CORTEXYME

# Investor Presentation

***September 2021***

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# Game-Changing Approach Focused Upstream

| | |
|---|---|
| **Disruptive MOA** | • Atuzaginstat is a proprietary, oral, small molecule with an MOA upstream of neurodegeneration<br>• Gingipain inhibitor to address the hypothesis that *P. gingivalis* infection is a causative agent for AD<br>• Completely novel class and unprecedented approach |
| **Lead Asset in Pivotal P2/3 with Data in 2021** | • GAIN is fully enrolled (N=643) global pivotal Phase 2/3 clinical trial of atuzaginstat for Alzheimer's disease<br>• Topline results from GAIN Trial expected by mid-November 2021<br>• Topline results from REPAIR Phase 2 periodontal disease sub-study of 233 GAIN patients expected by mid-November 2021 |
| **Expanding Evidence Base** | • Expanding evidence base with animal causation and human clinical studies<br>• Data supports expansion into other indications<br>• First patient planned for Phase 2 PEAK study in Parkinson's in Q1 2022 |
| **Growing Pipeline** | • COR588 is a lysine gingipain inhibitor that began Phase 1 study in Q3 2021<br>• Lead arginine gingipain inhibitors, COR788 and COR822, have been selected<br>• Lead 3CLpro inhibitors, COR803 and COR817, for coronavirus treatment have been selected |
| **Strong Capital Position** | • $153.5M in cash, equivalents, and short-term investments (as of June 30, 2021)<br>• Fully funded through 2023 to advance through multiple clinical and regulatory milestones |

# Expanding Pipeline

| Molecule | Target | Indication | Development Stage | | | | Anticipated Milestones |
|---|---|---|---|---|---|---|---|
| | | | Pre-clinical | Phase 1 | Phase 2 | Phase 3 | |
| **Atuzaginstat (COR388)** | Lysine gingipain inhibitor | Alzheimer's disease | | | | | Pivotal P2/3 GAIN trial results by mid-November 2021 |
| | Lysine gingipain inhibitor | Periodontal disease | | | | | Phase 2 REPAIR sub-study results by mid-November 2021 |
| | Lysine gingipain inhibitor | Parkinson's disease | | | | | Phase 2 PEAK trial first patient in Q1 2022 |
| **COR588** | Lysine gingipain inhibitor | Periodontal and other *P. gingivalis* driven disease | | | | | Phase 1 trial initiated September 2021 |
| **COR788/ COR822** | Arginine gingipain inhibitor | Undisclosed | | | | | |
| **COR803/ COR817** | CL3 Protease inhibitor | COVID-19 and other coronaviruses | | | | | |
| **Undisclosed** | Undisclosed | Undisclosed | | | | | |

## Amyloid-β peptide protects against microbial infection in mouse and worm models of Alzheimer's disease

Deepak Kumar, *Se Hoon Choi, *Kevin J. Washicosky, *William A. Eimer, Stephanie Tucker, Jessica Ghofrani, Aaron Lefkowitz, Gawain McColl, Lee E. Goldstein, Rudolph E. Tanzi, Robert D. Moir

## Alzheimer's Amyloid-b is an antimicrobial peptide: a review of the evidence

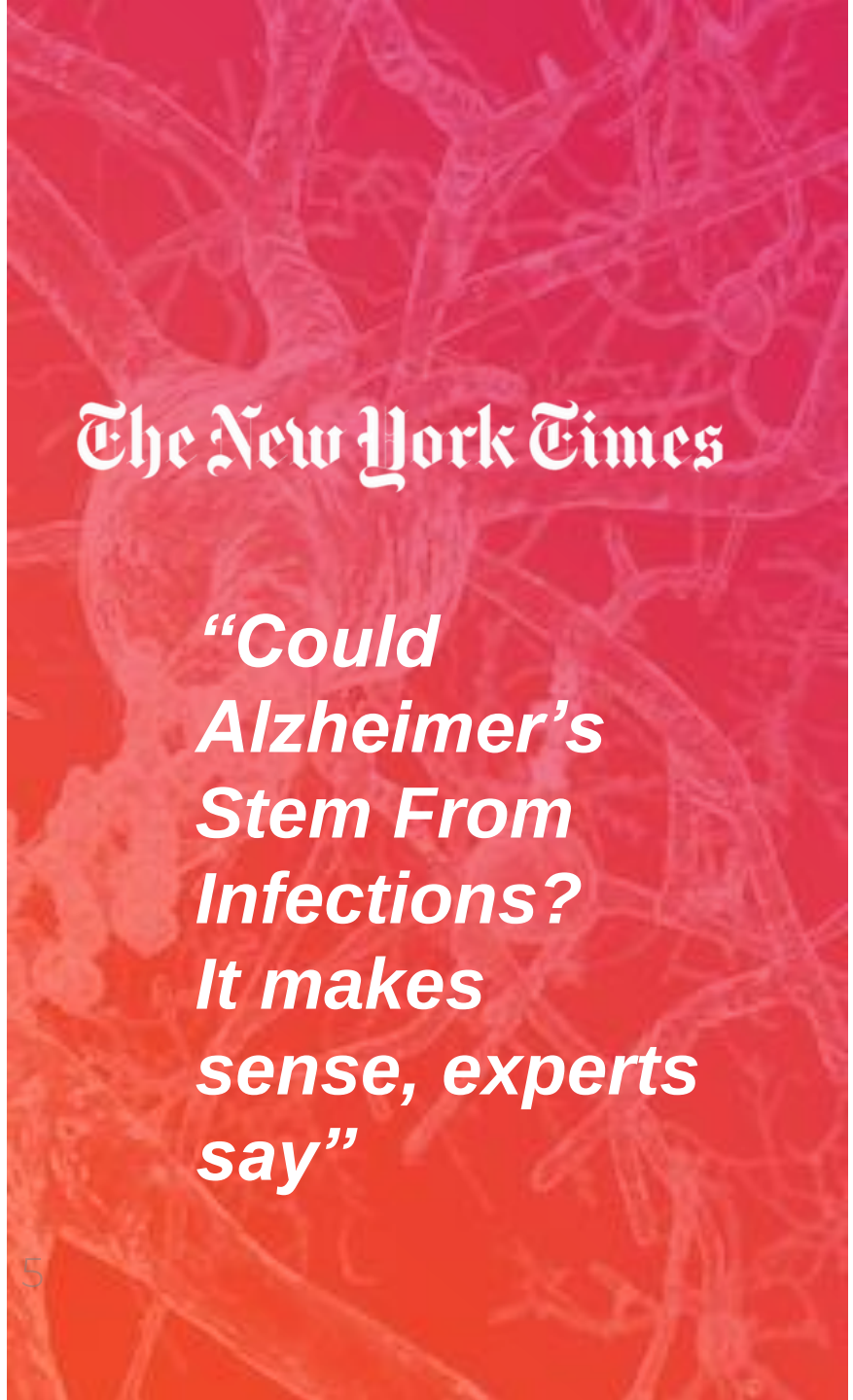
Gosztyla, M.G., Brothers, H.M., Robinson, S.R. (2018). Journal of Alzheimer's Disease, 64(4), 1495- 1506.

## The Alzheimer's Disease-Associated Amyloid β-Protein Is an Antimicrobial Peptide

Stephanie J. Soscia, James E. Kirby, Kevin J. Washicosky, Stephanie M. Tucker, Martin Ingelsson, Bradley Hyman, Mark A. Burton, Lee E. Goldstein, Scott Duong, Rudolph E. Tanzi, Robert D. Moir

## Antimicrobial Properties of Amyloid Peptides

Bruce L. Kagan, Hyunbum Jang, Ricardo Capone, Fernando Teran Arce, Srinivasan Ramachandran, Ratnesh Lal, and Ruth Nussinov




## Periodontal Disease and Incident Dementia: The Atherosclerosis Risk in Communities Study (ARIC)

Ryan T. Demmer, _Faye L. Norby, Kamakshi Lakshminarayan, Keenan A. Walker, James S. Pankow, Aaron R. Folsom, Thomas Mosley, Jim Beck, _Pamela L. Lutsey

## Tooth loss, dementia and neuropathology in the Nun Study

Pamela Sparks Stein, DMD; Mark Desrosiers, PhD; Sara Jean Donegan, SSND, DDS; Juan F. Yepes, DDS, MD, MPH; Richard J. Kryscio, PhD

## Periodontal disease associates with higher brain amyloid load in normal elderly

Angela R. Kamer, Elizabeth Pirraglia, Wai Tsui, Henry Rusinek, Shankar Vallabhajosula, Lisa Mosconi, Li Yi, Pauline McHugh, Ronald G. Craig, Spencer

## Tooth loss and Periodontal Disease Predict Poor Cognitive Function in Older Men

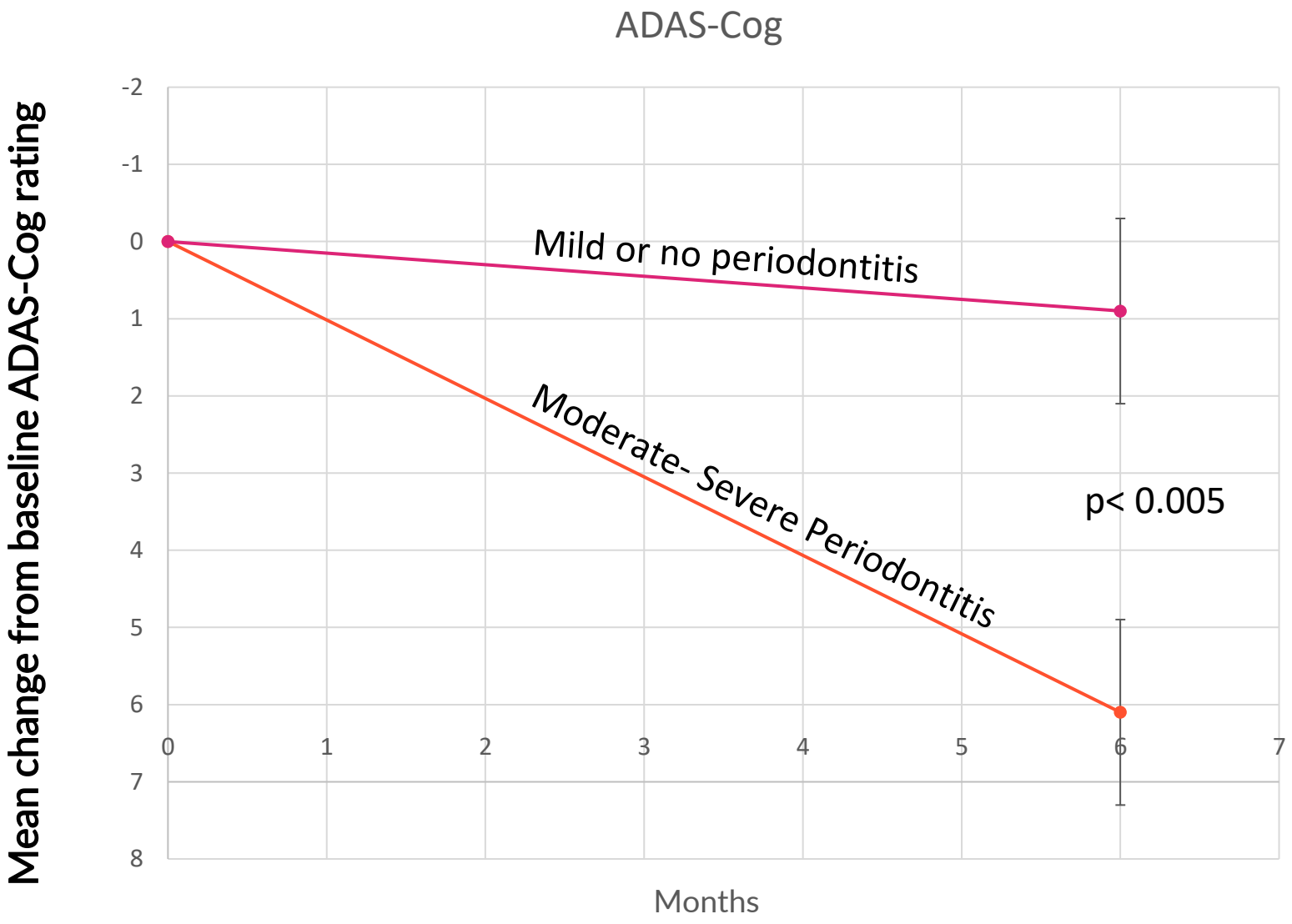
Elizabeth Krall Kaye, PhD, Aileen Valencia, BS, Nivine Baba, MA, Avron Spiro, III, PhD, Thomas Dietrich, DMD, and Raul I. Garcia, DMD

## Serum antibodies to periodontal pathogens are a risk factor for Alzheimer's disease

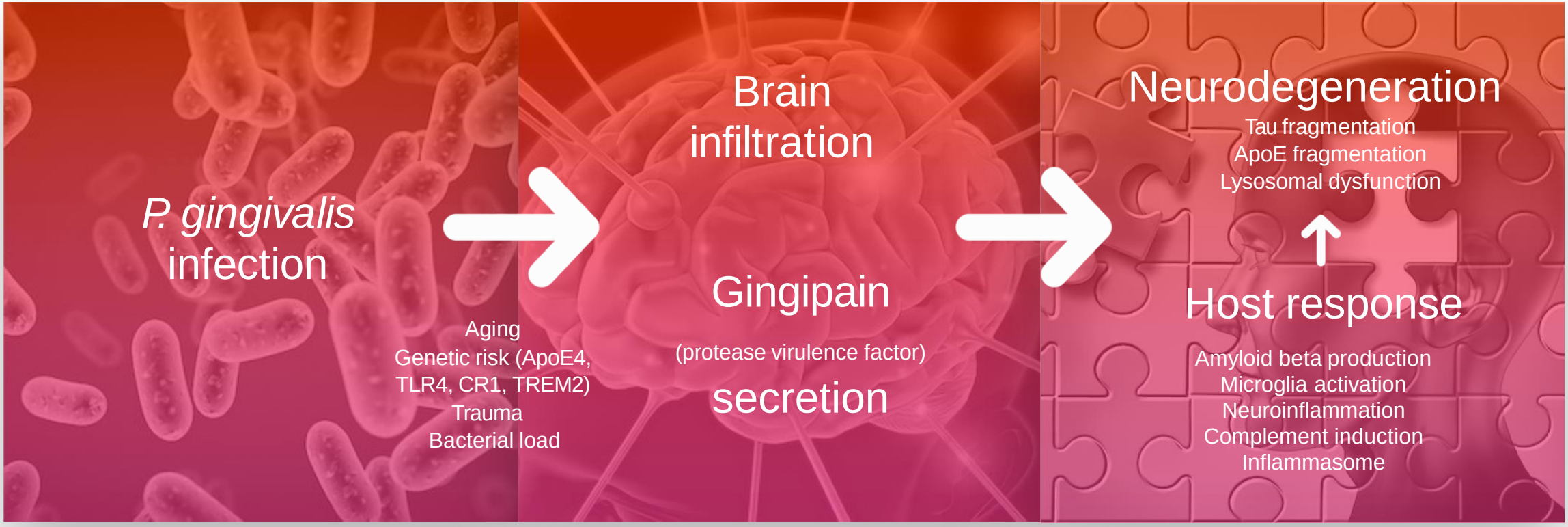
Pamela Sparks Stein, Michelle J. Steffen, Charles Smith, Gregory Jicha, Jeffrey L. Ebersole, Erin Abner, and Dolph Dawson III

# Active periodontal disease is associated with rapid decline in Alzheimer's patients

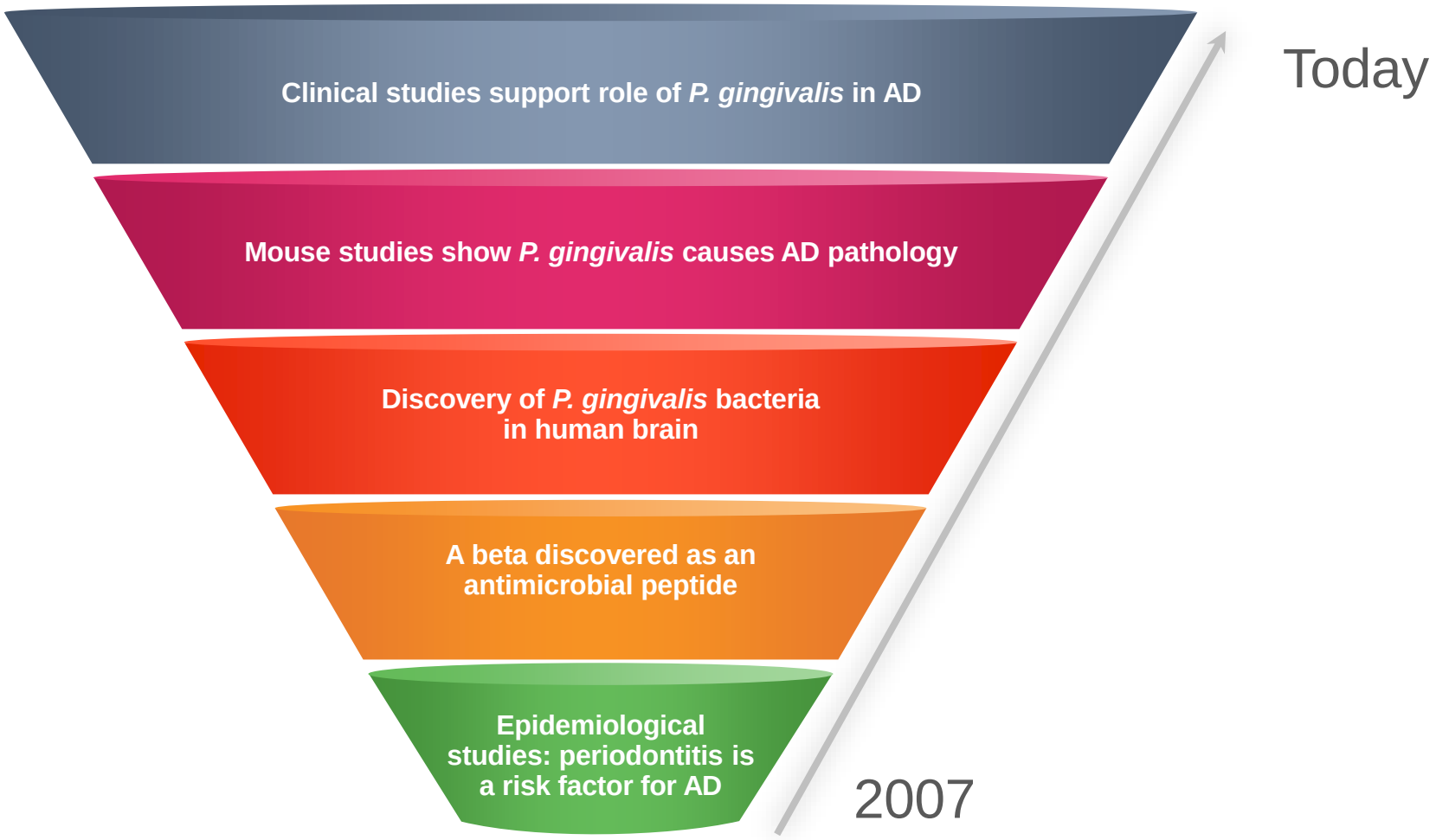
Ide M, et al (2016) Periodontitis and Cognitive Decline in Alzheimer's Disease. PLoS ONE 11(3)



# Evidence Shows *P. gingivalis* is a Key Driver of Alzheimer's Disease

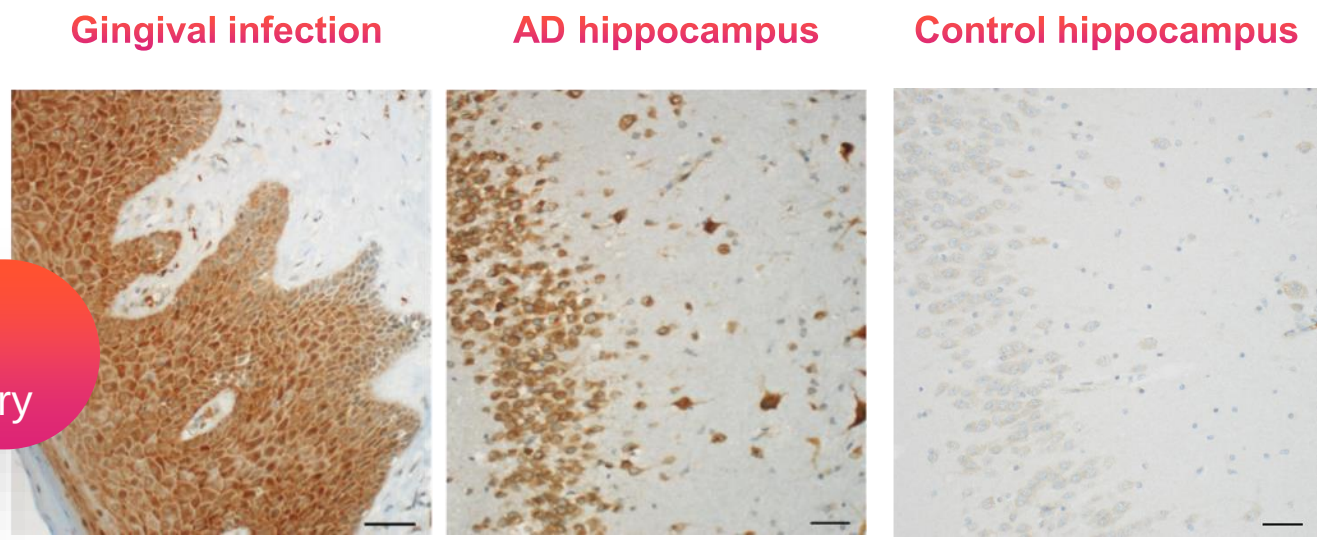


# Evidence & Support for Gingipain Hypothesis Gaining Momentum



# Seminal Discovery: *P. gingivalis* Found in Brains of >90% of AD Patients

Gingipain Immuno-histochemistry




*P. gingivalis* DNA also confirmed through sequencing of multiple genes in Alzheimer's brain tissue

Source: Cortexyme Human IHC study, Dominy et al 2019



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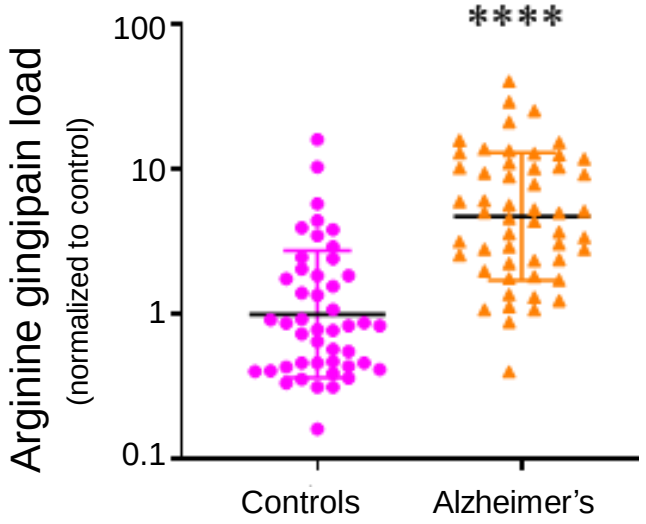
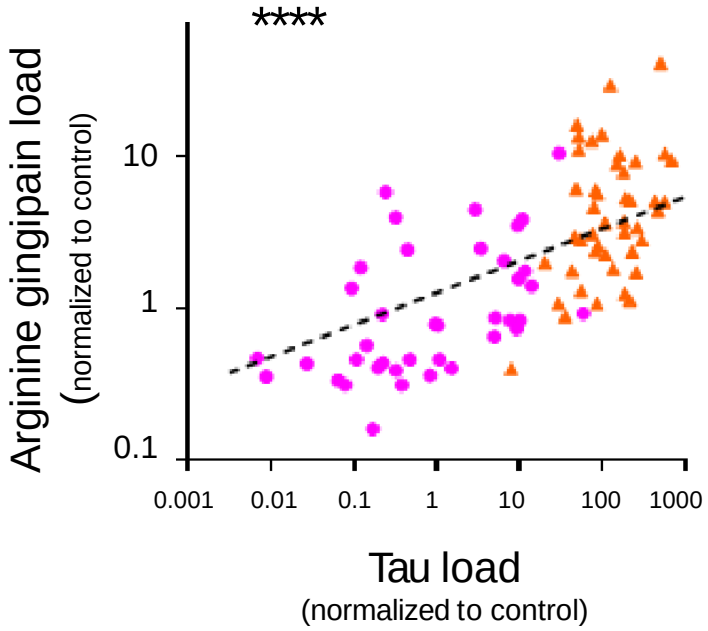
# Higher Gingipain Load is Associated with Symptoms and Correlates to Pathology



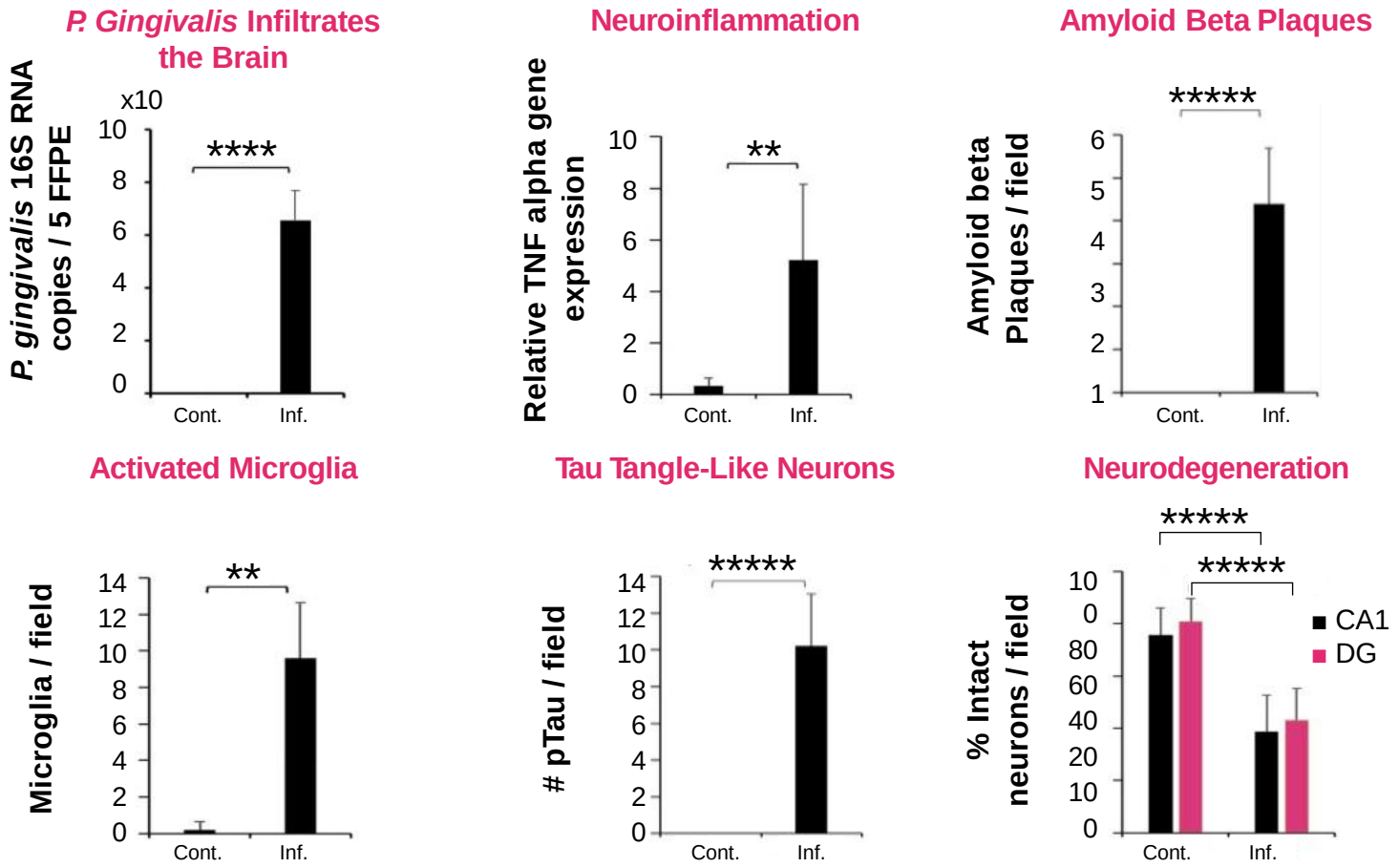




**Immunohistochemistry of middle temporal gyrus microarray**

Source: Collaboration with University of Auckland/ Neurovalida ****p<0.0001, Dominy et al. Science Advances, 2019

# Evidence of Causation: Oral Pg Infection Induces AD Pathology in Mice

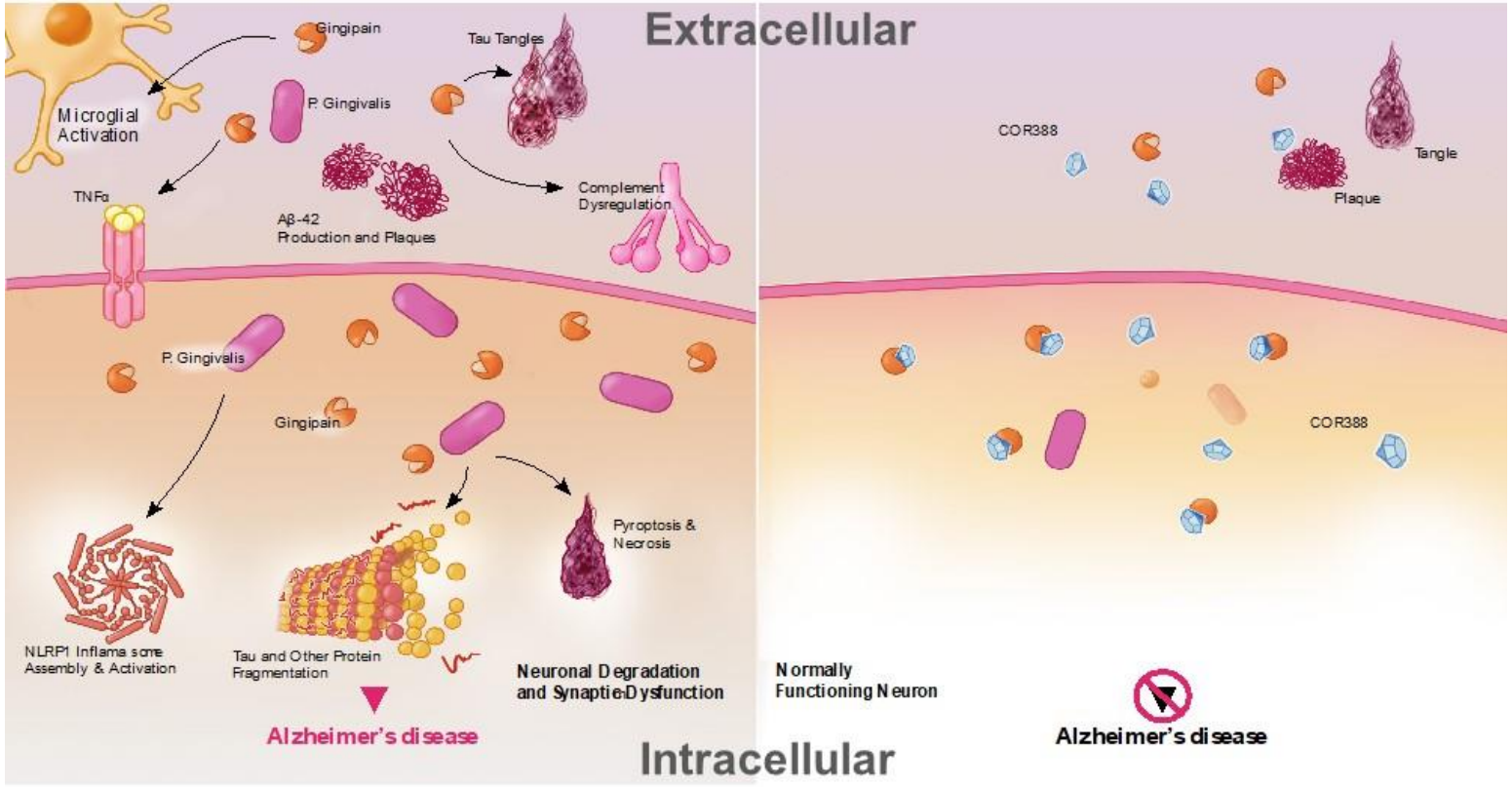
*Brain pathology at 22 weeks post oral infection of wild type mouse with P. gingivalis*




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

Source: Adapted from Ilievski, et al. Chronic oral application of a periodontal pathogen results in brain inflammation, neurodegeneration and amyloid beta production in wild type mice PLOS: One 2018

# Virulence Factor Inhibition (COR388) Blocks Downstream Damage, Reduces Bacterial Load, and Normalizes Immune Function




1. **Tau** is fragmented and aggregated in the AD brain and by Pg.
2. **ApoE** is fragmented in the AD brain and by gingipains.
3. **Abeta** is overproduced in the AD brain and triggered by Pg infection in WT mice.
4. **Microglia** are activated in the AD brain and by Pg.
5. **Inflammasomes** are activated in the AD brain and by Pg.
6. **Complement** is dysregulated in the AD brain and by gingipains.
7. **Neurodegeneration** is evident in the AD brain and caused by Pg gingipains in physiological models

# Atuzaginstat (COR388) First-in-Class Gingipain Inhibitor

- Gingipains are proteases secreted by *P. gingivalis*
  - Required for survival of intracellular assaccharolytic bacterium
  - Manipulate innate immune response
  - Promote chronic inflammation
  - Proposed causative agent for Alzheimer's disease
  - Tau and ApoE are targets of gingipain proteolysis

- Atuzaginstat specifically targets lysine gingipain (Kgp)[1]
  - Synthesized and optimized from proprietary library
  - Selective, potent (IC50 < 50 pM) small molecule inhibitor of Kgp
  - Superior PK properties: orally bioavailable, 100% brain penetrant
  - Composition of matter protection to at least 2037

- Atuzaginstat acts upstream of Alzheimer's pathology
  - Selectively blocks toxicity and reduces bacterial load
  - Reduced $Ab_{1-42,}$ TNFa, and protects neurons in mouse model
  - No evidence of Pg resistance

1. Dominy, et.al. 2019. Science Advances; 5: eaau333

CORTEXYME

**6.2M**

People in the U.S. with Alzheimer's

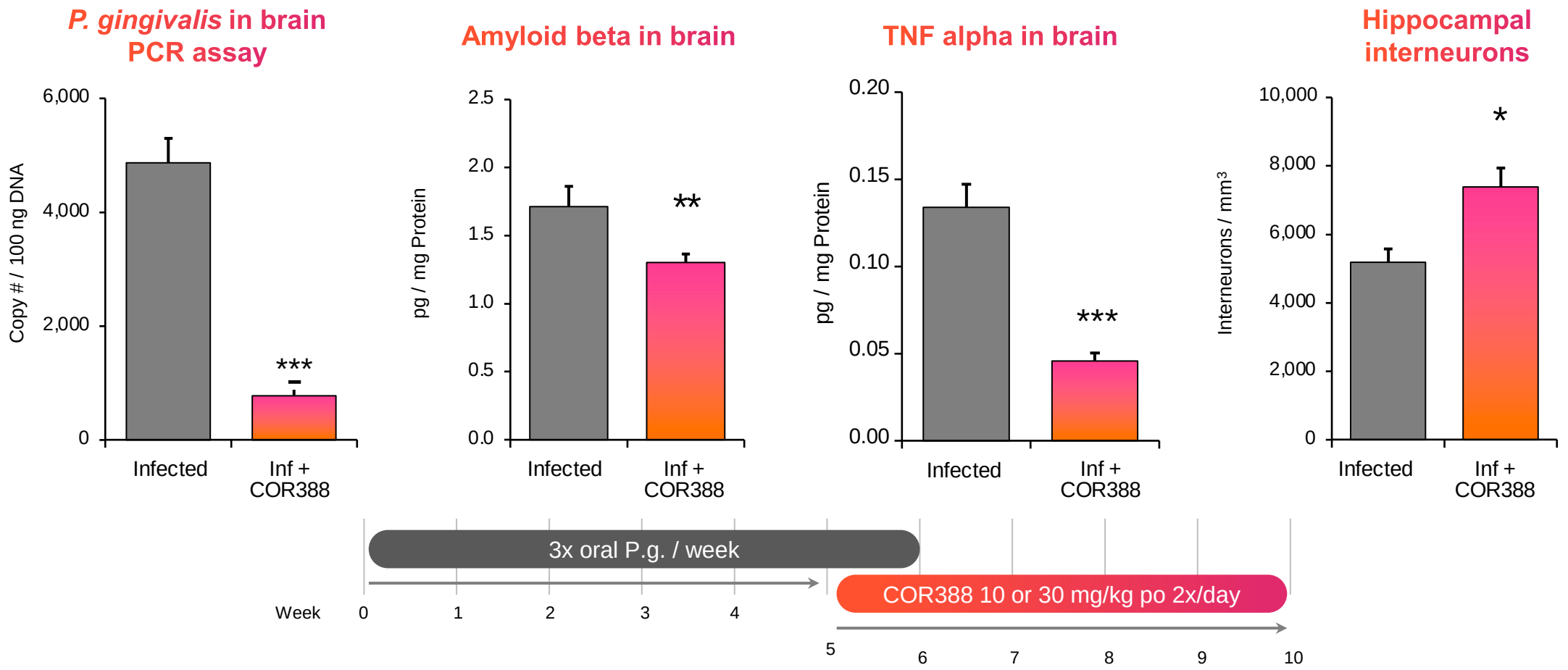
**$355B**

Economic burden

Source: Alzheimer's Association

# Atuzaginstat Acts Upstream of Alzheimer's Pathology

*Efficacious in wild type mouse model for sporadic Alzheimer's disease*




Source: Cortexyme atuzaginstat (COR388) dose response study, Mean +/- SEM *p< 0.05,**p<0.01, ***p<0.001, Science Advances, 2019

# Phase I: Atuzaginstat Well-Tolerated in Older Subjects & AD Patients

## *10-day MAD in Healthy Elderly and 28-day in Alzheimer's patients*

*Drug related adverse events*

| Cohorts 1-3: Older Healthy Volunteers; Treatment duration = 10 days | | | | |
|---|---|---|---|---|
| Dose | Plcbo BID | 25 mg BID | 50 mg BID | 100 mg BID |
| **Subjects dosed** | **N=6** | **N=6** | **N=6** | **N=6** |
| Dizziness[1] | 0 | 0 | 1 (17%) | 1 (17%) |
| Dysgeusia[1] | 1 (17%) | 0 | 0 | 0 |
| Nausea[1] | 0 | 0 | 0 | 1 (17%) |
| Presyncope[2] | 1 (17%) | 0 | 0 | 0 |
| Restlessness[1] | 0 | 0 | 0 | 1 (17%) |
| Tachycardia[1, 3] | 0 | 0 | 1 (17%) | 0 |

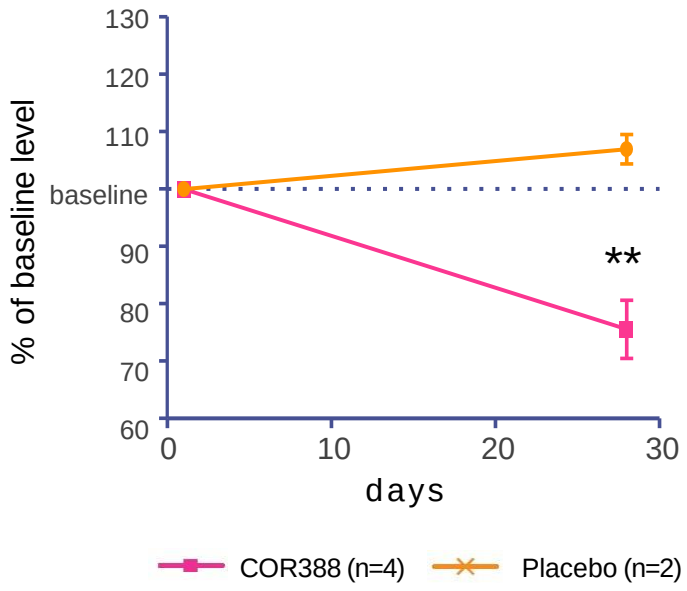
| Cohorts 4: Patients with AD; Treatment duration = 28 days | | | | |
|---|---|---|---|---|
| **Dose** | Placebo BID | 25 mg BID | 50 mg BID | 100 mg BID |
| **Subjects dosed** | **N=3** | | **N=6** | |
| Bradycardia[1] | 1 (33%) | | 0 | |
| Orthostasis[1] | 1 (33%) | | 0 | |
| Liver enzyme elevation[2] | 0 | | 1 (17%) | |
| Pancreatic enzyme elevation[1] | 0 | | 1 (17%) | |
| Transient QT Prolongation[1] | 1 (33%) | | 1 (17%) | |
| **Subjects with drug related TEAE** | **4 (44%)** | **0 (0%)** | **4 (33%)** | **2 (33%)** |

1 Mild AE severity,
2 Moderate AE severity.
3 AE consisted of 6 beats of SVT that occurred again 72 hours after stopping study drug and was designated unreleated to drug
Note: No Serious Adverse Events were reported

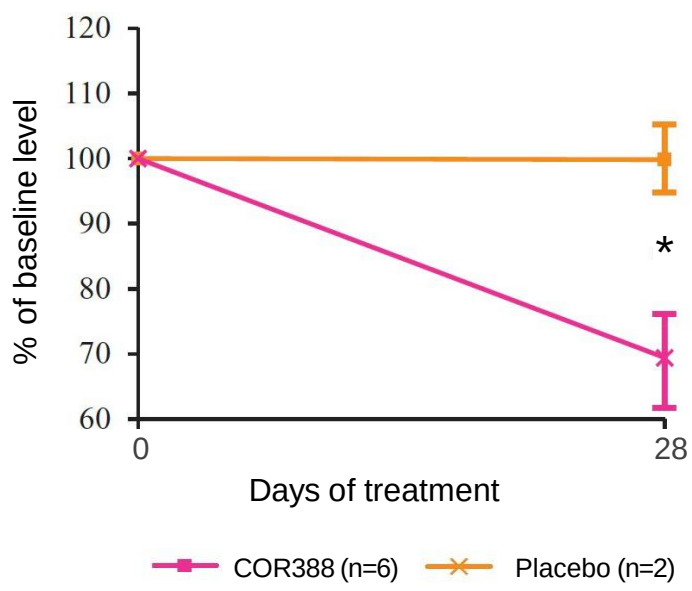
# Atuzaginstat Target Engagement of Key Endpoints

*28-day Phase 1b study 50 mg BID in AD patients*

**Plasma RANTES (CCL5) is reduced in Atuzaginstat treated subjects**




**CSF ApoE fragments are reduced in Atuzaginstat treated subjects**

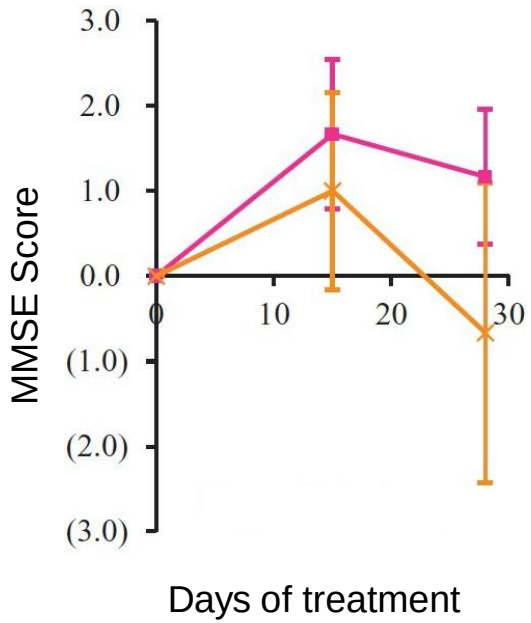



Source: Cortexyme ApoE and MAD study: *p< 0.05, ** p< 0.01

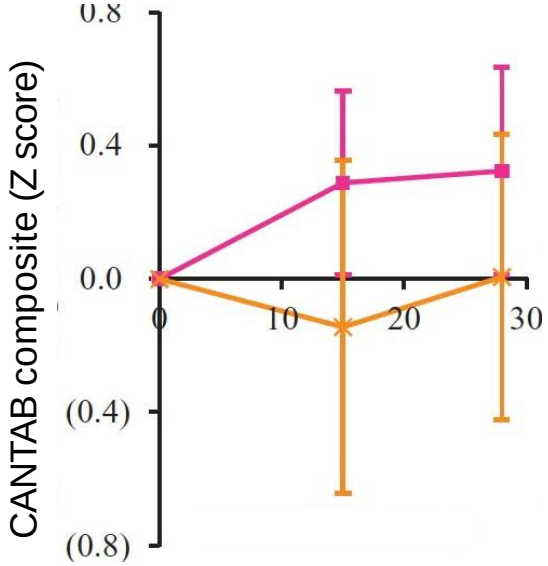
# Atuzaginstat Showed Favorable Trends on Multiple Cognitive Measures

*28-day Phase 1b study 50 mg BID in AD patients*

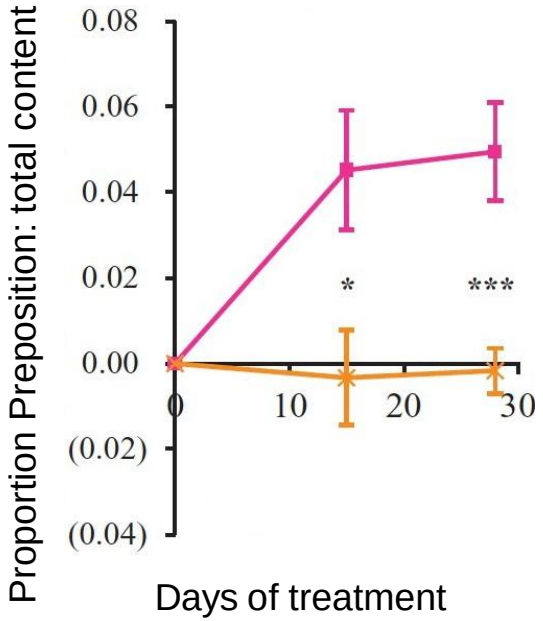
**MMSE**




**CANTAB Memory Composite of Cognitive Functions**




**Winterlight Assessment Prepositions & Conjunctions**




COR388 (n=6) Placebo (n=3)

Source: Cortexyme MAD study: *p< 0.05, ***p<0.001

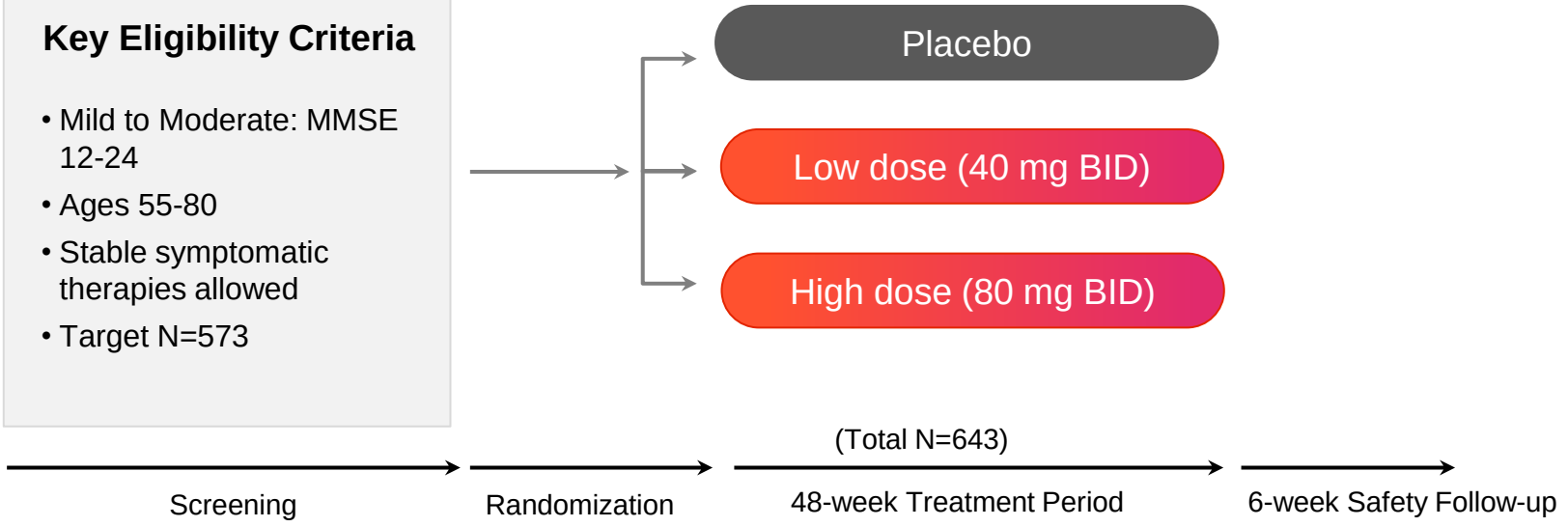
# Summary of Atuzaginstat Pre-clinical and Phase 1 Findings

- Pg causes Alzheimer's pathology after oral infection in rodent studies
- Atuzaginstat acts upstream of infection-induced Alzheimer's pathology in mouse model
- Top doses of chronic toxicology studies were no-observed-adverse-effect level (NOAEL)
- Well-tolerated in Phase 1a/b
- Favorable PK profile in therapeutic range
- Pharmacodynamic biomarkers demonstrate target engagement at 50 mg BID
- Favorable trends on multiple cognitive measures

# Pivotal P2/3 GAIN Trial Design: Atuzaginstat in Alzheimer's Disease

**Key Eligibility Criteria**

- Mild to Moderate: MMSE 12-24
- Ages 55-80
- Stable symptomatic therapies allowed
- Target N=573




## Endpoints

**Co-Primary:**
ADAS-Cog11 and ADCS-ADL

**Secondary:**
CDR-SB, MMSE and NPI

**Exploratory:**
Winterlight

**Primary biomarker:** MRI volumetric measures

**Biomarkers of Alzheimer's**:
CSF Aβ, tau, p-tau

**Biomarkers of Pg activity**:
blood, saliva, CSF

## Timelines

- Enrollment initiated Apr. 2019; completed Sept. 2020
- Interim analysis in December 2020 successfully completed with no sample size adjustment
- Top-line data expected on time in mid-November 2021

## Periodontal REPAIR sub-study

- 233 subjects
- Assessment of pocket depth and clinical attachment level at 6 and 12 months

More information: www.gaintrial.com

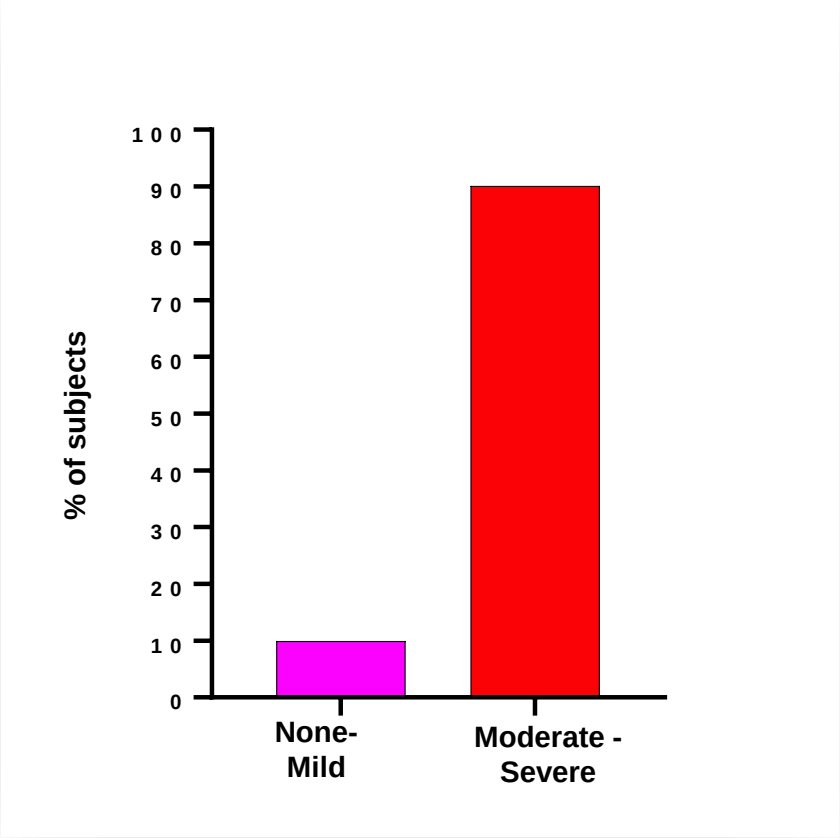
# GAIN Baseline Demo: Population and Stratification as Expected

| Parameter | Overall (N=643) |
|---|---|
| Age at Informed Consent (years) | 69.1 (55 – 80) |
| Sex | |
| Male | 278 (43%) |
| Female | 365 (57%) |
| Race and Ethnicity | |
| Black or African American | 42 (7%) |
| White, Hispanic or Latino | 68 (11%) |
| White, Not Hispanic/Latino | 505 (79%) |
| Other | 10 (2%) |
| Missing | 18 (3%) |

| Parameter | Overall (N=643) |
|---|---|
| Region | |
| North America | 447 (70%) |
| Europe | 196 (30%) |
| MMSE (Statum), n (%) | |
| Moderate >=12 to <=18 | 324 (50%) |
| Mild >=19 to <=24 | 319 (50%) |
| ApoE4 (Stratum), n (%) | |
| ApoE4 Positive | 414 (64%) |
| non-ApoE4 | 229 (36%) |
| Cholinesterase Inhibitor/Memantine Use | |
| Yes | 476 (74%) |
| No | 167 (26%) |

*Final data to be confirmed post data lock*

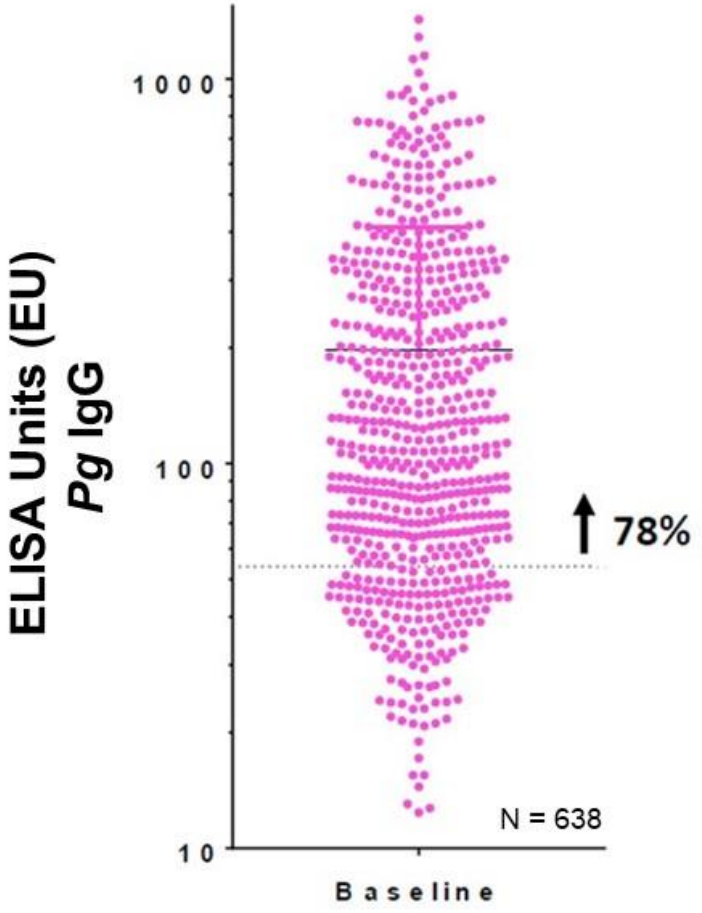
# Over 90% of GAIN Subjects in REPAIR Sub-Study Have Moderate to Severe Periodontal Disease at Baseline




**Diagnosis based on Pocket depth and Clinical attachment loss measures (N=233)**

*Final data to be confirmed post data lock*

# *P. gingivalis* Specific IgG Elevated in Serum at Baseline Indicating Systemic Infection



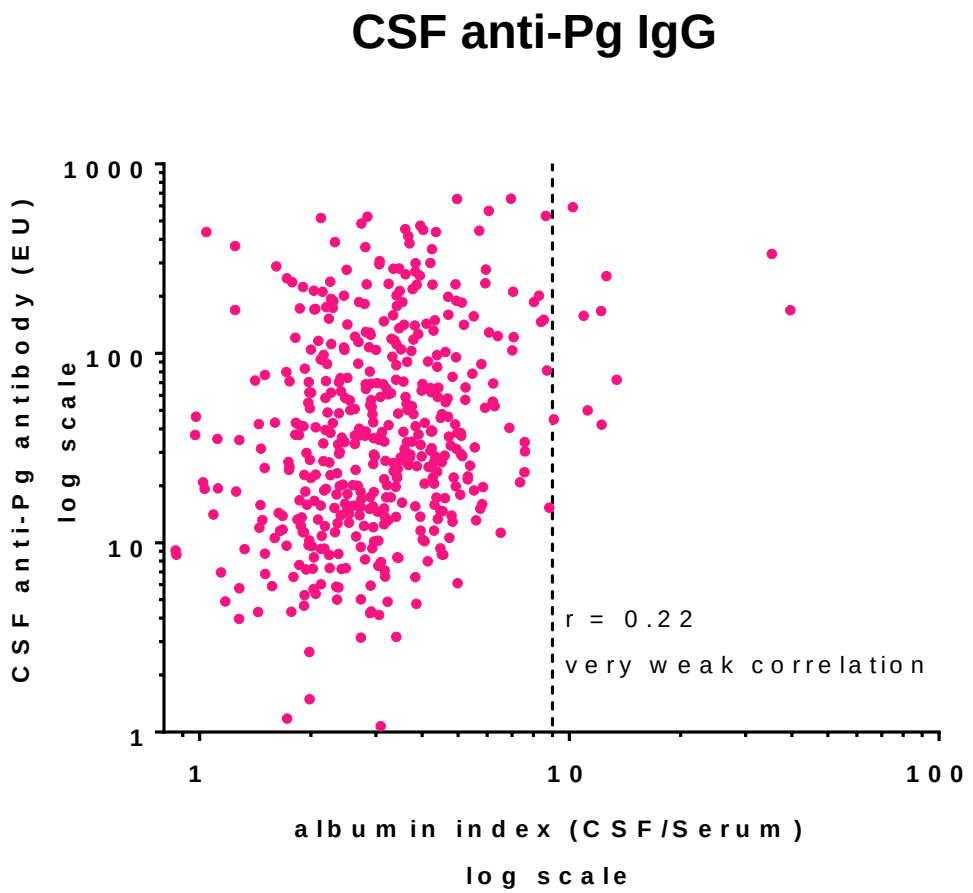

**100% of GAIN subjects have evidence of systemic *P. gingivalis* exposure with detectable antibodies**

**78% have higher IgG antibody titers associated with oral periodontal disease symptoms**

*Final data to be confirmed post data lock; Collaboration with H. Hasturk, Forsyth Institute; range and assay from Offenbacher et al. 2007*

# Baseline CSF Anti-*Pg* IgG Levels Provide Evidence of CNS Infection in AD

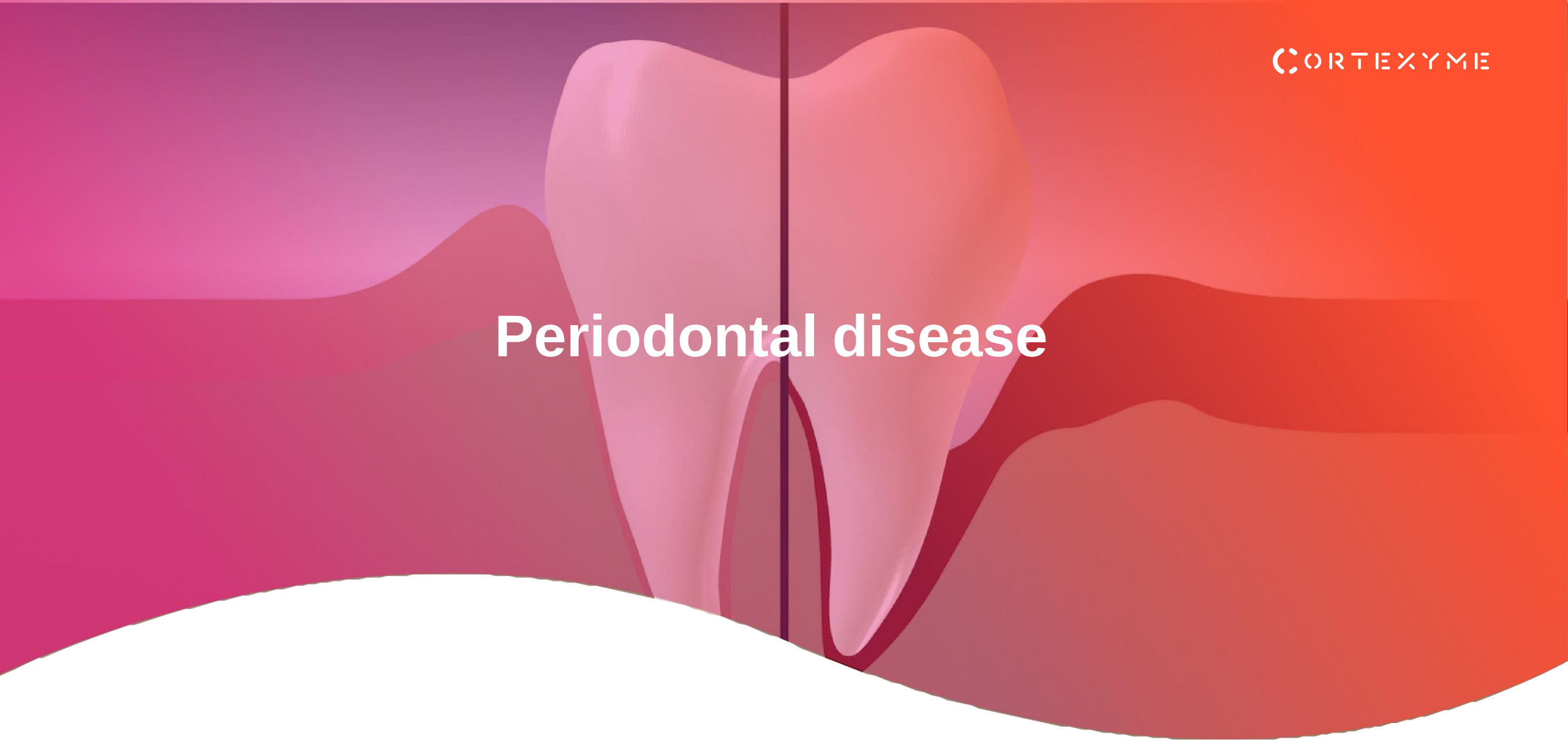
- Anti-*Pg* IgG concentration in CSF is largely independent of the albumin index indicating central nervous system production in addition to levels found in serum
- Only 2% of GAIN subjects (mean 69 yo) have loss of BBB integrity, as measured by albumin index >9
- The presence of these antibodies further supports a direct *P. gingivalis* infection in the central nervous system




*Final data to be confirmed post data lock; Collaboration with Hatice Hasturk, DDS PhD, Forsyth Institute*

# GAIN Pivotal Phase 2/3 Trial Status & Summary

- Fully enrolled on time and strategically over-enrolled to counter any potential impact of COVID
- Baseline demographics and biomarker data indicate appropriate population enrolled
- Patients enrolled have baseline biomarkers consistent with Alzheimer's and *P. gingivalis* infection
- Co-primary endpoints are well-established
- Topline data for GAIN and REPAIR expected by mid-November 2021
- Results of periodontal disease REPAIR sub-study will enable initiation of pivotal program



# Periodontal disease

# Periodontal Disease Program Overview

### REPAIR Ph2 Trial

Includes 233 subjects enrolled in periodontal study as part of the GAIN trial, reporting topline data mid-November 2021

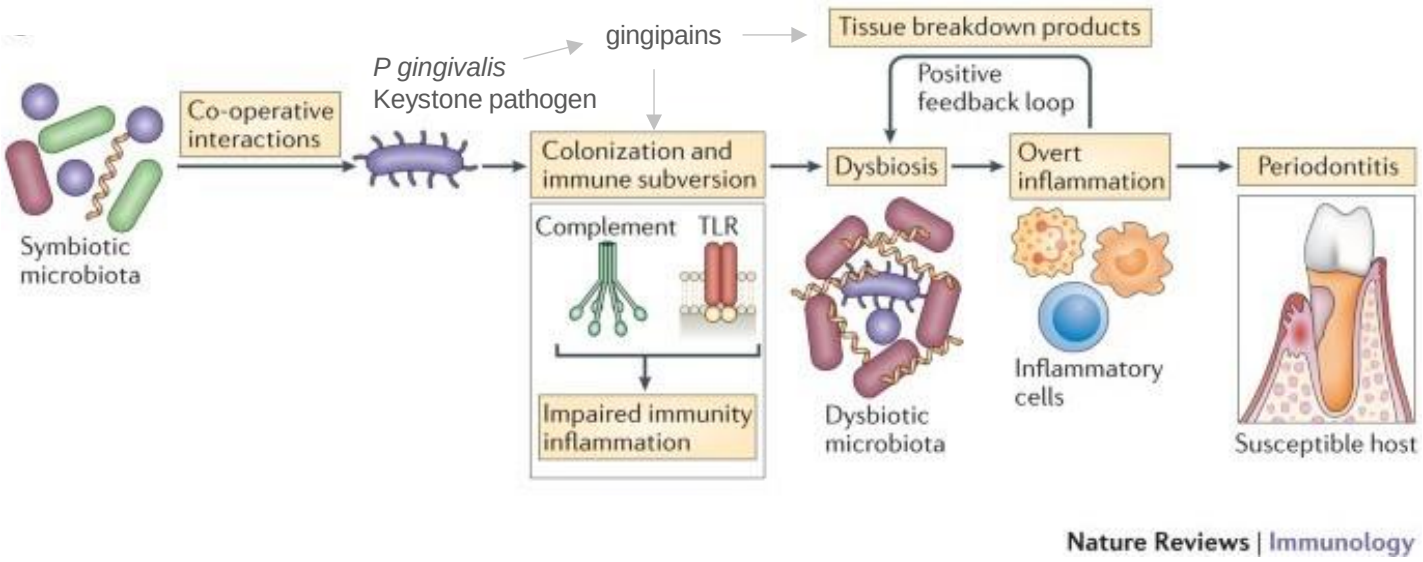
### Efficacy Endpoints

At 6 months and 1 year; Pocket Depth (PD) and clinical attachment level (CAL) are typical regulatory endpoints

### Milestones

Atuzaginstat efficacy data: mid-November 2021

COR588 Phase 1: Q3 2021



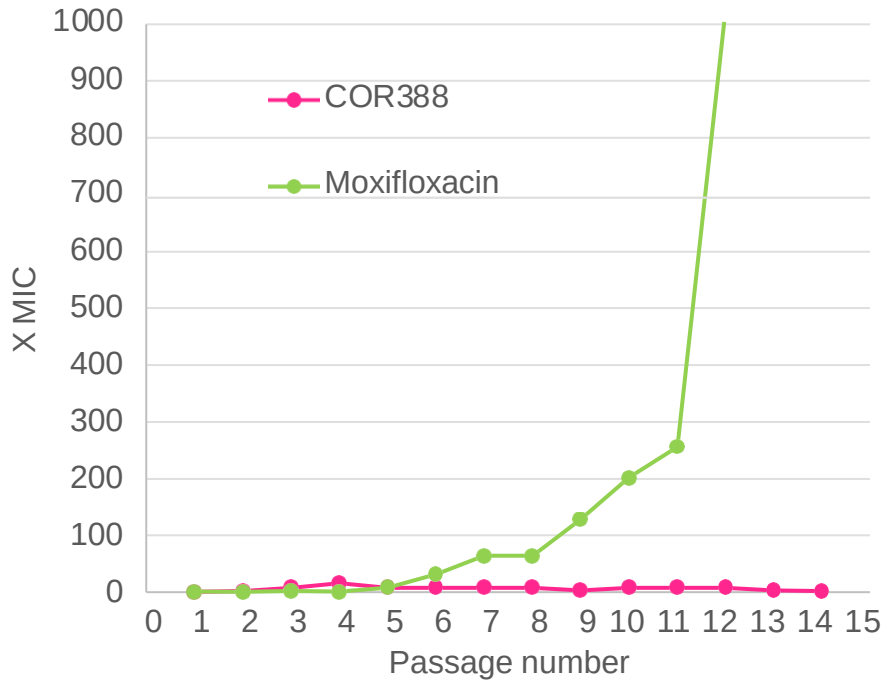

**65M**

People in the U.S. with periodontal disease

**> $2B**

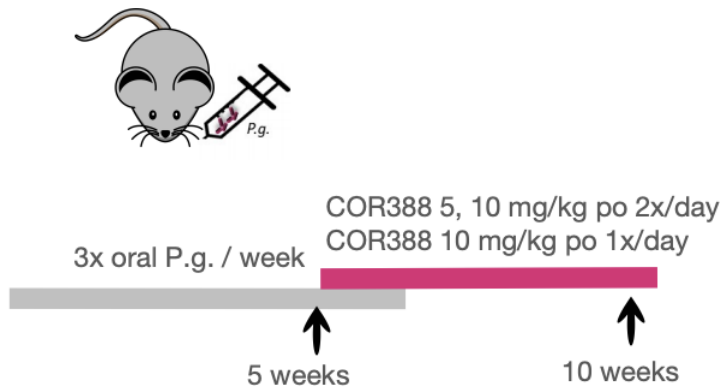
Estimated annual revenue opportunity

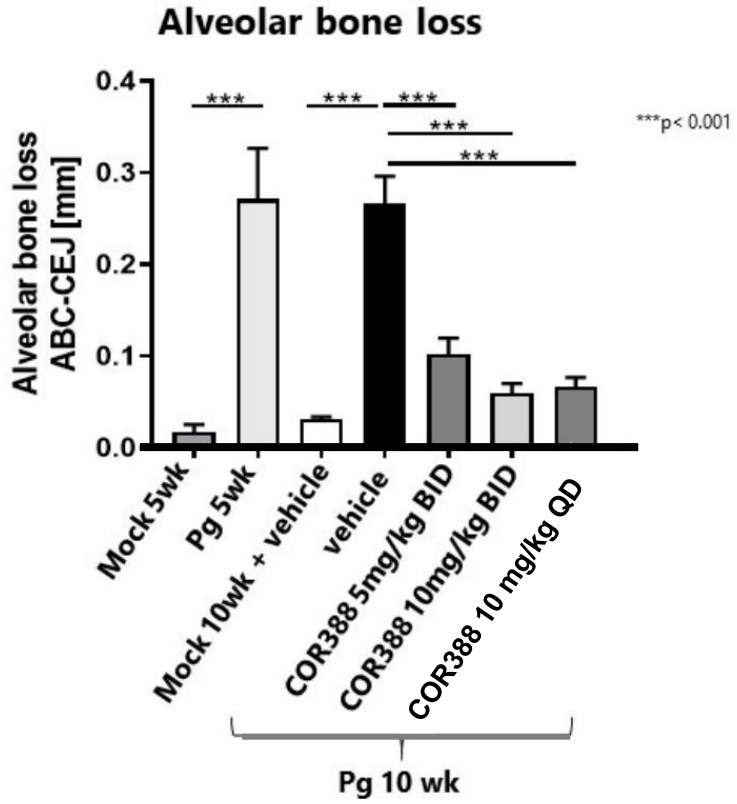
# Atuzaginstat Does Not Show Any Evidence of Pg Resistance




Dominy et al, 2019 Science Advances

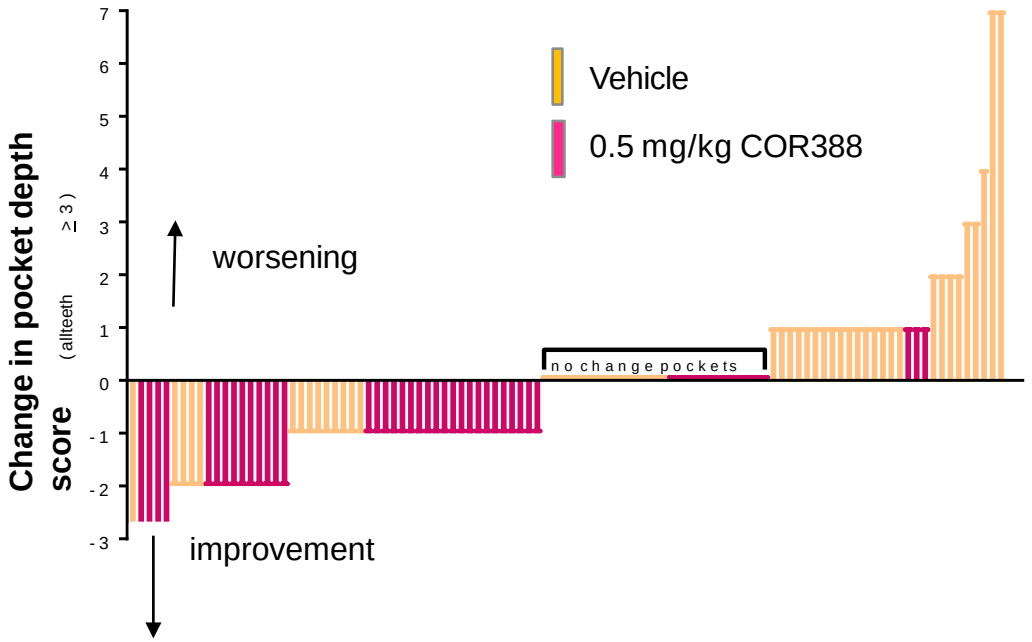
# Atuzaginstat Reverses Bone Loss in Mouse Periodontal Model

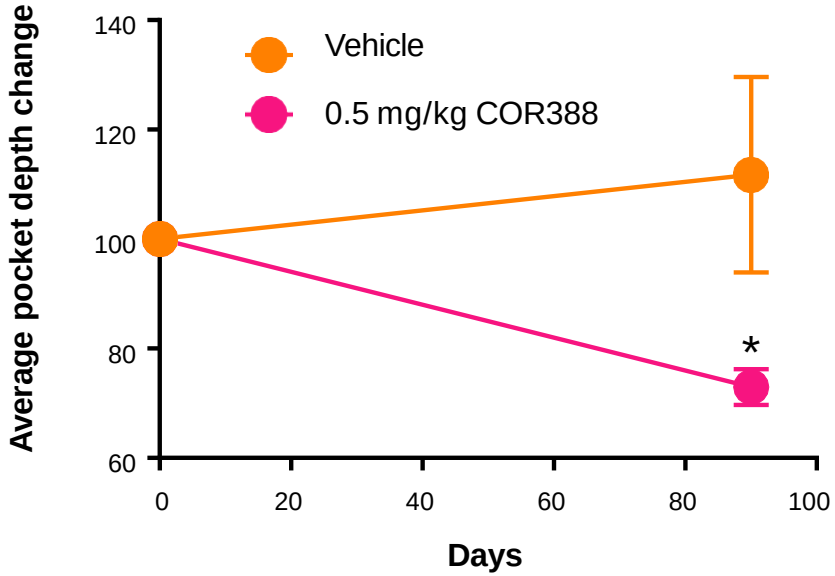


# Atuzaginstat is Efficacious in Treating Periodontitis in Aged Dogs

*Significant reduction in gingival pocket depth*



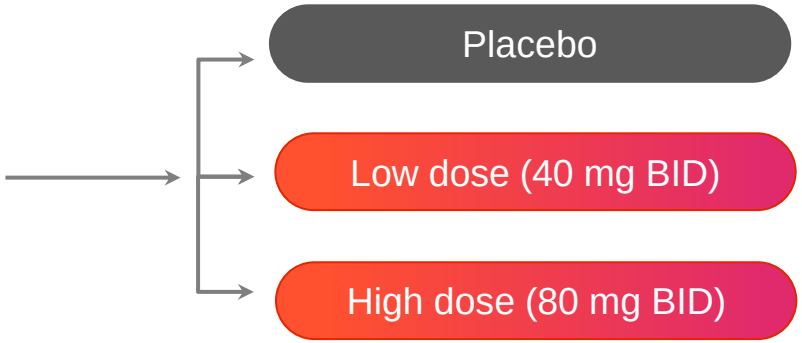



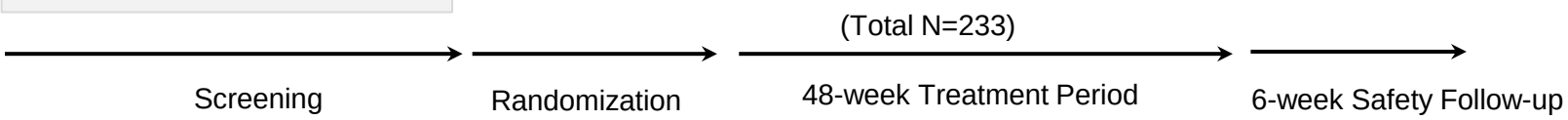

Kapur et al. Pharmacology Research and Perspectives

# REPAIR Phase 2 Periodontal Disease Sub-study Trial Design

**Key Eligibility Criteria**

- Mild to Moderate: MMSE 12-24
- Ages 55-80




## Timelines

- Enrollment initiated April 2019; completed September 2020
- Top-line data expected on time in mid-November 2021
- Phase 3 initiation expected in 2022

## Endpoints

**Endpoints**

- Pocket depth at 6 and 12 months
- Clinical attachment level at 6 and 12 months
- Bleeding on probing at 6 and 12 months

**Biomarkers**

- Pg in saliva

More information: www.gaintrial.com

# COR588 second generation lysine gingipain inhibitor

Small molecule optimized from proprietary library

- Potent and selective
- Novel structure vs. atuzaginstat
- Once a day dosing vs. twice a day
- Highly selective
- Orally available, brain penetrant
- Novel & proprietary small molecule
- Low COGS manufacturing
- Composition of matter patent pending
- Phase 1 study initiated September 2021

# Parkinson’s Disease

# Evidence Supports MOA in Parkinson’s Disease

## Unmet need

- Currently only symptomatic treatments
- Unmet need to stop or slow disease progression

## Pathological pattern

The famous pathologist, Braak originally postulated that Parkinson’s pathology begins when a neurotrophic pathogen enters the body via the gastric pathway spreading trans-synaptically from one vulnerable brain region to the next. Braak et al. 2003

## Periodontal disease is a risk factor for Parkinson’s

Chen et al. Periodontal inflammatory disease is associated with the risk of Parkinson’s disease: a population-based retrospective matched-cohort study

Woo et al. Association of Tooth Loss with New-Onset Parkinson’s Disease: A Nationwide Population-Based Cohort Study

Chen et al. Dental Scaling Decreases the Risk of Parkinson’s Disease: A Nationwide Population-Based Nested Case-Control Study

Kaur et al. Parkinson’s and periodontal disease – the missing link?

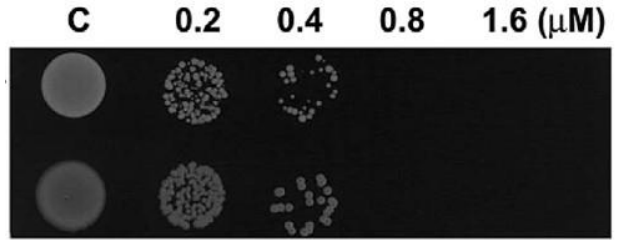
## Human data

Supports presence of gingipains in blood and relevant motor brain areas in PD patients

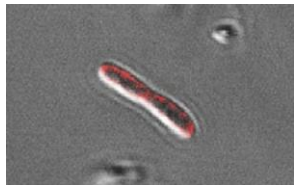
## Animal data

Shows ability of Pg to trigger alpha-synuclein and neurodegeneration in the substantia nigra in at risk populations

# Alpha-synuclein, like Aβ42, Behaves Like an Antimicrobial Peptide (AMP)




Interaction of positively charged alpha syn with negatively charged bacterial membranes similar to other AMPS



Inhibitory effects of recombinant α-Syn against bacterial and fungal cells.

| Pathogenic microbes | MIC (μM) | | |
|---|---|---|---|
| | α-Syn (1–140 a.a.) | α-Syn (1–60 a.a.) | α-Syn (61–140 a.a.) |
| Bacteria | | | |
| *E. coli* | 0.2 | 1.6 | >25.6 |
| *P. aeruginosa* | 0.2 | 1.6 | >25.6 |
| *S. aureus* | 0.2 | 3.2 | >25.6 |
| *S. epidermidis* | 0.2 | 3.2 | >25.6 |

Additional publications:

Gastrointestinal immunity and Alpha-synuclein

Holocranohistochemistry enables the visualization of alpha-synucleai expression in the murine olfactory system and discovery of its systemic antimicrobial effects

Alpha-synuclein Pathology and the role of the microbiota in Parkinson's disease

Amyloid-β peptide protects against microbial infection in mouse and worm models of Alzheimer's disease

Alzheimer's Amyloid-b is an antimicrobial peptide: a review of the evidence

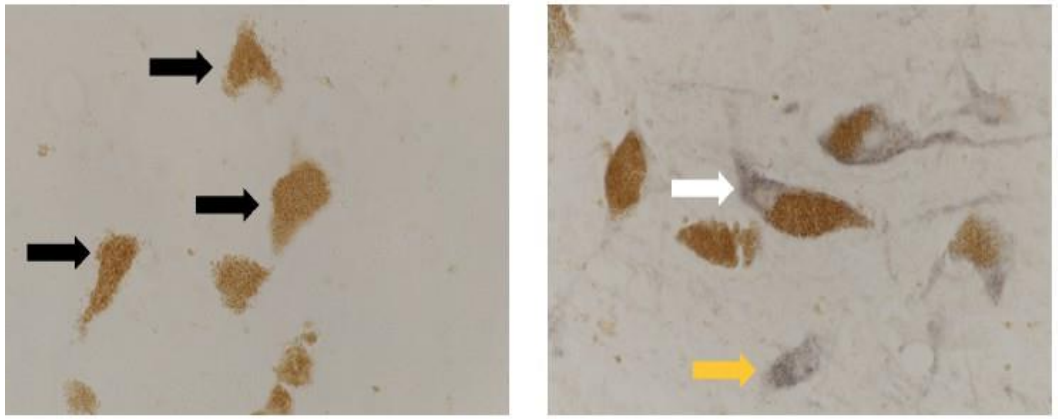
The Alzheimer's Disease-Associated Amyloid β-Protein Is an Antimicrobial Peptide

Source: Park et al. Functional characterization of Alpha-synuclein protein with antimicrobial activity. Biochemical and Biophysical Research Communications 2016

# Gingipains Found in the Substantia Nigra and blood of PD Patients

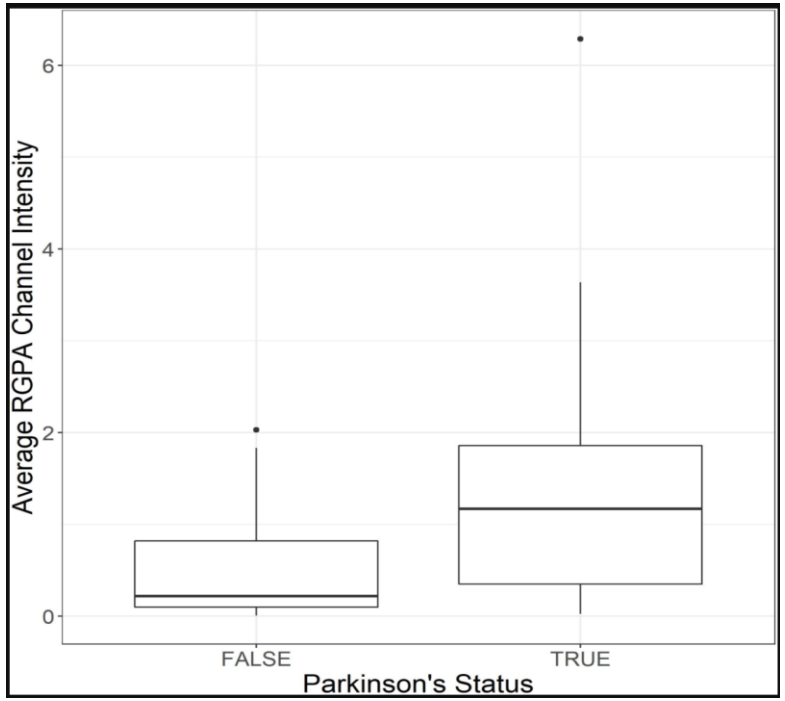
Preabsorption control showing melanin containing dopaminergic neurons

Lysine gingipain IHC



Source: University of Auckland/Neurovalida, December 2020

Arginine Gingipain increased in blood of Parkinson's patients




Source: Adams et al. Parkinson's Disease: A Systemic Inflammatory Disease Accompanied by Bacterial Inflammagens. 2019

# Oral Pg Infection of LRRK2 Mutant Mice Results in Alpha Synuclein Production and Degeneration of the Substantia Nigra

Feng *et al. Journal of Neuroinflammation* (2020) 17:347
https://doi.org/10.1186/s12974-020-02027-5

Journal of Neuroinflammation

RESEARCH Open Access

## Oral *P. gingivalis* impairs gut permeability and mediates immune responses associated with neurodegeneration in LRRK2 R1441G mice

Yu-Kun Feng[1,2†], Qiong-Li Wu[3†], Yan-Wen Peng[4], Feng-Yin Liang[1], Hua-Jing You[1], Yi-Wei Feng[1,5], Ge Li[6], Xue-Jiao Li[6], Shu-Hua Liu[6], Yong-Chao Li[6], Yu Zhang[6] and Zhong Pei[1*]

**Abstract**

**Background:** The R1441G mutation in the leucine-rich repeat kinase 2 (LRRK2) gene results in late-onset Parkinson's disease (PD). Peripheral inflammation and gut microbiota are closely associated with the pathogenesis of PD. Chronic periodontitis is a common type of peripheral inflammation, which is associated with PD. *Porphyromonas gingivalis* (Pg), the most common bacterium causing chronic periodontitis, can cause alteration of gut microbiota. It is not known whether Pg-induced dysbiosis plays a role in the pathophysiology of PD.

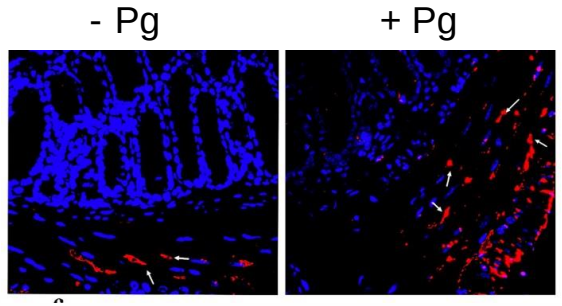
**Methods:** In this study, live Pg were orally administrated to animals, three times a week for 1 month. Pg-derived lipopolysaccharide (LPS) was used to stimulate mononuclear cells in vitro. The effects of oral Pg administration on the gut and brain were evaluated through behaviors, morphology, and cytokine expression.

**Results:** Dopaminergic neurons in the substantia nigra were reduced, and activated microglial cells were increased in R1441G mice given oral Pg. In addition, an increase in mRNA expression of tumor necrosis factor (TNF-α) and interleukin-1β (IL-1β) as well as protein level of α-synuclein together with a decrease in zonula occludens-1 (Zo-1) was detected in the colon in Pg-treated R1441G mice. Furthermore, serum interleukin-17A (IL-17A) and brain IL-17 receptor A (IL-17RA) were increased in Pg-treated R1441G mice.

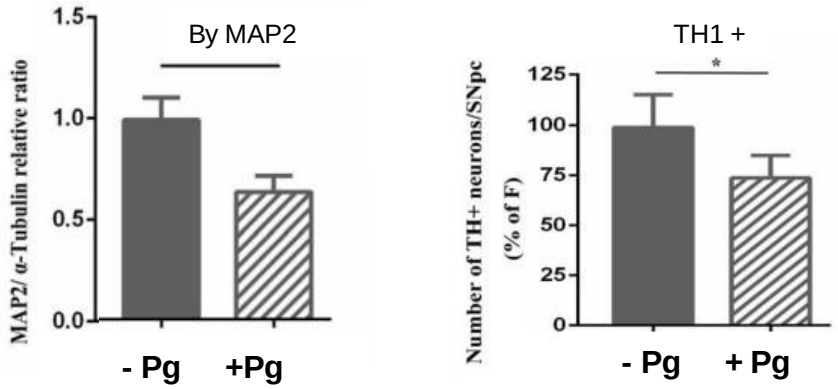
**Conclusions:** These findings suggest that oral Pg-induced inflammation may play an important role in the pathophysiology of LRRK2-associated PD.

**Keywords:** Chronic periodontitis, Parkinson's disease, Dopaminergic neurons, R1441G LRRK2, IL-17A

Increased Alpha synuclein in the colon (red)




Neurodegeneration in the substantia nigra




Similar effects of alpha syn. production, neurodegeneration in the SN, and inflammation seen after oral infection of in wild type mice, Renn et al. 2020

# Pg Inflammatory Marker RANTES (CCL5) Correlates to Severity of Parkinson's and is Reduced By COR388 Treatment

RANTES correlates with severity of Parkinson's disease

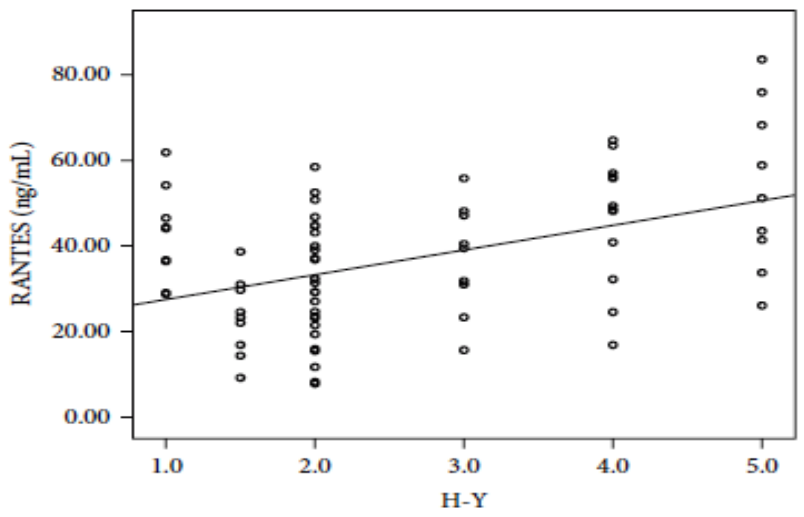
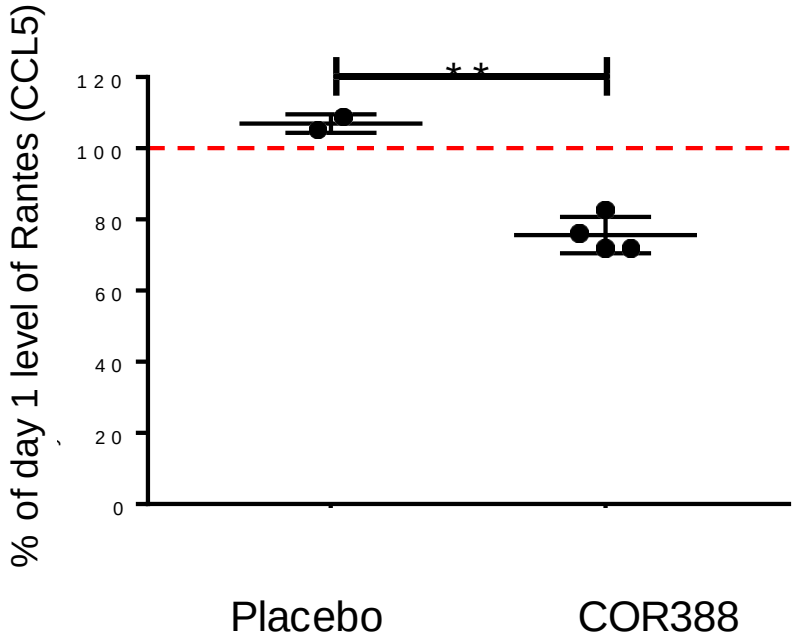



FIGURE 1: Significant positive correlation between RANTES and H-Y scale in PD patients ($n = 78$, $r = 0.362$, $P = 0.001$).

Tang et al. Correlation between Serum RANTES and Severity of Parkinson's disease

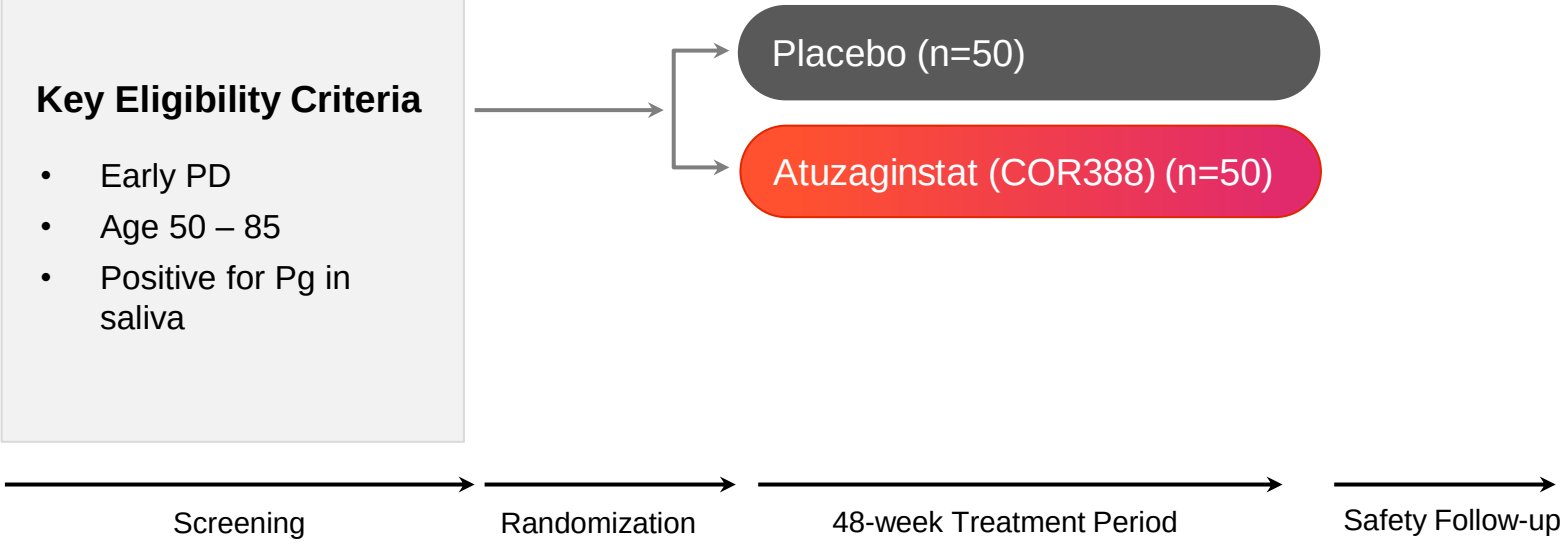



Atuzaginstat (COR388) 50 mg taken orally twice daily for for 28 days significantly reduced plasma levels of RANTES (CCL5) compared to placebo in AD patients. ***P < 0.001, **P < 0.01, *P < 0.05.

# Phase 2 PEAK Trial Design in Parkinson's Disease

**Key Eligibility Criteria**

- Early PD
- Age 50 – 85
- Positive for Pg in saliva




**Target Engagement Biomarkers**

- RANTES
- *P. gingivalis* DNA
- *P. gingivalis* IgG

**Endpoints**

- Digital motor endpoints
- MDS-UPDRS
- Non-Motor Symptoms scale (NMSS)
- Schwab and England ADLs
- GI Symptoms
- Standard Safety Outcomes (AEs, physical exams, ECGs, Vital Signs, Safety Labs, C-SSRS)

# Upcoming Milestones

| Timing | Indication | Milestone |
|---|---|---|
| **Atuzaginstat** | | |
| Q4 2020 ✓ | Alzheimer's disease | Enrollment Complete (GAIN Trial) |
| H1 2021 ✓ | Parkinson's disease | Study startup activities (PEAK Trial) |
| By mid- Nov 2021 | Alzheimer's disease | Top-line Data (GAIN Trial) |
| By mid -Nov 2021 | Periodontal disease | Top-line Data Phase 2 REPAIR sub-study (GAIN Trial) in Periodontal disease |
| Q1 2022 | Parkinson's disease | First patient in (PEAK Trial) |
| **COR588** | | |
| Q3 2020 ✓ | Periodontal and other diseases | Candidate Selection/Advancement to IND enabling studies |
| Q2 2021 ✓ | Periodontal and other diseases | IND Enabling Studies Complete |
| Q3 2021 ✓ | Periodontal and other diseases | Phase 1 initiation |
| Q2 2021 | Periodontal and other diseases | Phase 1 SAD/MAD complete |
| **COR788/COR882** | | |
| Q1 2021✓ | Potential in AD, Parkinson's, Perio, Cancer, and other indications | Selection of arginine gingipain inhibitor leads (COR787/788) |
| Q3-Q4 2021 | Potential in AD, Parkinson's, Perio, Cancer, and other indications | Candidate selection and initiation of IND enabling studies |
| **COR803/COR817** | | |
| Q3 2021✓ | Coronavirus | Lead Selection |

# Changing The Way We Think About Degenerative Diseases

- Top-line efficacy data in Alzheimer's disease pivotal GAIN Trial by mid-November 2021
- Top-line efficacy data in periodontal disease REPAIR sub-study by mid-November 2021
- COR588 phase 1 initiated in Q3 2021 for periodontal and other diseases
- New PEAK trial in Parkinson's disease study start up 2021, first patient is anticipated Q1 2022

- MOA upstream of neurodegeneration and other pathology
- Additional indications and compounds in pre-clinical development; expect advancement into the clinic in 2022
- Fully funded through 2023, Q2 2021 cash, equivalents and investments: $153.5 million

CORTEXYME

# THANK YOU