSFORMATIONAL
Advances in pre-clinical models and clinical dosing
IKT-148009 drives functional recovery inside and outside of the brain
IKT-148009 drives clearance of the toxic form of α-synuclein
Low oral doses in humans achieve therapeutic exposure levels observed in animal efficacy studies
Early clinical outcomes with IkT-148009 have accelerated development and provide a path for early entry into Parkinson's patients
Targeting c-Abl we believe is transformational to treatment of neurodegeneration
Inhibikase Therapeutics 32