Results of a Phase 1, randomized, placebo-controlled, double-blind study to evaluate the safety, tolerability, and pharmacokinetics of ascending single IV doses of VY7523, a tau-targeting therapeutic, in healthy adult participants

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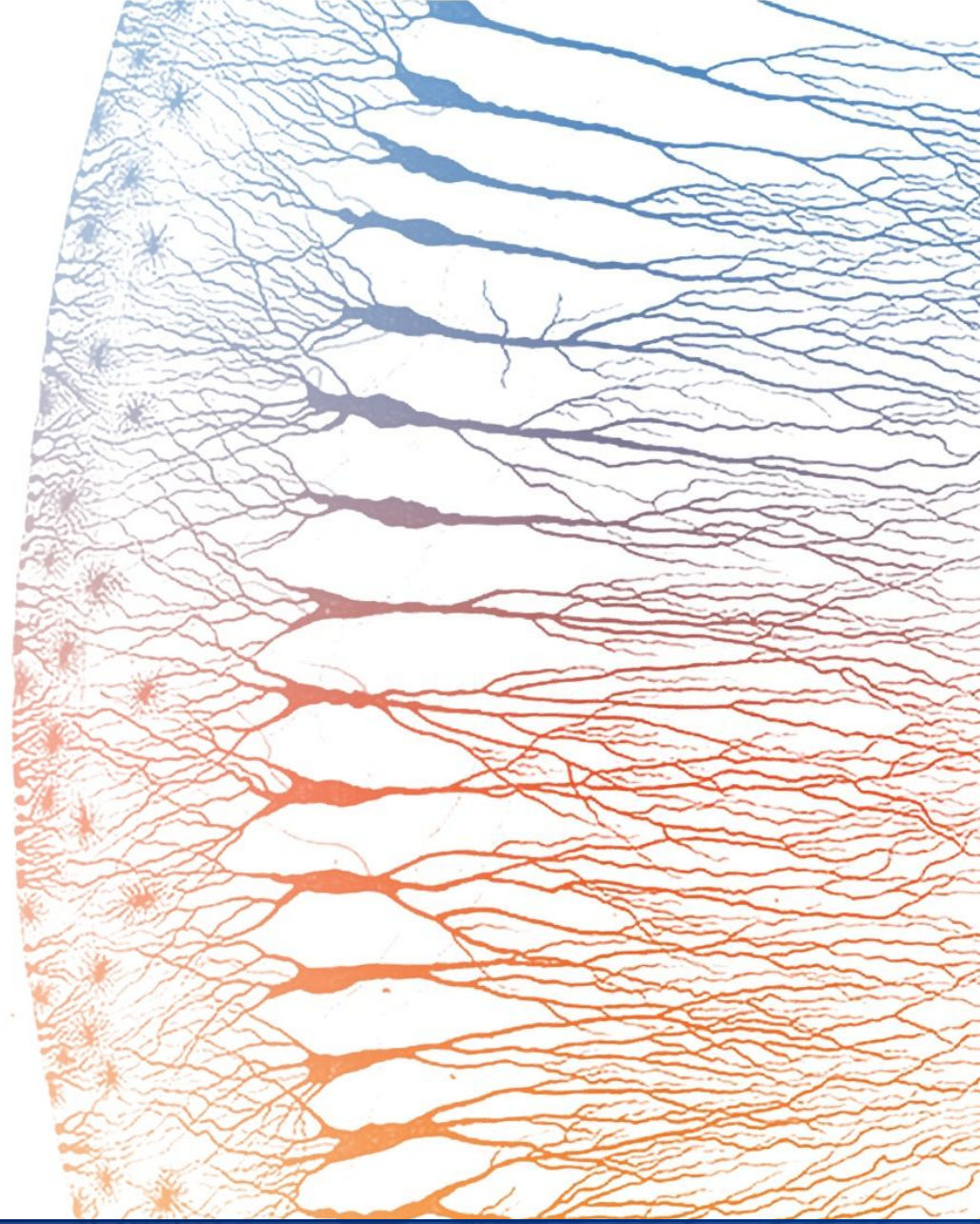

Affiliations

Elena Ratti is a full-time employee of Voyager Therapeutics, Inc.

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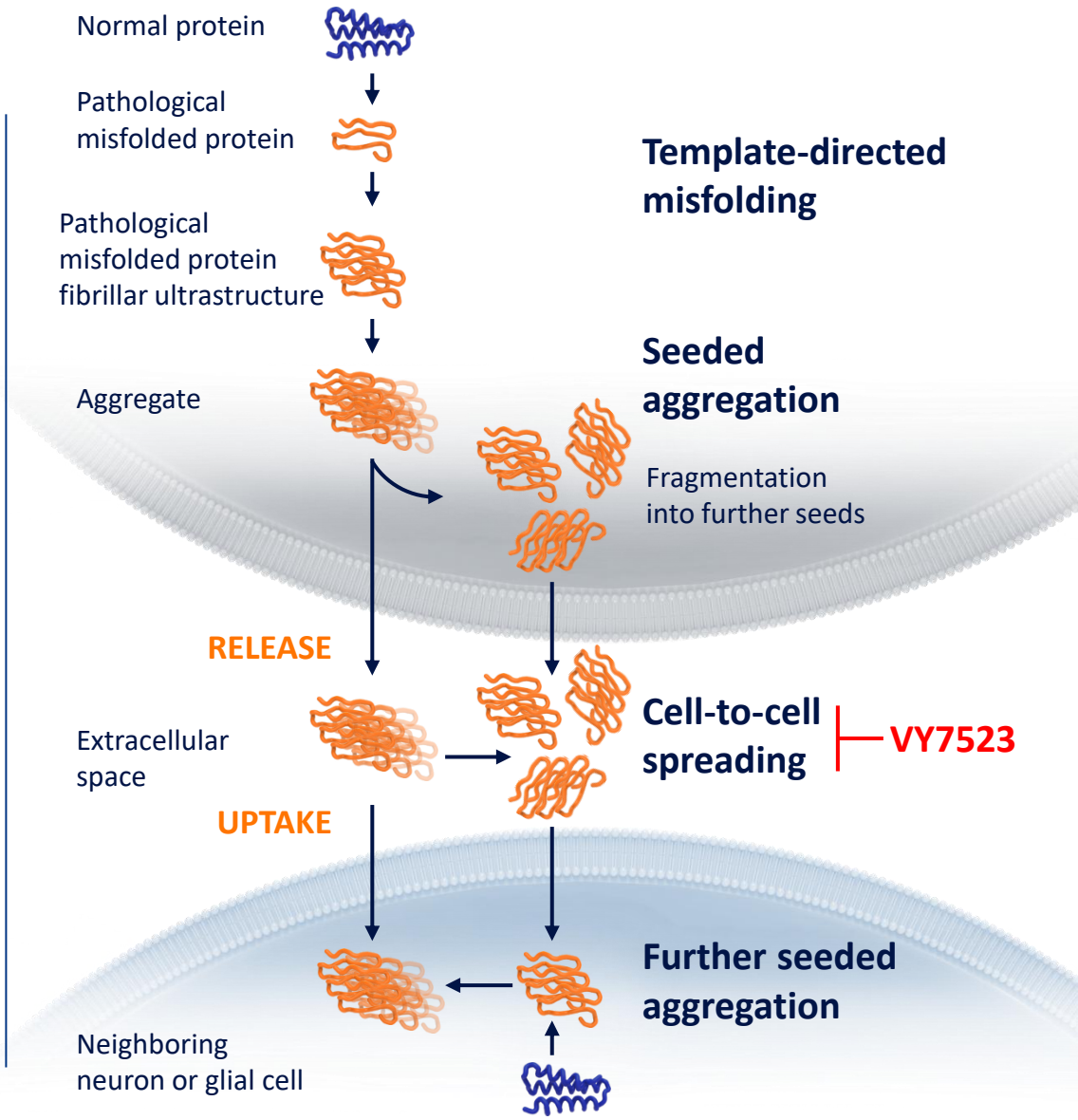
Background

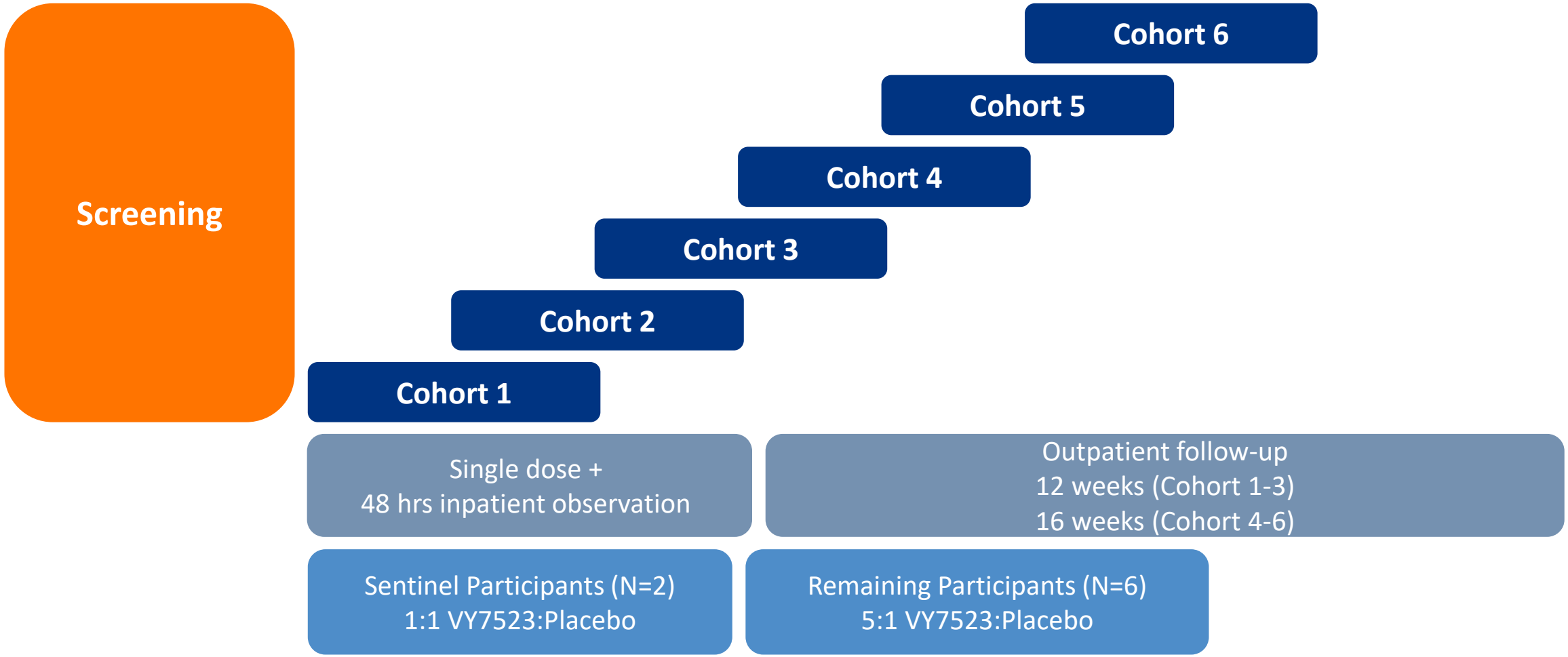
- Accumulation and seeding of **pathological tau** in Alzheimer's disease (AD) is believed to propagate preferentially through brain regions that are synaptically and functionally connected
- The pattern of tau protein spread in AD correlates with the development and progression of **cognitive symptoms** and **functional decline**
- **VY7523** (formerly VY-TAU01) is a humanized immunoglobulin gamma 4 (IgG4) monoclonal antibody that targets a specific epitope on the C-terminal region of tau
- VY7523 is hypothesized to inhibit the extracellular spread of pathological tau and, thereby, potentially **prevent AD progression**



Adapted from Brettschneider, *Nature Rev Neurosci*, 2015

First-in-Human Study of VY7523

SINGLE ASCENDING DOSE STUDY IN HEALTHY ADULT PARTICIPANTS



First-in-Human Study of VY7523

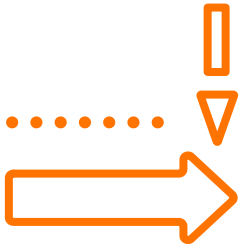
SINGLE ASCENDING DOSE STUDY IN HEALTHY ADULT PARTICIPANTS

Population

- Up to 48 healthy adult participants
- BMI 18-32 kg/m2
- Age 18-75 years

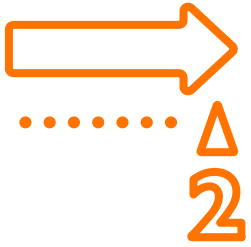
Objectives

- Safety, tolerability, and pharmacokinetics (PK) of 6 single IV ascending doses of VY7523



Primary Endpoints

- Incidence of treatment-emergent adverse events (TEAEs)
- Incidence of clinically relevant changes from baseline in vital signs, electrocardiograms (ECGs) and clinical laboratory parameters



Secondary Endpoints

- Serum VY7523 PK parameters
- Cerebrospinal fluid (CSF) concentration of VY7523
- Incidence of treatment emergent anti-drug antibodies (ADAs)

Administration

- Intravenous (IV), single dose, 6 dose levels

Sites

- 1 site (Clinical Pharmacology Phase 1 Unit)

Demographics and Dispositions

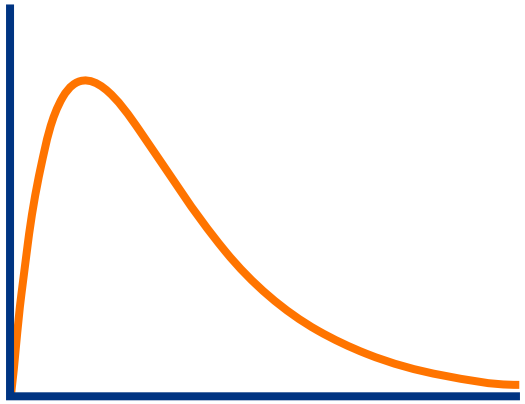
		Pooled Placebo (N = 12)	All VY7523 (N = 36)
Sex	Female	**5 (42%)**	**16 (44%)**
	Male	**7 (58%)**	**20 (56%)**
Race	Black or African American	**3 (25%)**	**3 (8%)**
	White	**9 (75%)**	**31 (86%)**
	White, American Indian or Alaska Native	**0 (0%)**	**1 (3%)**
	White, Black or African American	**0 (0%)**	**1 (3%)**
Ethnicity	Hispanic or Latino	**2 (17%)**	**4 (11%)**
	Not Hispanic or Latino	**10 (83%)**	**32 (89%)**
Age (yrs)	Mean	**46.7**	**44.9**
	SD	**15.5**	**13.7**
Body Mass Index (kg/m^2)	Mean	**26.6**	**26.5**
	SD	**3.3**	**2.9**

- All participants received entire dose
- 2 participants discontinued study prematurely (after receiving treatment) due to lost to follow up (placebo participant) or personal reason (treated participant)

SAD Safety Summary

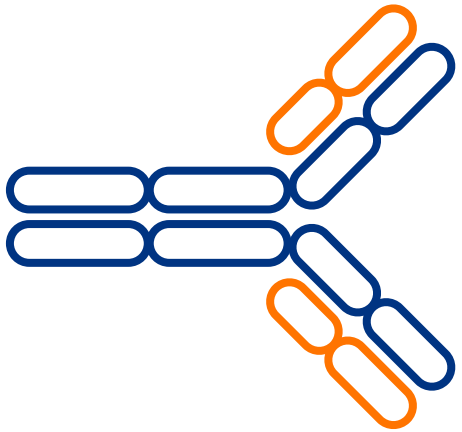
- **No** deaths, SAEs or severe AEs, No infusion related reactions (IRRs)
- All TEAEs were **mild to moderate** in severity; **no trends in AE severity** across the ascending doses
- **No clinically significant changes** in Labs (chemistry, hematology, coagulation), vital signs (including orthostatic testing), ECG and urinalysis
- No TEAEs leading to **treatment discontinuation**
- 55 TEAEs overall reported by 17 (35%) participants [11 (31%) treated; 6 (50%) placebo]
- Most frequent TEAE overall was **headache**, experienced by 4 (8%) participants [2 (6%) treated; 2 (17%) placebo]
- 5 TEAEs in treated participants (dizziness, nausea, headache and 2 events of chest pain) considered **related** to study product by Investigator

Pharmacokinetics Summary



Pharmacokinetics

- VY7523 demonstrated dose proportional and linear PK
  - Mean half-life ranged between 22 to 29 days which supports monthly dosing
  - Demonstrated CNS penetrance with %CSF-to-serum of approximately 0.3% typical of IgGs



Immunogenicity

- Low immunogenicity profile following single dose
  - One possible treatment emergent ADA observed – not associated with neutralizing antibody formation or with impact on PK or safety

Summary and Conclusions

- VY7523 was well tolerated, no SAEs, no infusion related reactions

- VY7523 showed dose proportional and linear pharmacokinetics
  - Half-life supports monthly dosing
  - Demonstrated CNS penetrance with %CSF-to-serum of ~0.3%

- Phase 1 SAD and chronic GLP toxicology data support continuation of the ongoing multiple ascending dose (MAD) study in participants affected by Alzheimer's disease (AD) (NCT06874621)