Alterity Therapeutics

(NASDAQ:ATHE, ASX:ATH)

David Stamler, MD / 医学博士
CEO / 首席执行官

June 2022 / 2022年6月

Forward Looking Statements / 前瞻性陈述

This presentation may contain some statements that may be considered “Forward-Looking Statements”, within the meaning of the US Securities Laws. Thus, any forward-looking statement relating to financial projections or other statements relating to the Company’s plans, objectives, expectations or intentions involve risks and uncertainties that may cause actual results to differ materially. For a discussion of such risks and uncertainties as they relate to us, please refer to our 2021 Form 20-F, filed with US Securities and Exchange Commission, in particular Item 3, Section D, titled “Risk Factors.’’

Alterity is dedicated to creating an alternate future for people living with neurodegenerative diseases. / **Alterity**致力于为神经退行性疾病患者创造一个不同的未来。

Alterity means **the state of being different / Alterity**的意思是不同的状态

Our goal is to **modify the course of disease /** 我们的目标是改变疾病的进程

We're here to **disrupt the trajectory** of illness and improve quality of life / 我们**打破疾病的轨迹**，改善生活质量

Investment Highlights / 投资亮点

- Addressing **the underlying pathology of disease /** 解决**疾病的基本病理问题**
- **Strong and highly experienced management team** with significant R&D experience including **3 drug approvals by US FDA / 强大、经验丰富的管理团队，**拥有丰富的研发经验，**包括美国FDA批准的3种药物**
- ATH434 is a **novel drug candidate targeting key proteins** implicated in neurodegeneration of Parkinson's Disease and related disorders / ATH434是**一种新型候选药物**，靶向与帕金森病和相关疾病的神经退行性变有关的关键蛋白
- First therapeutic target: Multiple System Atrophy (MSA), a **devastating disease with no approved treatments / 第一个治疗目标：多系统萎缩症（MSA），这是一种没有获批疗法的毁坏性疾病**
- Orphan Drug designation in the U.S. and EU / 获得美国和欧盟的孤儿药资格认定
- Randomized, double-blind, placebo-controlled **Phase 2 clinical trial** ongoing / 随机、双盲、安慰剂对照的**二期临床试验**正在进行中
- Strong patent portfolio / 强大的专利组合

Recent Progress / 近期进展

- Launch of Phase 2 Clinical Trial / 启动二期临床试验
- Presented supportive imaging data from bioMUSE Natural History study in early MSA / 报告了来自bioMUSE Natural History研究的早期多系统萎缩症（MSA）的支持性成像数据
- Presentation of advanced quantitative MRI as potential novel biomarker in early MSA / 先进的定量MRI作为早期多系统萎缩症（MSA）的潜在新型生物标志物的报告
- Two new US patents expand portfolio of next generation compounds for neurodegenerative diseases / 两项新的美国专利，扩大了治疗神经退行性疾病的下一代化合物组合
- Publication demonstrating neuroprotective effect of ATH434 in animal model of MSA /证明ATH434在多系统萎缩症（MSA）动物模型中的神经保护作用的出版物
- Michael J. Fox Foundation grant for ~US$500K for Parkinson's disease / Michael J. Fox基金会为帕金森病提供约50万美元的资助
- EMA endorses clinical strategy for Phase 2 study in early MSA patients / 欧洲药品管理局（EMA）认可了早期多系统萎缩症（MSA）患者的二期研究的临床策略
- US FDA provides development pathway for ATH434 in Multiple System Atrophy / 美国FDA为ATH434治疗多系统萎缩症提供开发途径

Experienced Leadership Team with Multiple FDA Approvals in Neurology / 经验丰富、在神经病学领域获得多项FDA批准的领导团队

Alterity THERAPEUTICS

David Stamler, M.D. / 医学博士

Chief Executive Officer / 首席执行官

Auspex/Teva | Abbott | Prestwick Xenoport | Fujisawa

- **3 FDA Approvals in Neurology / 在神经病学领域获得3项FDA批准**
- Former CMO, Auspex / 前Auspex的首席营销官
- VP, Clinical Development & Therapeutic Head, Movement Disorders, Teva Pharmaceuticals / 梯瓦制药副总裁、运动障碍领域的临床开发和治疗主管
- Part of Teva's US$3.5 billion acquisition of Auspex in 2015 / 梯瓦制药在2015年以35亿美元收购了Auspex
- Led development of AUSTEDO® (deutetrabenazine) for treatment of Huntington disease and Tardive dyskinesia, both approved in 2017 / 领导AUSTEDO®（deutetrabenazine）的开发，用于治疗亨廷顿病和迟发性运动障碍，均在2017年获批

Kathryn Andrews, CPA / 注册会计师

Chief Financial Officer / 首席财务官

Antisense Therapeutics | Rio Tinto | Consultant / 顾问

- Extensive experience advising private and public CFOs, mainly in the biotechnology sector / 在为私营和上市公司首席财务官提供咨询方面有丰富的经验，主要是在生物技术领域
- Prior CFO and Company Secretary of Antisense Therapeutics Limited / 曾任Antisense Therapeutics Limited的首席财务官和公司秘书
- 15+ years in finance and accounting roles at Rio Tinto Limited and BP Australia Limited / 在力拓和BP Australia Limited担任财务和会计职务15年以上

Margaret Bradbury, Ph.D. / 博士

VP, Nonclinical Development / 非临床开发副总裁

Auspex/Teva | Neurocrine | Merck

- Auspex - led strategic planning and program management in Huntington Disease chorea from IND through NDA filing / Auspex——领导亨廷顿舞蹈症的战略规划和项目管理，从IND到NDA申请
- Teva - led non-clinical development of several neuroscience programs / 梯瓦制药——领导多个神经科学项目的非临床开发

Cynthia Wong, M.P.H.

Senior Director, Clinical Operations / 临床运营部高级总监

Auspex/Teva | Nextwave | Astex | Intermune | Impax Labs

- Clinical Operations leadership at Auspex/Teva. / 在Auspex/梯瓦担任临床运营领导
- Led clinical trial activities for the registration study of AUSTEDO® in Huntington Disease chorea. / 领导AUSTEDO®在亨廷顿舞蹈症的注册研究中的临床试验活动
- Prior, led Phase 1-3 studies, including registration studies for marketing approval for Quillichew ER, Esbriet and Infergen. / 在此之前，领导1-3期研究，包括Quillichew ER、Esbriet和Infergen的注册研究，以获得上市许可。

Parkinsonian Disorders: A Significant Unmet Need / 帕金森病：显著未满足的需求

Parkinsonism is a syndrome of motor symptoms that includes slowed movement, stiffness and tremor / 帕金森病是一种运动症状综合征，包括运动迟缓、僵硬和震颤

- A major source of disability / 残疾的一个主要原因

Parkinsonian disorders also include atypical forms such as Multiple system atrophy (MSA) and Progressive supranuclear palsy (PSP) / 帕金森病还包括非典型形式，比如多系统萎缩（MSA）和进行性核上性麻痹(PSP)

- “Atypical” as have prominent non-motor symptoms and a limited response to available treatments / "非典型"具有突出的非运动症状，对现有疗法的反应有限

Current therapies treat the symptoms and NOT the underlying pathology of disease / 目前的疗法只治疗症状，而不是疾病的基本病理

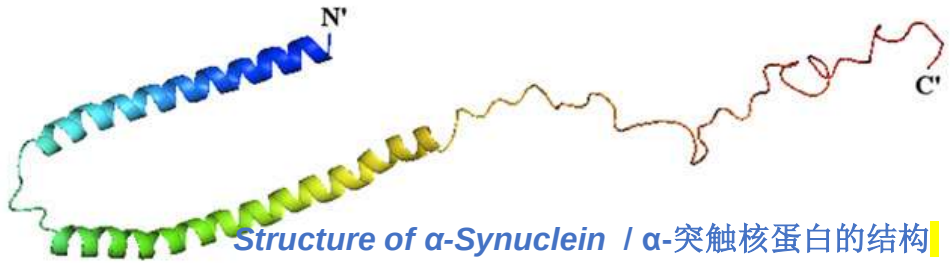
PARKINSONIAN DISORDERS / 帕金森病

Discovery and Development Portfolio in Neurodegenerative Diseases / 神经退行性疾病的发现和开发组合

Program / 项目	Indication / 适应症	Current Status / 现状	Future Plans / 未来计划
ATH434	Multiple System Atrophy / 多系统萎缩症	Phase 2 Ongoing / 正在进行第二期	Expand enrollment globally / 在全球范围内扩大招募
bioMUSE Natural History Study / bioMUSE Natural History研究	Multiple System Atrophy / 多系统萎缩症	Ongoing / 进行中 Partner: / 合作伙伴：VANDERBILT UNIVERSITY MEDICAL CENTER	Enrolling up to 20 patients / 正在招募20名患者
ATH434	Parkinson's Disease / 帕金森病	Preclinical studies to optimize dosing / 临床前研究以优化剂量 Partner: / 合作伙伴：THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH	Proof of concept study in Parkinson's disease / 帕金森病的概念验证研究
Drug Discovery / 药物发现	Neurodegenerative diseases / 神经退行性疾病	Discovery ongoing / 正在发现	Generate new IND candidates / 产生新的IND候选药物

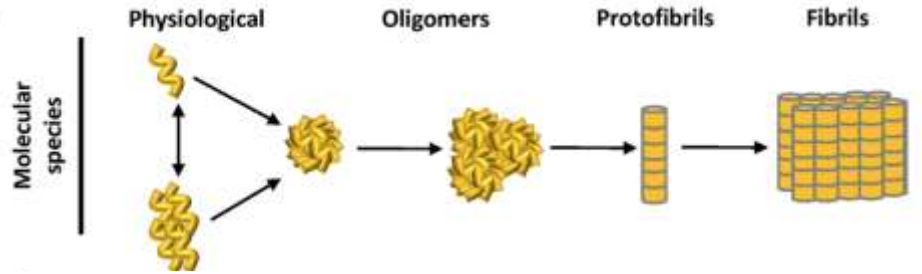
Alterity's Approach to Treating Parkinsonian Disorders / Alterity治疗帕金森病的方法

Alpha-Synuclein: A Major Focus for Treating Parkinsonian Disorders / α-突触核蛋白：治疗帕金森病的一个主要焦点



Structure of α-Synuclein / α-突触核蛋白的结构

Health / 健康 **Disease / 疾病**



- α-Synuclein is an intracellular protein critical for normal function of neurons / α-突触核蛋白是一种对神经元的正常功能至关重要的细胞内蛋白质
- Native, unfolded protein enables neurotransmission / 原生的、未折叠的蛋白质能实现神经传导
- α-Synuclein *aggregates* in Parkinson's Disease and Multiple System Atrophy / 帕金森病和多系统萎缩症中的α-突触核蛋白聚集

Our Strategy / 我们的策略

- Inhibit oligomerization and aggregation of intracellular α-Synuclein / 抑制细胞内α-突触核蛋白的寡聚和聚集
- Target misfolding α-synuclein by redistributing excess iron in areas of pathology / 通过在病理区重新分配过量的铁来靶向错误折叠的α-突触核蛋白
- Address underlying pathology of disease / 解决疾病的基本病理学问题

Sources: Ritchie et al, 2012; DOI:10.4236/health.2012.431175; Bengoa-Vergniory et al, 2017.DOI 10.1007/s00401-017-1755-1 / 来源：Ritchie et al, 2012; DOI:10.4236/health.2012.431175; Bengoa-Vergniory et al, 2017.DOI 10.1007/s00401-017-1755-1

Iron is Critical in the Pathogenesis of Parkinsonian Disorders / 铁在帕金森病症的发病机制中至关重要

α-Synuclein and iron are strong contributors to the pathogenesis of MSA / α-突触核蛋白和铁是MSA(多系统萎缩症)发病机制的重要因素

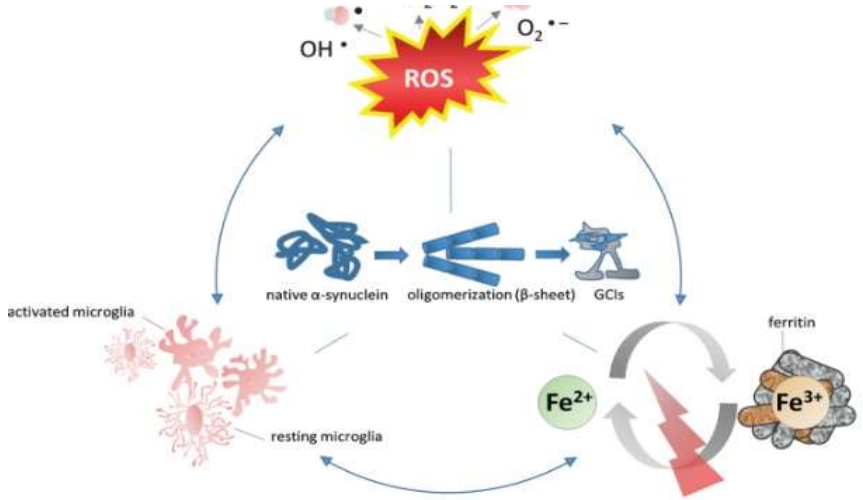
Prominent pathology in Oligodendroglial cells (ODG) / 少突胶质细胞（ODG）的突出病理学特征

- ODGs are vital support cells for neurons / ODG是神经元的重要支持细胞
- Cells with highest iron content in the CNS / 中枢神经系统中铁含量最高的细胞
- Demonstrate prominent α-synuclein pathology / 显示出突出的α-突触核蛋白病理学特征
- Hallmark of MSA: accumulation of α-synuclein within ODGs and neuron loss in multiple brain regions / MSA(多系统萎缩症)的标志：α-突触核蛋白在少突胶质细胞（ODG）内的积累和多个脑区的神经元损失

Adverse impact of increased labile iron / 不稳定的铁含量增加会产生不利影响

- Promotes α-synuclein aggregation / 促进了α-突触核蛋白的聚集
- Root cause of oxidative stress which damages intracellular structures and leads to neuroinflammation / 氧化应激的根源，损害细胞内结构并导致神经炎症

Oxidative Stress / 氧化应激



Neuroinflammation / 神经炎症

Iron Dyshomeostasis / 铁失衡

Sources: / 来源：Kaindlstorfer, J. Alzheimers Dis. 2018; Rodgers, J Neural Transm (Vienna). 2011

Our Approach: Dual Mode of Action to Address the Underlying Pathology of Disease / 我们的方法：解决疾病基本病理的双重行动模式

Alterity THERAPEUTICS

Bind and redistribute **excess iron** in the CNS of patients with Parkinsonian disorders / 结合并重新分配帕金森病患者中枢神经系统中的**多余的铁**

→

Reduce **α-synuclein aggregation** and oxidative stress / 减少**α-突触核蛋白的聚集**和氧化应激

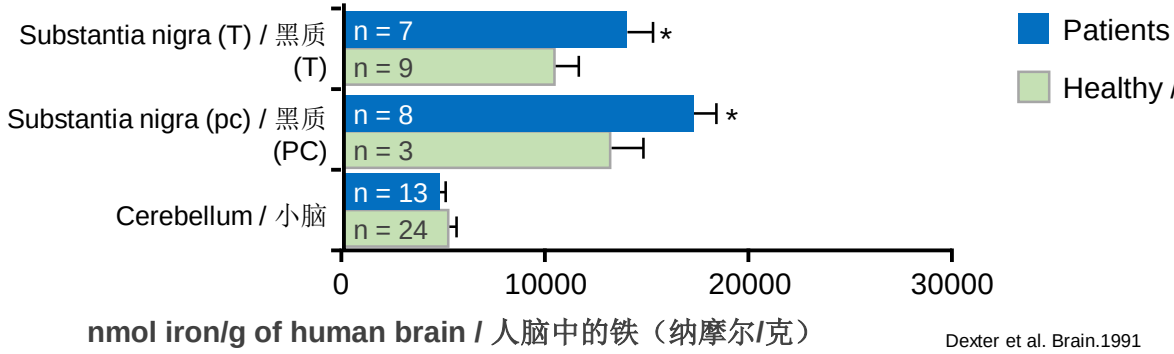
→

Rescue neurons in multiple brain regions to address underlying pathology / **拯救多个脑区的神经元**，解决根本病理问题

Targeting protein misfolding aggregation by binding and redistributing iron / 通过结合和重新分配铁来靶向蛋白质的错误折叠聚集

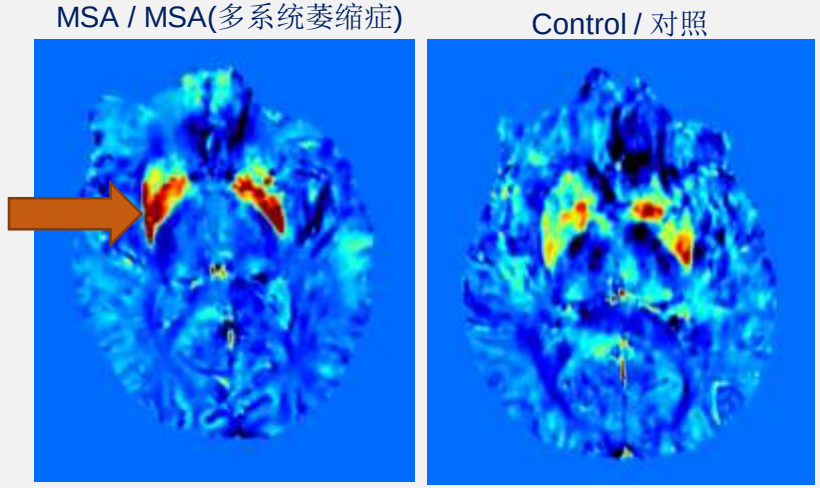
Increased Brain Iron in Synuclein-related Diseases / 突触核蛋白相关疾病中的脑铁增加

Parkinson's disease / 帕金森病



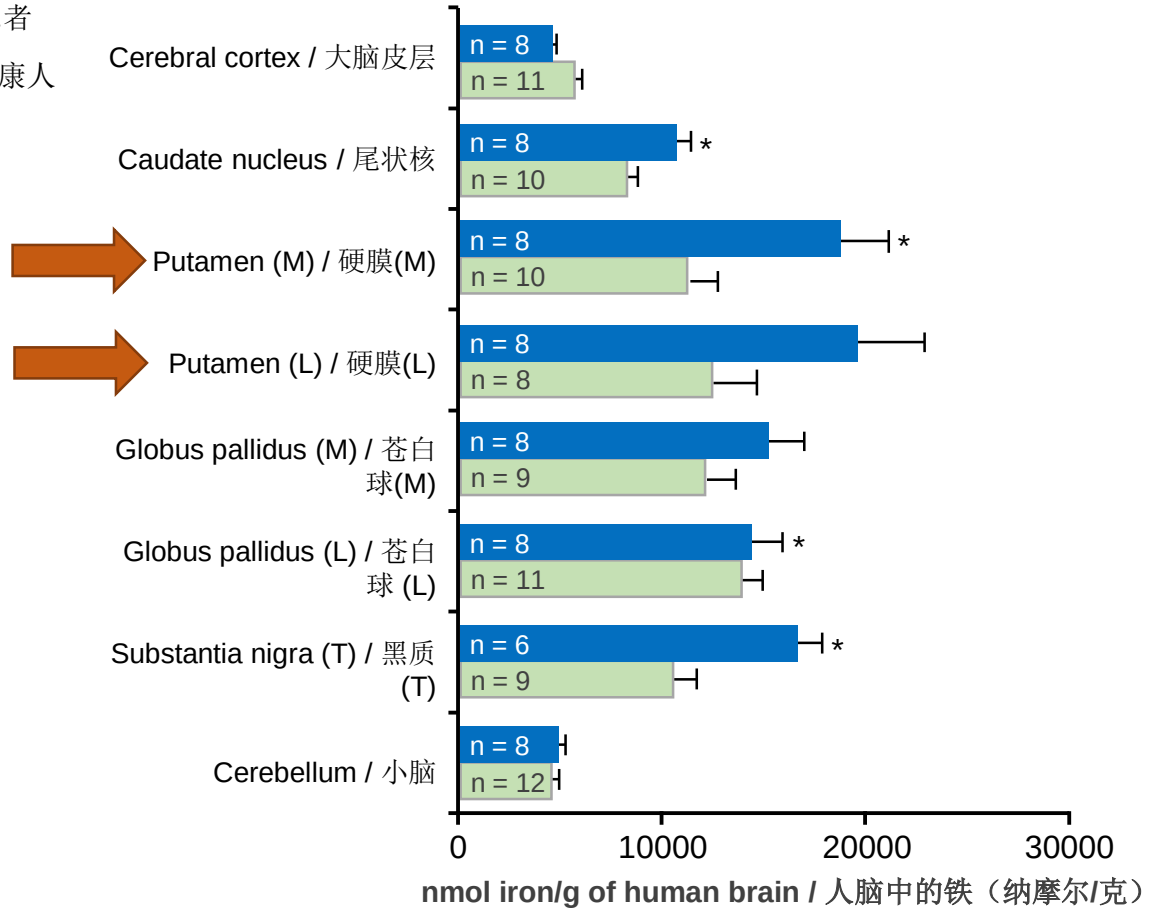
Dexter et al. Brain.1991

Advanced Quantitative MRI to measure brain iron / 用先进的定量MRI来测量脑铁



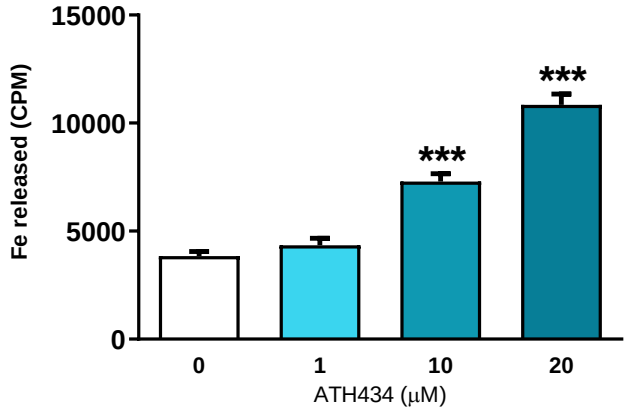
Courtesy of P. Trujillo, D. Claassen

Multiple System Atrophy / 多系统萎缩症



Pharmacologic Actions of ATH434 / ATH434的药理作用

ATH434 redistributes excess iron / ATH434重新分配多余的铁

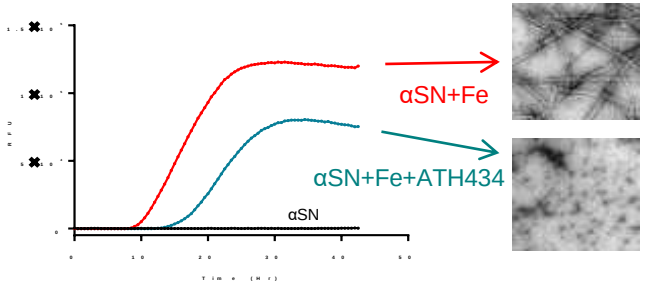


Ligand / 配体	Kd for Fe^{3+}
α-Synuclein / α-突触核蛋白	10^{-5}
ATH434	10^{-10}
Ferritin / 铁蛋白	10^{-22}
Transferrin / 转铁蛋白	10^{-23}

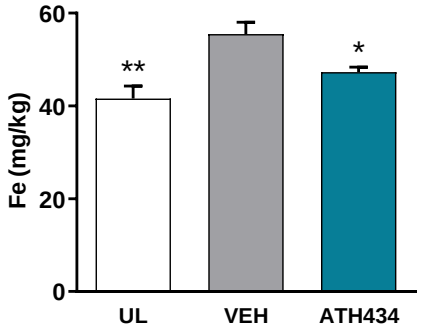
Stronger binding / 结合力更强

Iron trafficking proteins > **ATH434** > α-synuclein / 铁转运蛋白 > ATH434 >α-突触核蛋白

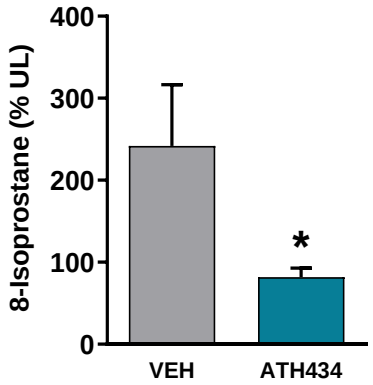
Reduces α-synuclein aggregation / 减少α-突触核蛋白的聚集



Blocks increase in brain iron / 阻断脑铁的增加



Inhibits oxidative stress in vivo / 抑制体内的氧化应激



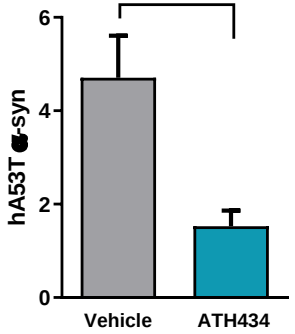
Finkelstein, et al. Acta Neuropath Comm. 2017; Friedlich, et al. Mol Psychiatry. 2007; * P < 0.05, ** P < 0.01, *** P < 0.001

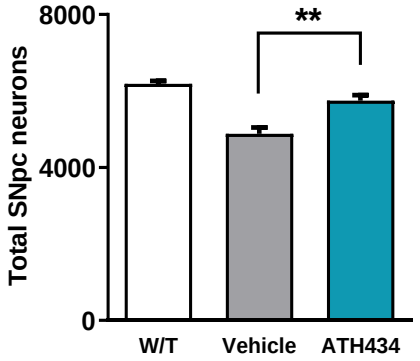
ATH434 Reduces Alpha-Synuclein-related Neuropathology in Parkinson's Disease Animal Models / ATH434可减少帕金森病动物模型中与α-突触核蛋白有关的神经病理现象

↓ α-Synuclein / α-突触核蛋白

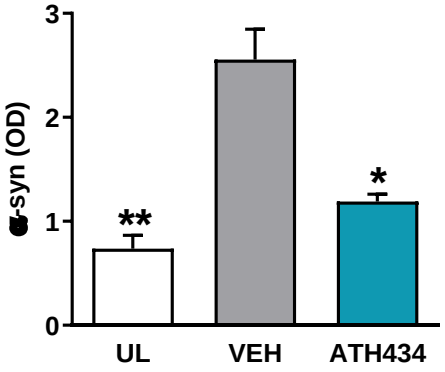
Preserves Neurons / 保留神经元

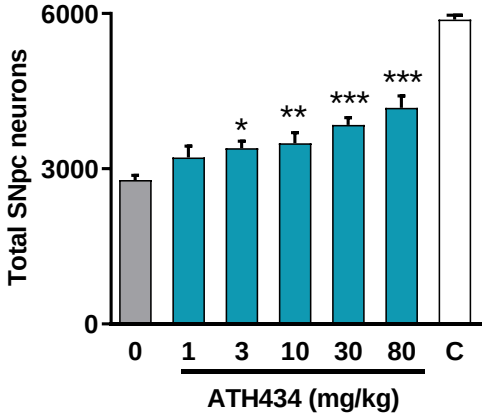
***h*A53T Mouse / 小鼠**





MPTP Mouse / 小鼠





Finkelstein, et al. Acta Neuropath Comm. 2017
TG: transgenic, W/T: wild type, UL: unlesioned, C: control
TG：转基因，W/T：野生型，UL：无损伤，C：对照

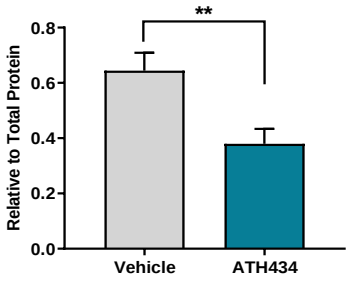
* P < 0.05, ** P < 0.01, *** P < 0.001

ATH434 Reduces α-Synuclein-related Neuropathology and Improves Motor Function in Animal Model of MSA / ATH434可在MSA(多系统萎缩症)动物模型减少α-突触核蛋白相关的神经病理并改善运动功能

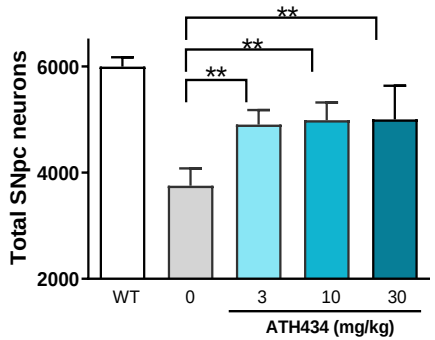
Alterity THERAPEUTICS

Exp. #1 / 实验#1

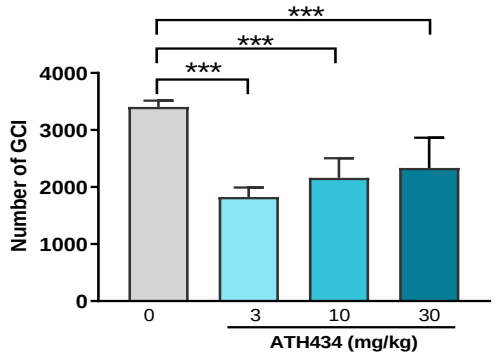
α-Synuclein /α-突触核蛋白



SN neurons / 黑质神经元

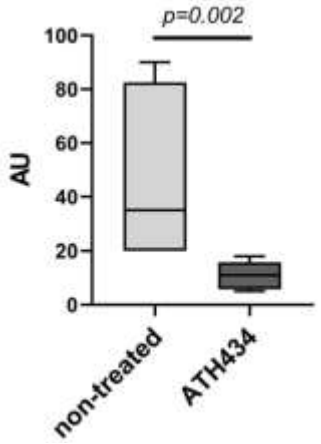


Glial inclusions / 胶质内含物

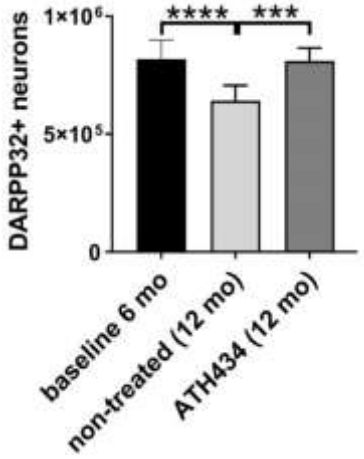


Exp. #2 / 实验 #2

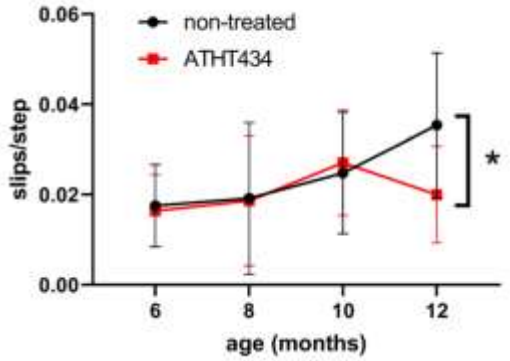
Iron in SN / 黑质中的铁



Striatal neurons / 纹状体神经元



Motor Function / 运动功能

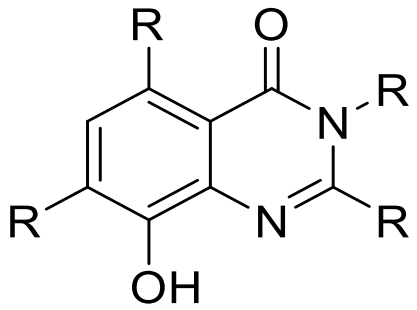


Finkelstein, et al. J. Parkinsons Disease 2022
Heras-Garvin, et al. Mov. Disorders 2021

* P < 0.05, ** P < 0.01, *** P < 0.001

ATH434: Clinical Development Program / 临床开发项目

ATH434: Potential Use Across Multiple Indications / 在多个适应症中的潜在用途



ATH434

- **Small molecule** designed to cross the blood brain barrier and inhibit α-synuclein aggregation / 旨在穿越血脑屏障和抑制α-突触核蛋白聚集的小分子
- Potential to treat various Parkinsonian disorders / 具有治疗各种帕金森病的潜力
- **Orphan Drug Designation granted** by FDA and EU for the treatment of Multiple System Atrophy / 美国FDA和欧盟授予治疗多系统萎缩症孤儿药资质
  - First indication: Treatment of MSA / 第一个适应症：治疗MSA(多系统萎缩症)
- Development pathway endorsed by FDA and EMA / FDA和欧洲药品管理局（EMA）认可的开发途径
- **Oral agent for ease of use / 口服制剂，便于使用**

Multiple System Atrophy (MSA) is a Rare, Neurodegenerative Disorder / 多系统萎缩症（MSA）是一种罕见的神经退行性疾病

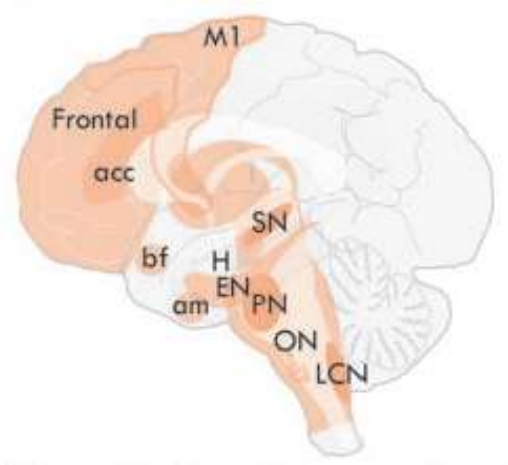
Characterized by Parkinsonism, autonomic instability and/or cerebellar impairments / 以帕金森症、自主神经不稳定和/或小脑损伤为特征

Affects the body's involuntary (autonomic) functions, including blood pressure, bladder control and bowel function / 影响身体的不自主（自律神经）功能，包括血压、膀胱控制和肠道功能

Current treatments only address symptoms of MSA / 目前的疗法只能解决MSA(多系统萎缩症)的症状

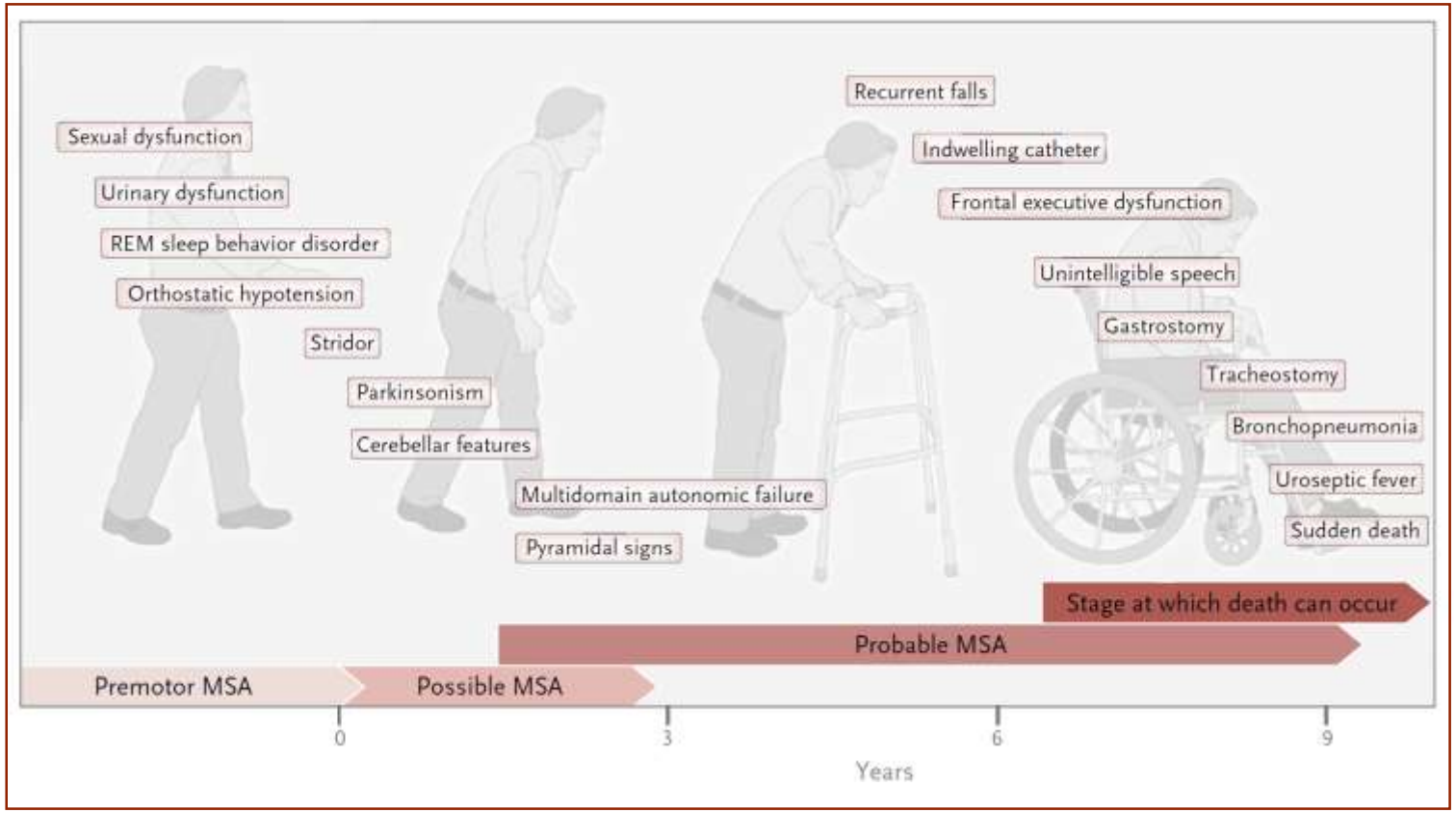
Development strategy / 发展战略

- Target early stage MSA patients / 针对早期MSA(多系统萎缩症)患者
- Explore the effect of ATH434 treatment on biomarkers and preliminary effects on clinical measures / 探索ATH434治疗对生物标志物的影响和对临床措施的初步效果



Halliday *Brain* 2015, based on Cykowski, *Brain 2015*

MSA is Highly Debilitating and Rapidly Progressive / MSA(多系统萎缩症)是高度衰弱和快速进展的疾病



60% require wheelchair confinement within 5 years / 60%的人会在5年内需要用上轮椅

Fanciulli, Wenning. NEJM 2015;372:249-63.

Excellent Progress with Lead Drug Candidate ATH434 / 领先的候选药物ATH434取得卓越进展

Robust efficacy in animal models of disease / 在患病的动物模型中具有强大的疗效

- Evidence of neuroprotection in PD and MSA animal models / 有证据表明，在帕金森病（PD）和MSA(多系统萎缩症)动物模型中具有神经保护作用
- Findings corroborated in multiple labs / 多个实验室的研究结果得到证实

Completed Phase 1 / 已完成第一期

- Orally bioavailable, brain penetrant / 口服生物制剂，大脑渗透性强
- Well tolerated / 耐受性良好
- Achieved brain levels comparable to efficacious levels in animal models of MSA / 实现了与MSA(多系统萎缩症)动物模型有效水平相当的大脑水平

Phase 2 Execution / 第二期执行

- bioMUSE Natural history study ongoing / bioMUSE Natural History研究正在进行中
- Long term toxicology completed / 长期的毒理学研究已经完成
- Drug product (tablet) manufactured and packaged / 药物产品（片剂）的生产和包装
- FDA and European regulatory advice / 美国FDA和欧洲监管部门的建议

Phase 1 Clinical Trial Design / 第一期临床试验设计

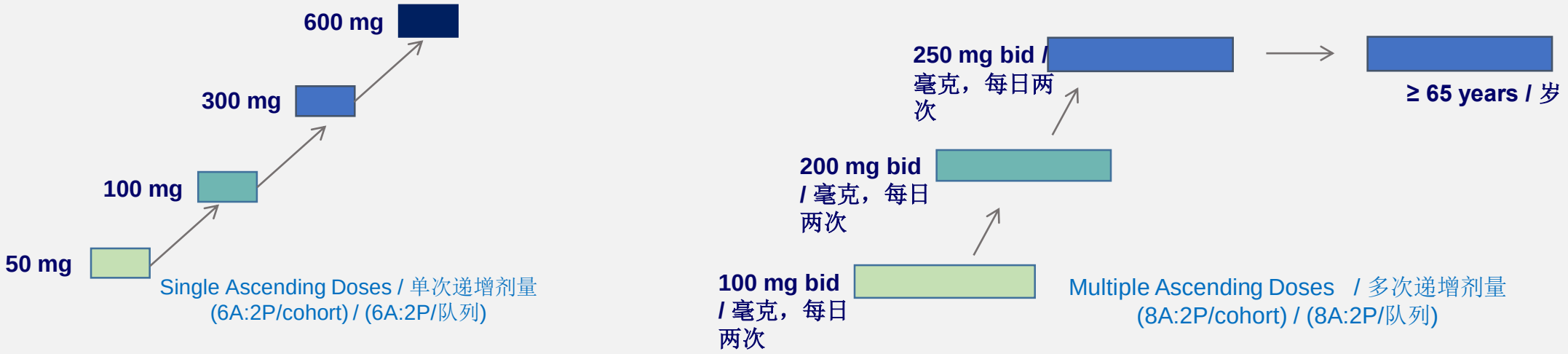
Design: Randomized, double blind, placebo-controlled, healthy adult and older adults (≥65 yo) / 设计：随机、双盲、安慰剂对照、健康成人和老年人（≥65）

Objectives: Assess safety and pharmacokinetics of ATH434 after single and multiple oral doses / 目标：评估单次和多次口服ATH434的安全性和药代动力学

Plasma PK in each cohort, CSF sampled in two top multiple dose levels / 在每个队列中进行血浆PK，在两个顶级多剂量水平中进行脑脊液采样

Safety: Adverse events, clinical labs, vital signs including orthostatics / 安全性：不良事件、临床实验室、生命体征（包括正位）

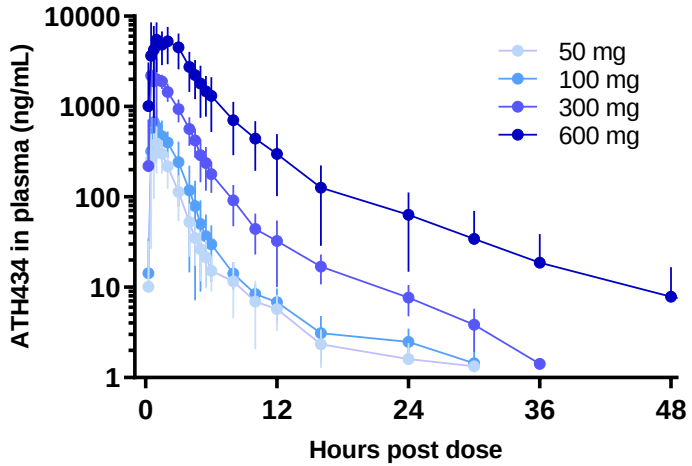
Continuous 12-lead digital ECGs for QT assessment / 用于QT评估的连续12导联数字心电图



Phase 1 Achieved Target Drug Concentrations Associated with Efficacy in Animal Models / 第一期实现的目标药物浓度与动物模型的疗效有关

Alterity THERAPEUTICS

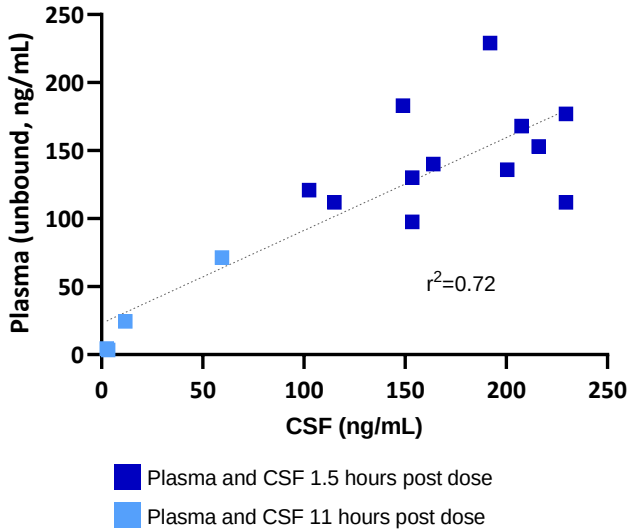
Plasma Profile after Single Dose Administration / 单剂量给药后的血浆概况



- Rapid absorption after oral administration / 口服后快速吸收
- Dose dependent pharmacokinetics / 剂量依赖药代动力学
  - Single doses up to 600 mg / 单次剂量达600毫克
  - Multiple doses up to 250 mg bid / 多剂量达 250毫克，每日两次
- Mean elimination half-life up to 9.3 hrs / 平均消除半衰期长达9.3小时

Source: / 来源： Stamler et al. Neurology 2019; 92 (15 Suppl.)

Plasma and CSF Levels at Steady-State / 稳定状态下的血浆和脑脊液水平



- CSF and free plasma levels strongly correlated and within 2-fold of each other / 脑脊液和游离血浆水平密切相关，并在2倍以内
- CSF concentrations at steady state exceed those associated with efficacy in animal models of PD and MSA / 稳定状态下的脑脊液浓度超过与帕金森病（PD）和MSA(多系统萎缩症)动物模型的疗效相关的浓度

ATH434 Well-Tolerated
No Serious Adverse Events / ATH434耐受性良好，无严重不良事件

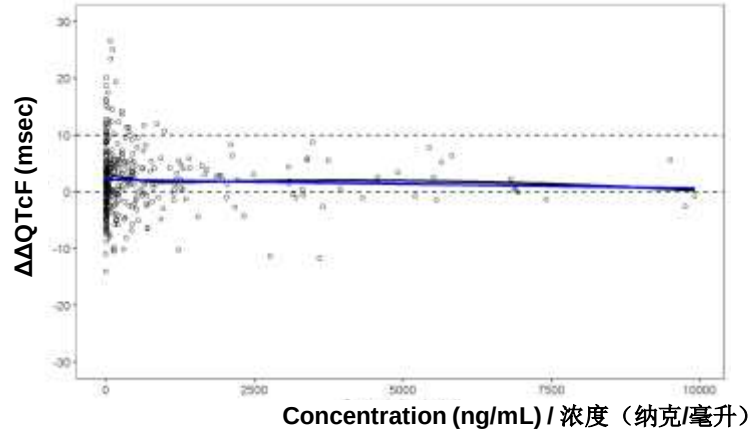
Single Doses / 单剂量	Placebo / 安慰剂 (N=8)	50 mg (N=6)	100 mg (N=6)	300 mg (N=6)	600 mg (N=6)
Patients with ≥ 1 AE / 有≥1个不良事件的患者	3 (38%)	0	0	1 (17%)	1 (17%)
Patients with AEs leading to Withdrawal / 出现不良事件导致停药的患者	0	0	0	0	0
Patients with Serious AEs / 有严重不良事件的患者	0	0	0	0	0
Multiple Doses / 多剂量	**Placebo / 安慰剂 (N=8)**	**100 mg BID / 毫克，每日两次 (N=8)**	**200 mg BID / 毫克，每日两次 (N=8)**	**250 mg BID / 毫克，每日两次 (N=8)**	**250 mg BID / 毫克，每日两次 ≥65 (N=8)**
Patients with ≥ 1 AE / 有≥1个不良事件的患者	5 (63%)	3 (38%)	6 (75%)	4 (50%)	5 (63%)
Patients with AEs leading to Withdrawal / 出现不良事件导致停药的患者	0	0	0	0	0
Patients with Serious AEs / 有严重不良事件的患者	0	0	0	0	0

Source: Phase 1 clinical trial; Alterity data on file /来源：一期临床试验；Alterity数据存档

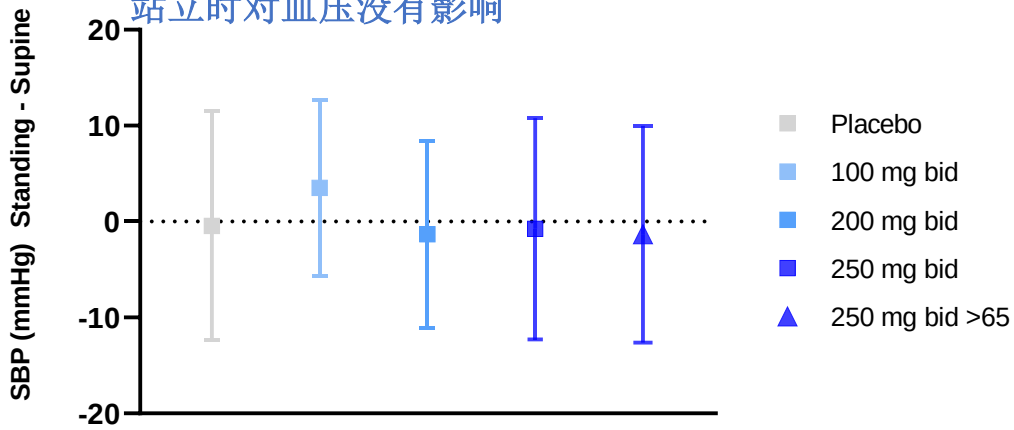
Favorable Safety Profile / 良好的安全状况

- All AEs were mild to moderate in severity / 所有不良事件的严重性都是从轻度到中度
- Most common AE reported in ATH434 subjects was headache / ATH434受试者中最常见的不良事件是头痛
- Similar AE profile for adults and older adults (≥ 65 years) / 成人和老年人（≥65岁）的不良事件情况相似
- No significant findings observed in vital signs, clinical labs or 12-lead ECGs / 在生命体征、临床实验室或12导联心电图中没有观察到重大发现
- Favorable cardiovascular safety profile / 良好的心血管安全状况

No evidence of QT prolongation / 没有证据表明QT间期延长



No effect on BP with Standing / 站立时对血压没有影响



Source: Phase 1 clinical trial; Alterity data on file / 来源：一期临床试验；Alterity数据存档

ATH434 Phase 2 Clinical Trial in Early-Stage MSA Patients / ATH434在早期MSA(多系统萎缩症)患者中的二期临床试验

Design / 设计	• Randomized, double-blind, placebo controlled / 随机、双盲、安慰剂对照
Objectives / 目的	• Assess efficacy and safety of ATH434 in subjects with MSA / 评估ATH434对MSA(多系统萎缩症)受试者的疗效和安全性 • Assess target engagement based on imaging and fluid biomarkers of disease severity / 根据疾病严重程度的成像和液体生物标志物评估目标参与情况
Population / 研究对象	• Early-stage patients with clinical diagnosis of MSA who are ambulatory, not severely impaired, and do not have long standing motor symptoms / 临床诊断为MSA(多系统萎缩症)的早期患者，可自由活动、无严重障碍、无长期运动症状
Sample Size / 样本规模	• N=60 at ~30 sites in Australia, New Zealand, Europe and the U.S. / 在澳大利亚、新西兰、欧洲和美国的约30个地点，N=60
Treatment / 治疗	• 12 months / 12个月 • Three arms: Two dose levels of ATH434 or placebo / 三组：两个剂量水平的ATH434或安慰剂
Primary Endpoint / 主要终点	• Change in iron content as measured by brain MRI / 通过脑部MRI测量铁含量的变化
Secondary Endpoints / 次要终点	• Clinical: Activities of daily living inventory (UMSARS I), motor exam, autonomic function / 临床：日常生活活动量表（统一MSA评定量表 I）、运动检查、自主神经功能 • Additional imaging biomarkers and fluid biomarkers (aggregating α-synuclein, NfL protein) / 其他的成像生物标志物和液体生物标志物（聚集的α-突触核蛋白，NfL蛋白）

BioMUSE: Biomarkers of Progression in MSA Natural History Study / BioMUSE：MSA(多系统萎缩症)进展的生物标志物

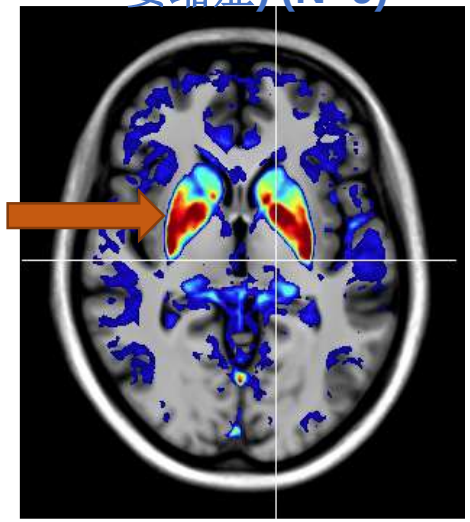
Design / 设计	• Observational / 观察
Objectives / 目的	• Inform and de-risk Phase 2 / 为第二期试验提供信息并降低风险 • Identify biomarker endpoint(s) for treatment study / 确定治疗研究的生物标志物终点 • Evaluate the change in biomarkers and clinical manifestations in early MSA / 评估早期MSA(多系统萎缩症)的生物标志物和临床表现的变化
Population / 研究对象	• Early-stage MSA patients similar to Phase 2 population /类似于2期人群的早期MSA(多系统萎缩症)患者 • Expanding to n=20 subjects / 扩大到n=20名受试者
Observation period / 观察期	• 12 months / 12个月
Biomarkers / 生物标志物	• MRI: Iron (QSM/R2*), regional blood flow (ASL), neuromelanin / MRI：铁（QSM/R2*）、局部血流（ASL）、神经黑色素 • Fluid: NfL protein (CSF, plasma), Aggregating α-synuclein (CSF), phos-α-synuclein (skin) / 液体：NfL蛋白（脑脊液，血浆）、聚集α-突触核蛋白（脑脊液）、phos-α-突触核蛋白（皮肤） • Wearable movement sensors / 可穿戴的运动传感器
Clinical Endpoints / 临床终点	• Clinical: Motor exam, autonomic function, activities of daily living inventory, global measures of severity and change (clinician, patient) / 临床：运动检查、自主神经功能、日常生活活动量表、严重程度和变化的整体测量（临床医生、患者） • Functional: Timed Up and Go, 2 min Walk Test / 功能性：行走计时，2分钟步行测试

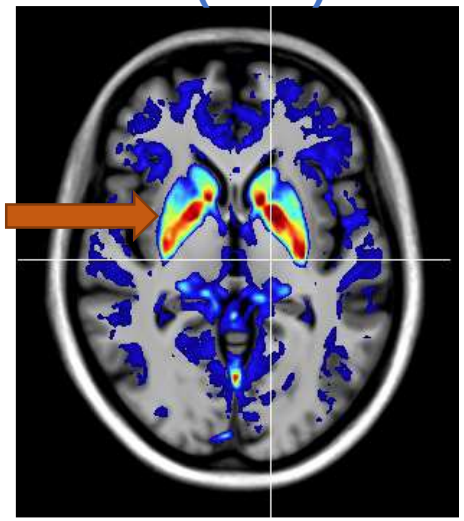
bioMUSE Interim Results: Increased Brain Iron in MSA and PD / bioMUSE中期结果：MSA(多系统萎缩症)和帕金森病（PD）的脑铁含量增加

MSA (N=9) / MSA(多系统萎缩症) (N=9)

PD (N=17) / 帕金森病（PD） (N=17)

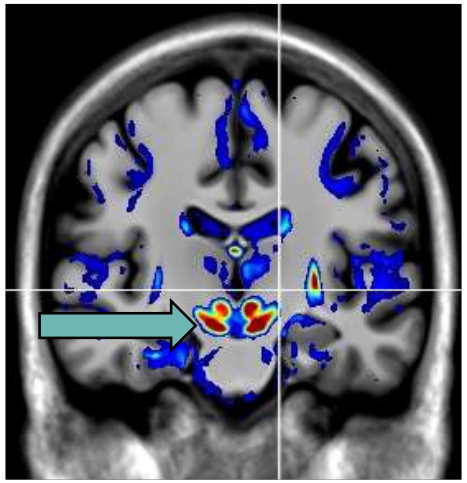
Basal ganglia / 基底神经节

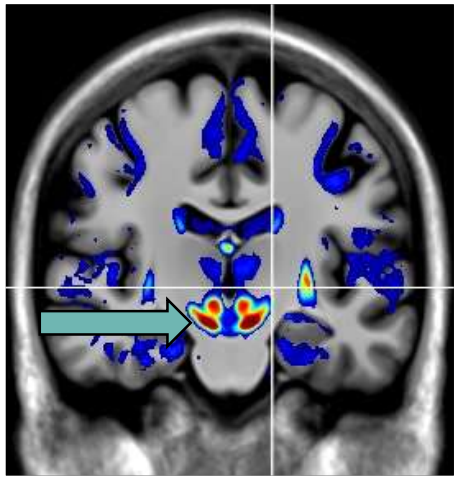




MSA patients have higher iron in basal ganglia / MSA(多系统萎缩症)患者基底神经节中的铁含量更高

S. nigra / 黑质





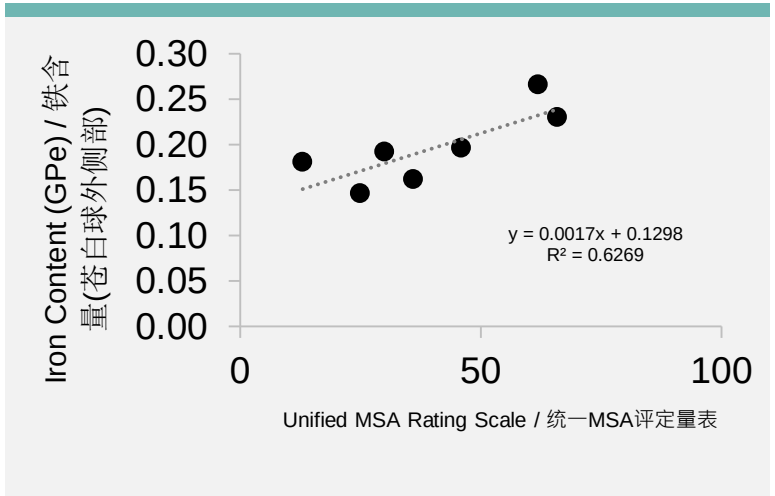
MSA and PD patients have increased iron in s. nigra / 多发性硬化症和帕金森病患者的黑质铁含量增加

Iron Content by Region of Interest /按感兴趣区划分的铁含量	
ROI /感兴趣区	MSA vs PD† / MSA(多系统萎缩症) vs 帕金森病（PD）†
PT	0.03*
Gpe/ 苍白球外侧部	0.04*
Gpi /苍白球内侧部	0.18
SN / 黑质	0.94

† P-value / P值

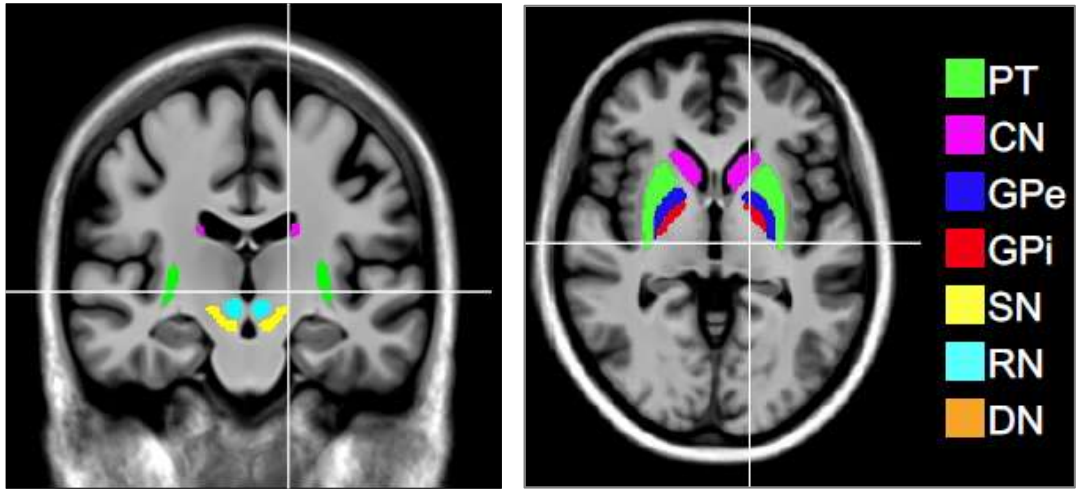
Source: / 来源：Claassen,et al; MDS 2021

Phase 2 Primary Endpoint: Change in Brain Iron by MRI / 第二期主要终点：核磁共振成像显示的脑铁变化



Brain iron correlates with disease severity in MSA / 脑铁与MSA(多系统萎缩症)的疾病严重程度相关

BioMUSE images registered with PD25 MNI template / 用帕金森病（PD）25 MNI模板注册的BioMUSE图像



Goal: Develop New MSA template from bioMUSE to improve precision of iron quantification in Phase 2 / 目标：从bioMUSE中开发新的MSA(多系统萎缩症)模板，以提高第二期铁定量的精度

Source: / 来源： Claassen,et al; MDS 2021

Significant Commercial Opportunity in Treating Multiple System Atrophy / 治疗多系统萎缩症的重要商业机会

Substantial Unmet Need / 大量满足的需求

Severely debilitating illnesses with no current treatments are ripe for new entrants targeting what may be the actual cause of the disease. / 目前没有疗法的严重衰弱性疾病，对于可能靶向疾病实际原因的新进入者来说，时机已经成熟。

Unique MOA / 独特的MOA

Inhibition of protein aggregation is a novel mechanism of action that may prove to impact more than motor symptoms. / 抑制蛋白质聚集是一种新的作用机制，可能被证明对运动症状有更大的影响。

Strong Intent to Prescribe / 强烈的处方意向

Motivated by efficacy of treating the underlying disease and not just the symptoms, clinicians intend to offer ATH434 to most of their patients with MSA. / 在治疗根本疾病而不仅仅是症状的功效的激励下，临床医生打算为大多数MSA(多系统萎缩症)患者提供ATH434。

Ease of Use / 易于使用

Twice daily oral administration of ATH434 preferred by physicians / ATH434每天口服两次，是医生们的首选

Source: Survey of U.S. neurologists / 来源：对美国神经病学家的调查

Alterity: Poised for Progress / Alterity：有望取得进展

Alterity THERAPEUTICS

- ✓ Targeting Orphan disease with no approved treatments / 针对没有获批疗法的孤儿病
- ✓ Development team with proven track record and multiple FDA approvals / 开发团队拥有成熟的业绩记录和获得多项FDA认证
- ✓ Lead drug candidate ATH434 Progressing to Phase 2 / 主要候选药物ATH434正在进入第二期
  - Completed Phase 1 demonstrating well-tolerated safety profile and delivery of drug to site of action / 已完成第一期，显示出良好的耐受性安全状况和将药物输送到作用部位
  - Recent publications validating mechanism of action targeting α-synuclein / 最近发表的文章验证了针对α-突触核蛋白的作用机制
- ✓ Drug discovery team generating patentable compounds as next generation therapies / 药物研发团队研发了可作为下一代疗法的专利化合物
- ✓ Strong balance sheet with 32.6M AUD as of 31 March 2022 / 截至2022年3月31日，资产负债表强劲，有3260万澳元资金

Milestones / 里程碑

- ✓ Q1 2022: Submit ATH434 European Clinical Trial Application (CTA) / 2022年第一季度：提交ATH434欧洲临床试验申请（CTA）
- ✓ Q2 2022: Launch ATH434 Phase 2 Clinical Trial in New Zealand / 2022年第二季度：在新西兰启动ATH434的第二期临床试验
- Q3 2022: Present bioMUSE Natural History biomarker data / 2022年第三季度：提交bioMUSE Natural History生物标志物数据
- 2H 2022: Launch ATH434 Phase 2 in Europe / 2022年下半年：在欧洲启动ATH434二期临床试验
- 2H 2022: Submit ATH434 U.S. IND / 2022年下半年：提交ATH434的美国IND
- 2H 2022: Launch ATH434 Phase 2 in U.S. / 2022年下半年：在美国启动ATH434的二期试验


Alterity
THERAPEUTICS