


EVIDENCE OF TARGET ENGAGEMENT IN A PHASE 1 CLINICAL TRIAL OF UB-312 IN PARKINSON'S DISEASE

Jean-Cosme Dodart, on behalf of the UB-312 program team

jc@vaxxinity.com

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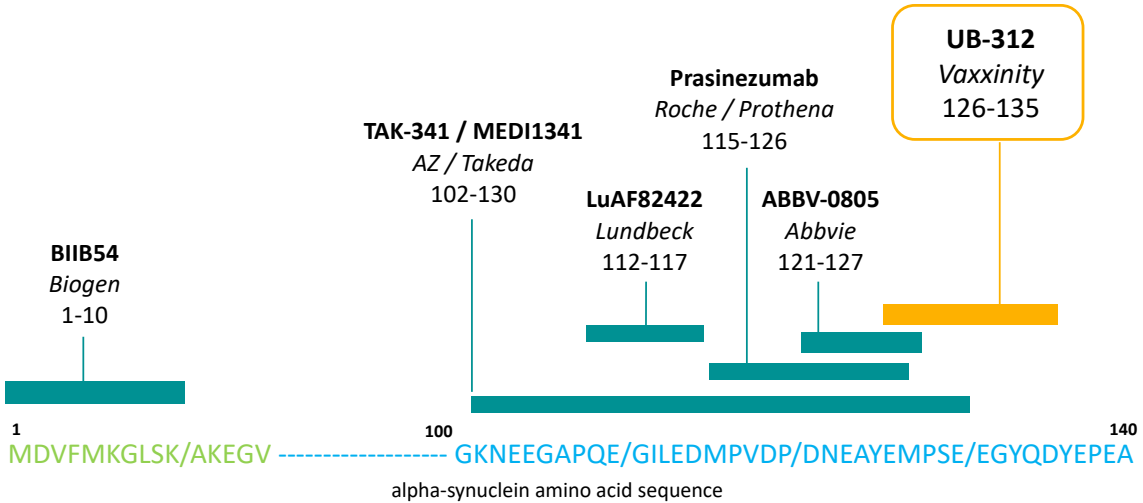
Disclosures

Jean-Cosme Dodart, Hui Jing Yu and Justin Boyd are employees of Vaxxinity.

Luis Concha-Mariambo is employee of Amprion.

UB-312 is an active immunotherapy designed to target pathological αSyn



- Preclinical studies showed that UB-312 induces antibodies preferentially bind to aggregated αSyn, inhibit αSyn toxicity and significantly reduce aggregated αSyn in brain and gut of transgenic mice.
- Phase 1 in healthy volunteers demonstrated good safety, tolerability and immunogenicity.

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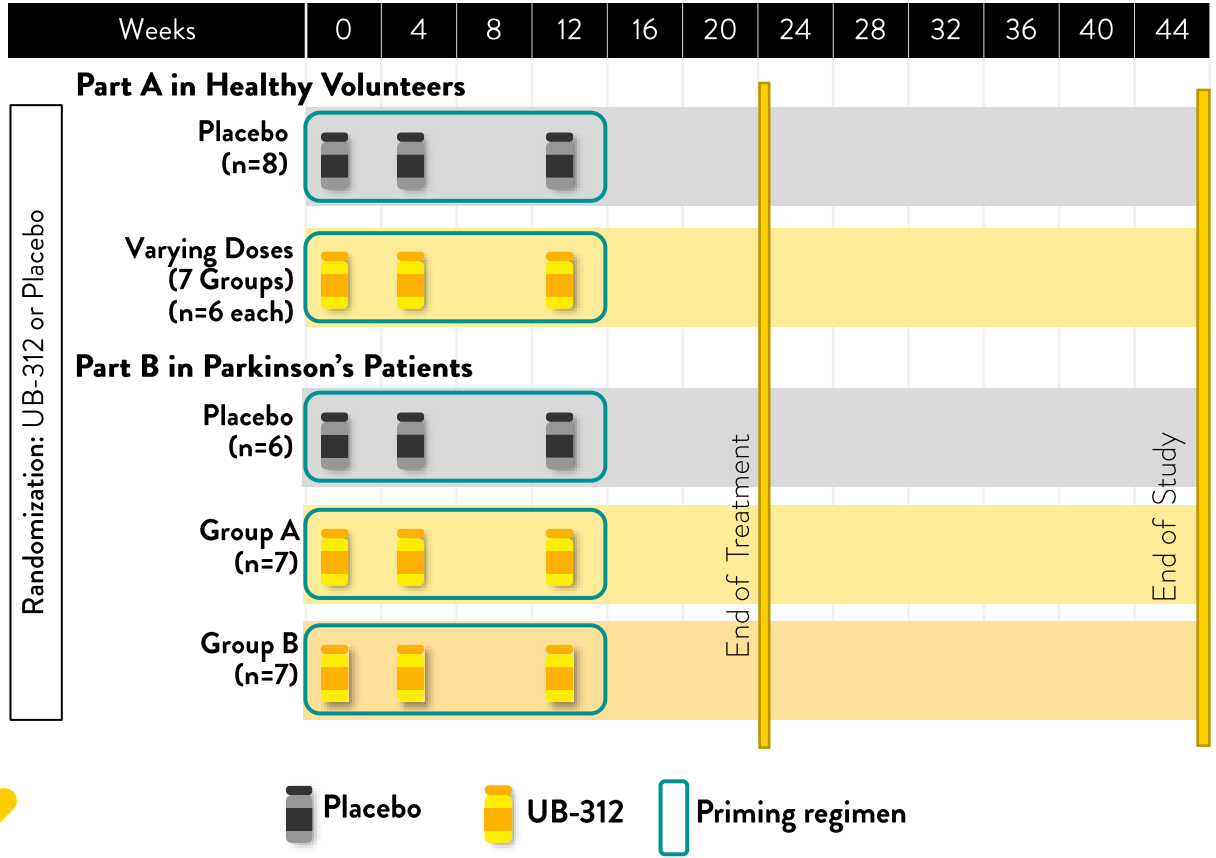
Nimmo et al., Alzheimer's Research & Therapy (2020)
Nimmo et al., Acta Neuropathologica (2022)
Yu et al., Movement Disorders (2022)

UB-312 Phase 1 Design

Part A Healthy Volunteers & Part B Parkinson's Disease Patients (H&Y≤3)



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Trial demographics, safety and immunogenicity

Shift 1 – 0463

A RANDOMIZED, DOUBLE BLIND, PLACEBO-CONTROLLED STUDY WITH UB-312, AN ANTI-ALPHA-SYNUCLEIN PEPTIDE VACCINE IN PARKINSON'S DISEASE PATIENTS.

POSTER SHIFT 01 (MARCH 6-7): THEME C: A-SYNUCLEINOPATHIES / C03.A. DRUG DEVELOPMENT, CLINICAL TRIALS: IMMUNOTHERAPY

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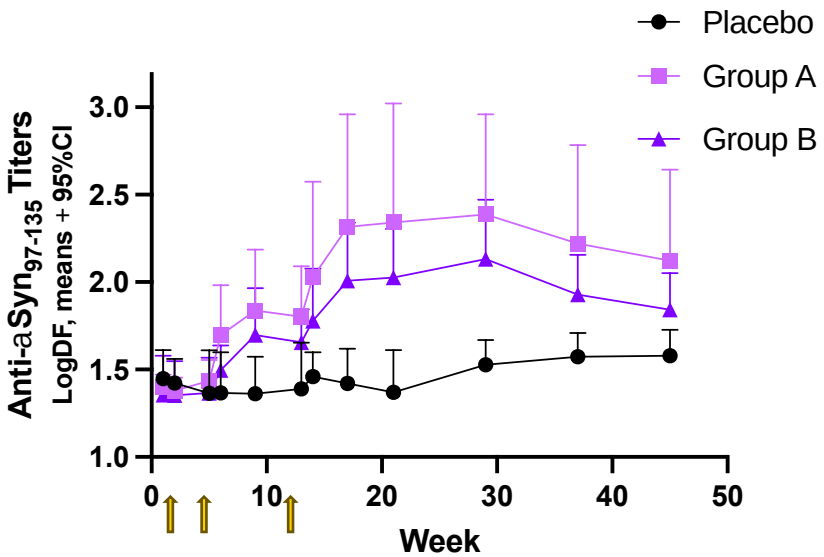
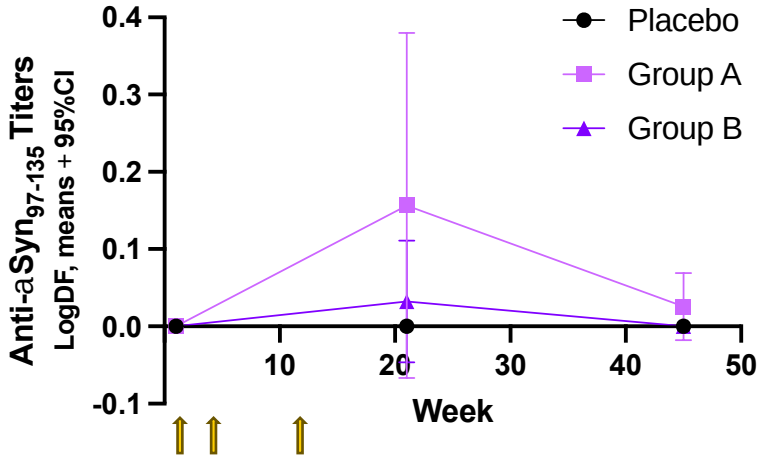
UB-312 is immunogenic in Parkinson's patients

Serum titers



92% responder rate
12 out of 13 patients with 3 doses

CSF titers



0.35% CSF:serum ratio

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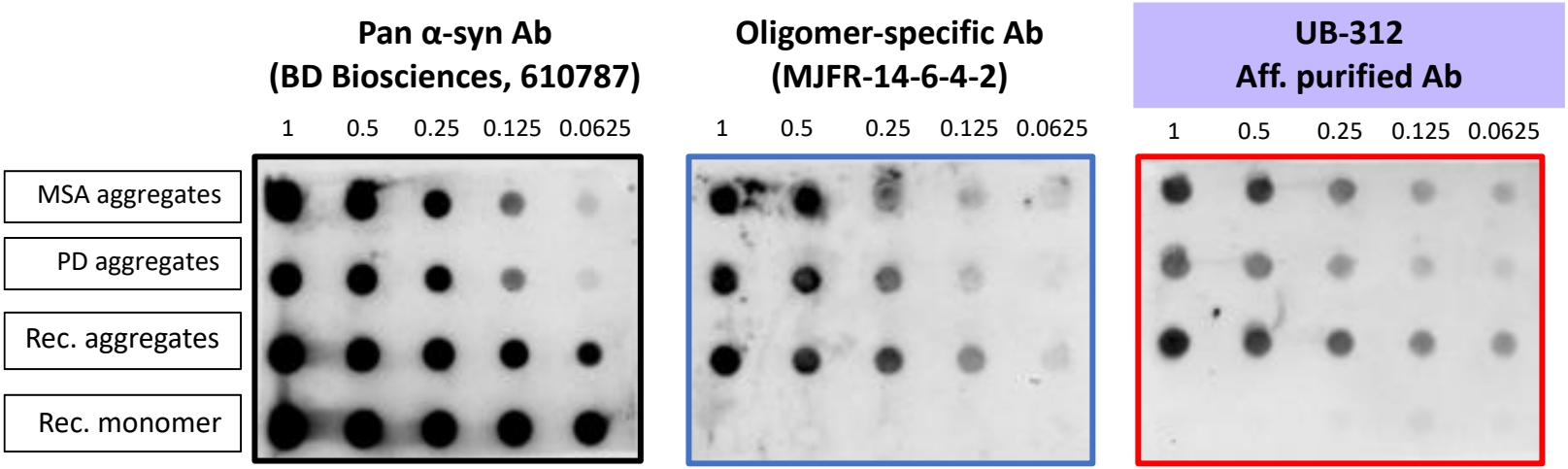
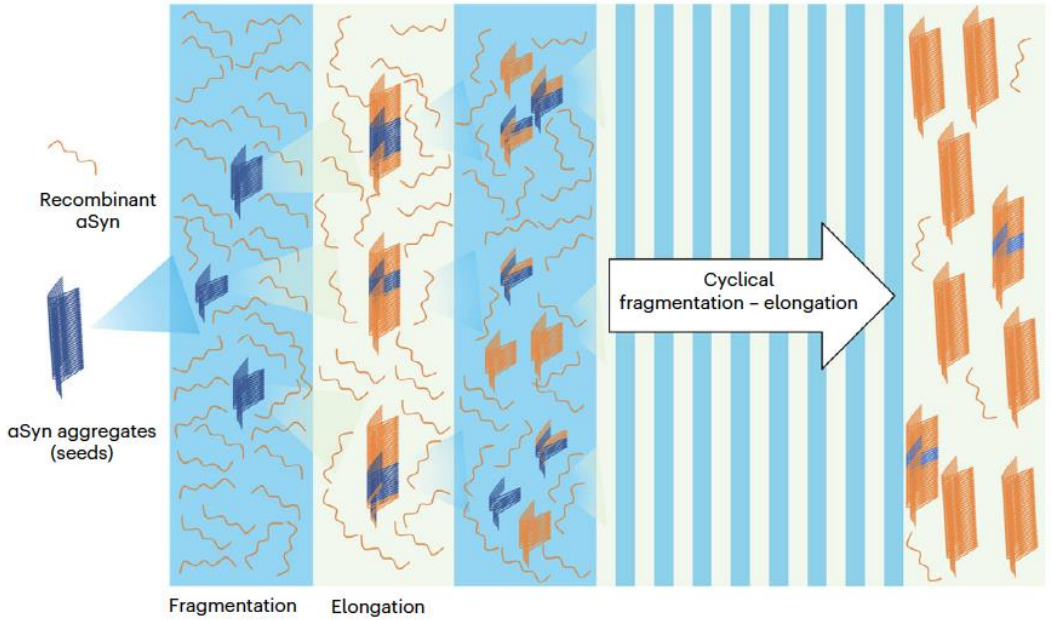
UB-312 antibodies preferentially bind aggregated species of αSyn



Antibodies were affinity purified from pooled serum samples from immunized HV.

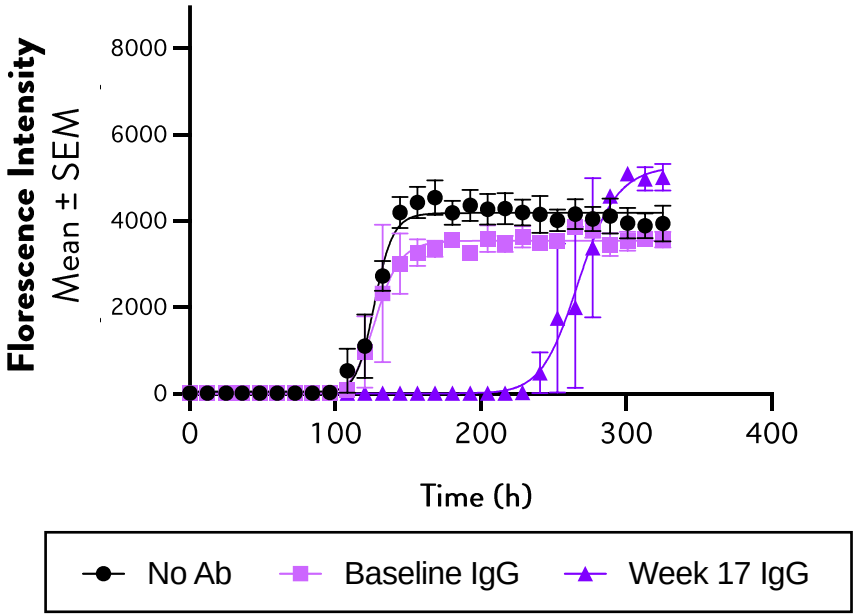
αSyn Seed Amplification Assay to assess target engagement



Concha-Mariambo et al., Nature Protocols (2023).

Target engagement: UB-312 antibodies alter αSyn aggregation in vitro

Antibodies spiked in a CSF sample from a PD patient



Total IgG fractions from healthy volunteers (Phase 1 part A) were isolated from sera collected before (baseline) or after (Week 17) immunization.

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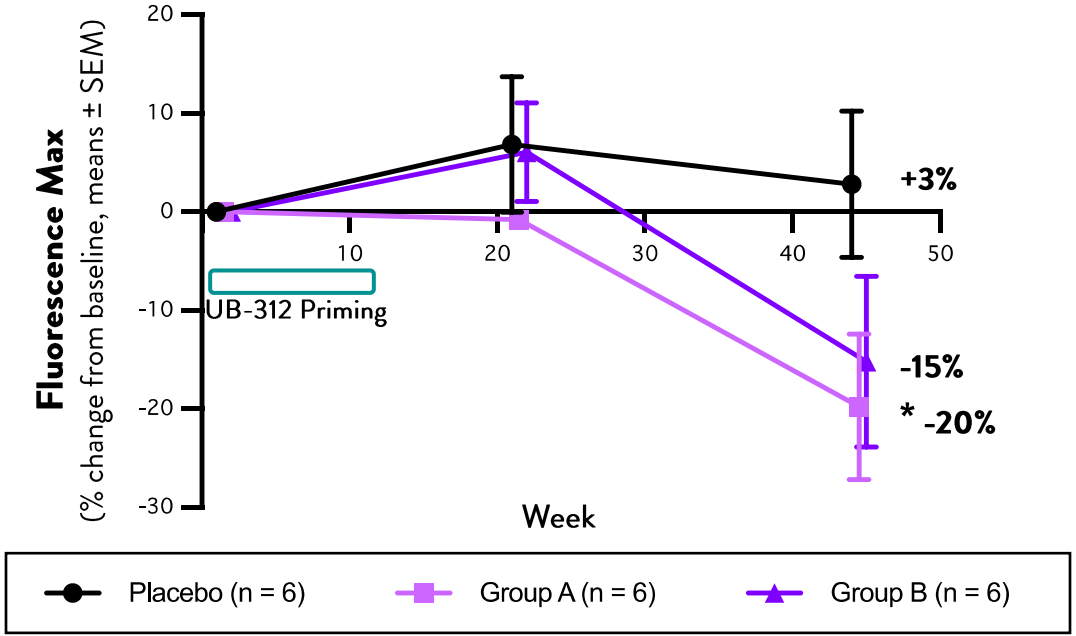
Target engagement: UB-312 reduces αSyn-SAA signal in CSF of Parkinson's patients



*Two-way RM ANOVA (Group A vs. placebo): $F_{2,19} = 4.047$, $p = 0.034$

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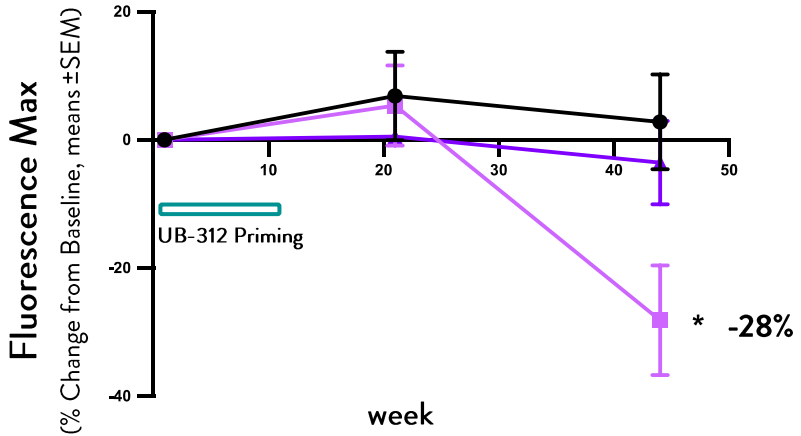
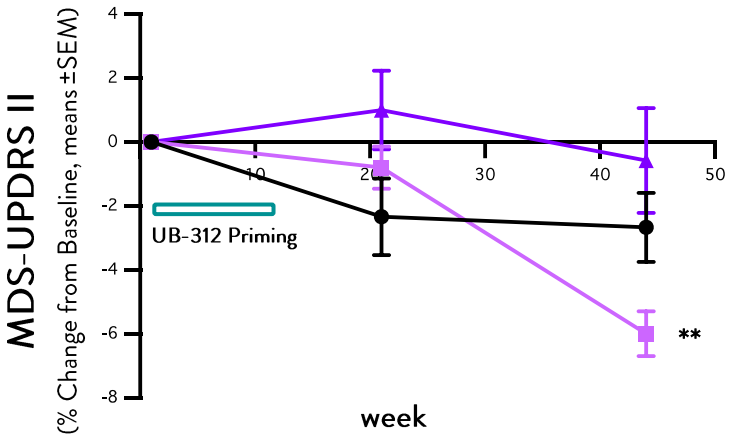
Patients with detectable antibodies in CSF show significant reduction in aggregated αSyn and improvement in MDS-UPDRS II

Reduction of aggregated αSyn in CSF Seed Amplification Assay (SAA)



*Two-way RM ANOVA: $F_{4,31} = 3.783$, $p = 0.01828$

Change in Activities of Daily Living MDS-UPDRS II



**Two-way RM ANOVA: $F_{4,31} = 4.162$, $p = 0.0082$

Placebo (n = 6) CSF titers (n = 5) No CSF Titers (n = 8)

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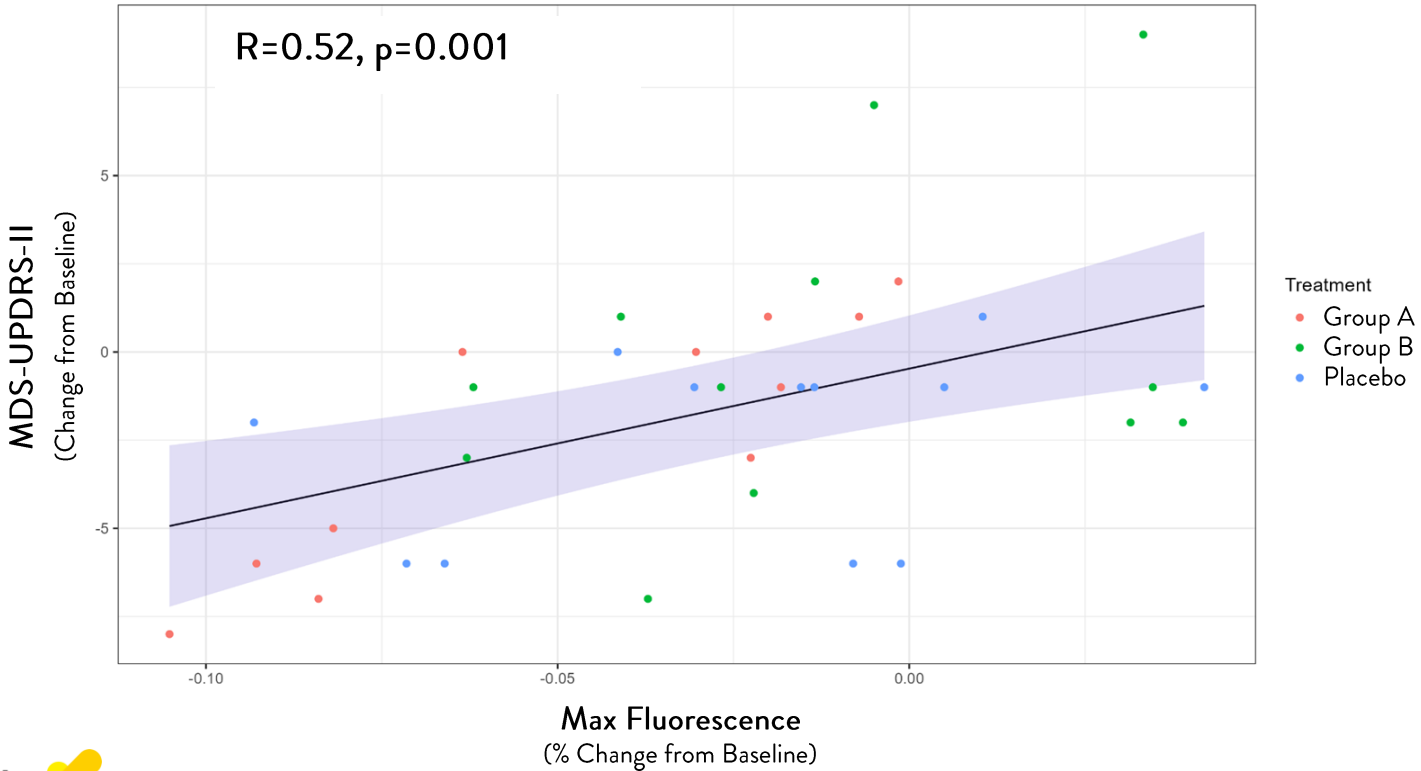
Correlation between reduction in aggregated αSyn in brain and change in MDS-UPDRS-II



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Summary

- UB-312 is first immunotherapy candidate to report reduction of pathological αSyn in Parkinson's patients
  - UB-312-induced antibodies are specific to pathological αSyn and alter aggregation in vitro
  - UB-312 immunization reduces pathological αSyn in CSF of Parkinson's Disease patients, as measured by αSyn-SAA
  - Early indication of clinical improvement correlated with reduction of pathology
  - Limitations: small cohort size, limited dosing regimens,
- Next step: Phase 2 study will further investigate optimal dose regimen and confirm target engagement in PD patients

Thank you!

Luis Oliveira, Katharina Klapper, Brian Fiske, Mark Frasier

Mohammad Shahnawaz, Claudio Soto

Pinaki Misra, Wolfgang Singer

Luis Concha-Mariambo, Carly Farris, Yihua Ma

... the patients, their families, and the CHDR and Vaxxinity teams