

## Strong Scientific Evidence Supports Anti- $\alpha$ -synuclein Therapies for Parkinson's Disease (PD)

### Alpha-synuclein pathology (Lewy bodies/neurites) is strongly implicated in PD

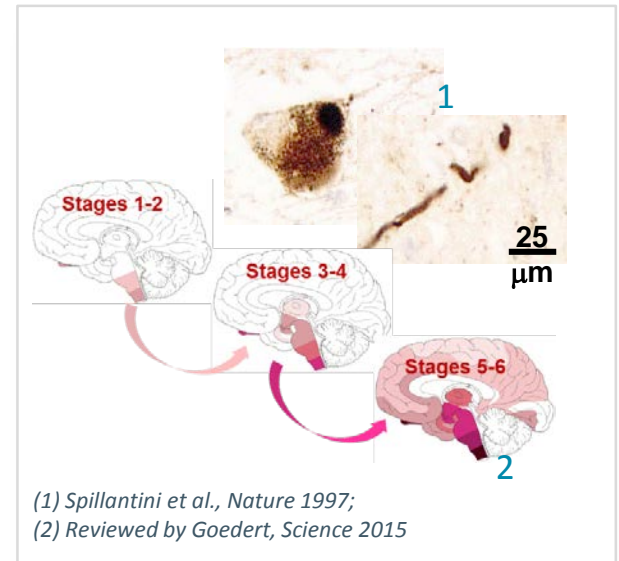
- Lewy pathology affects midbrain/SNc DA neurons and progresses to neurons in the entire CNS
- $\alpha$ -Syn is a genetically validated target (missense mutations, gene dose)

### Alpha-synuclein is an extracellular target during pathogenesis

- Caudal-rostral staging, host-to-graft transfer, propagation models
- Aggregated extracellular  $\alpha$ -Syn causes propagation of  $\alpha$ -Syn pathology, neuronal and functional loss in preclinical models of PD

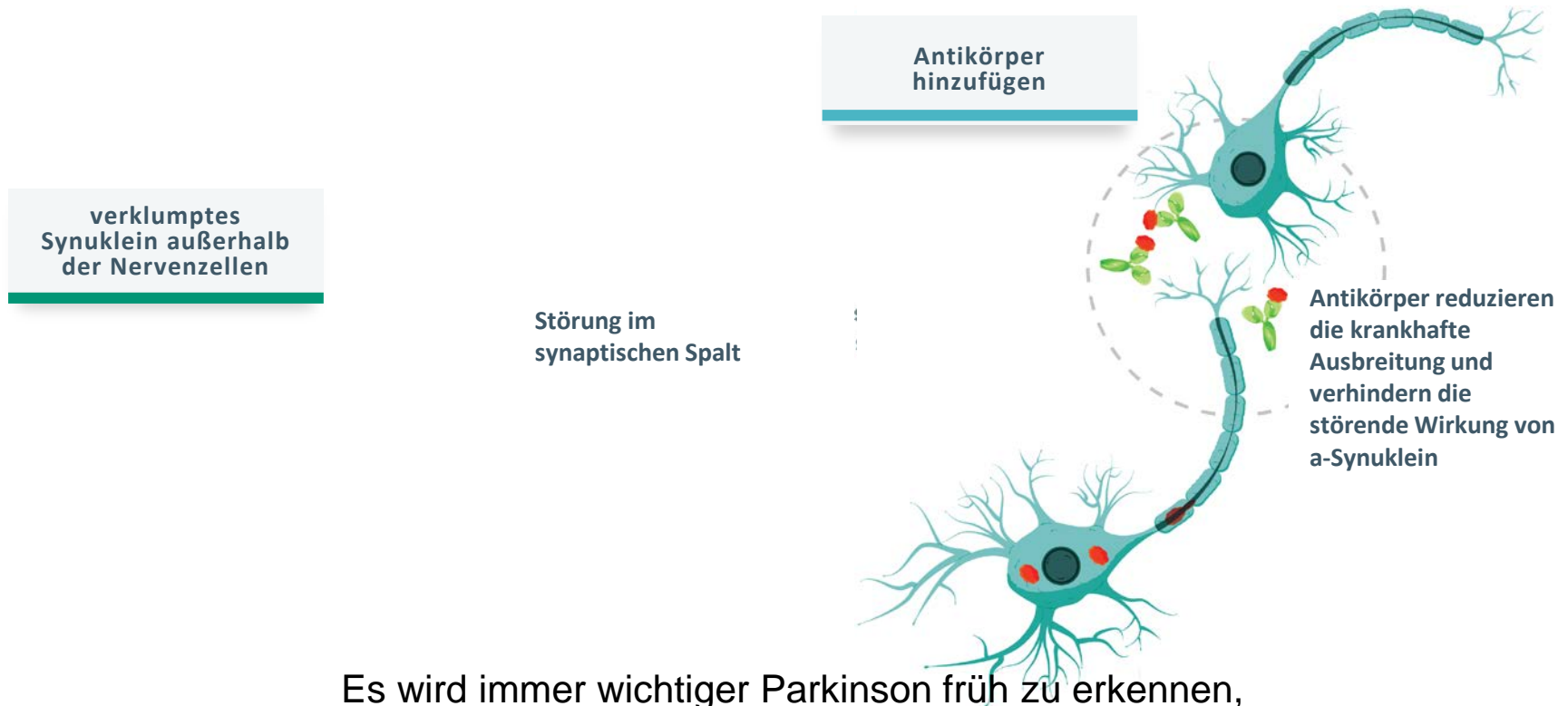
### Passive anti- $\alpha$ -synuclein immunization is a potential disease-modifying therapy for PD

- Strong preclinical efficacy in various *in vivo*-synuclein-aggregation disorder models



## Hypothese:

Anti- $\alpha$ -synuclein Immunotherapie kann die durch Synuclein verursachte Störung in den Nervenzellen evtl. abmildern und den Weitertransport, die "Ansteckung" der Nervenzellen verhindern

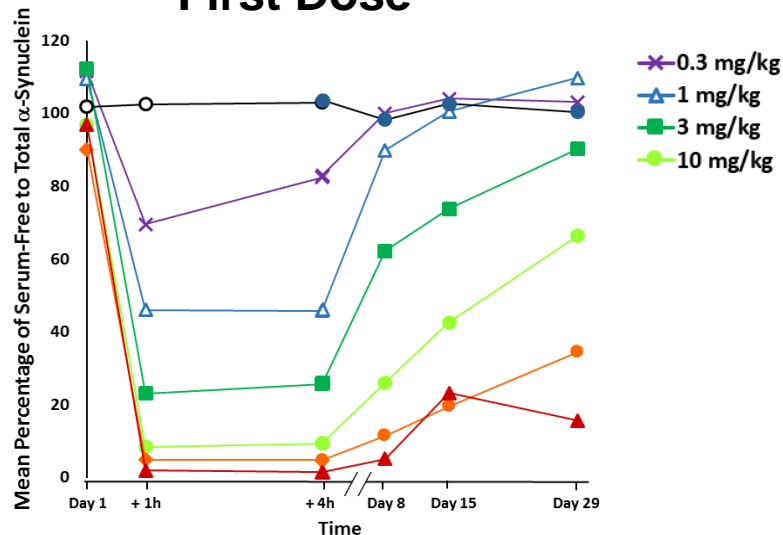


Es wird immer wichtiger Parkinson früh zu erkennen, da in Zukunft die Therapie viel früher einsetzen wird!

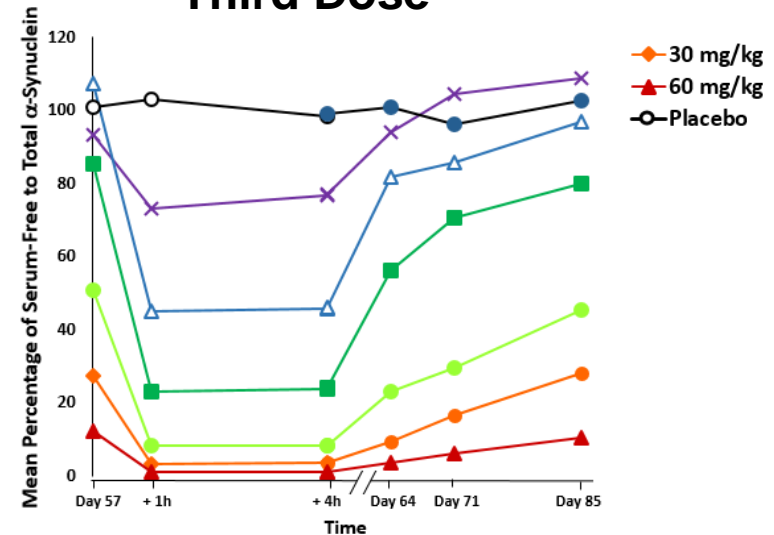
## First Study With RG7935/PRX002 in PD Patients

- Randomized, Double-blind, Placebo-controlled, **Multiple Ascending Dose**, Safety, Tolerability and Pharmacokinetic Study in Patients with Parkinson's Disease
- 80 patients randomly assigned to 1 of 6 sequential dose cohorts, up to 60 mg/kg (RG7935/PRX002: placebo ratio: cohorts 1-4, 8:4; cohort 5, 11:5; cohort 6, 12:4)
- Each patient received 3 IV doses (baseline, week 4, and week 8)
- 12 weeks of clinical assessments; 24 weeks of safety observation

### First Dose



### Third Dose



Free serum -synuclein levels normalized to total  $\alpha$ -synuclein (free-to-total ratio)

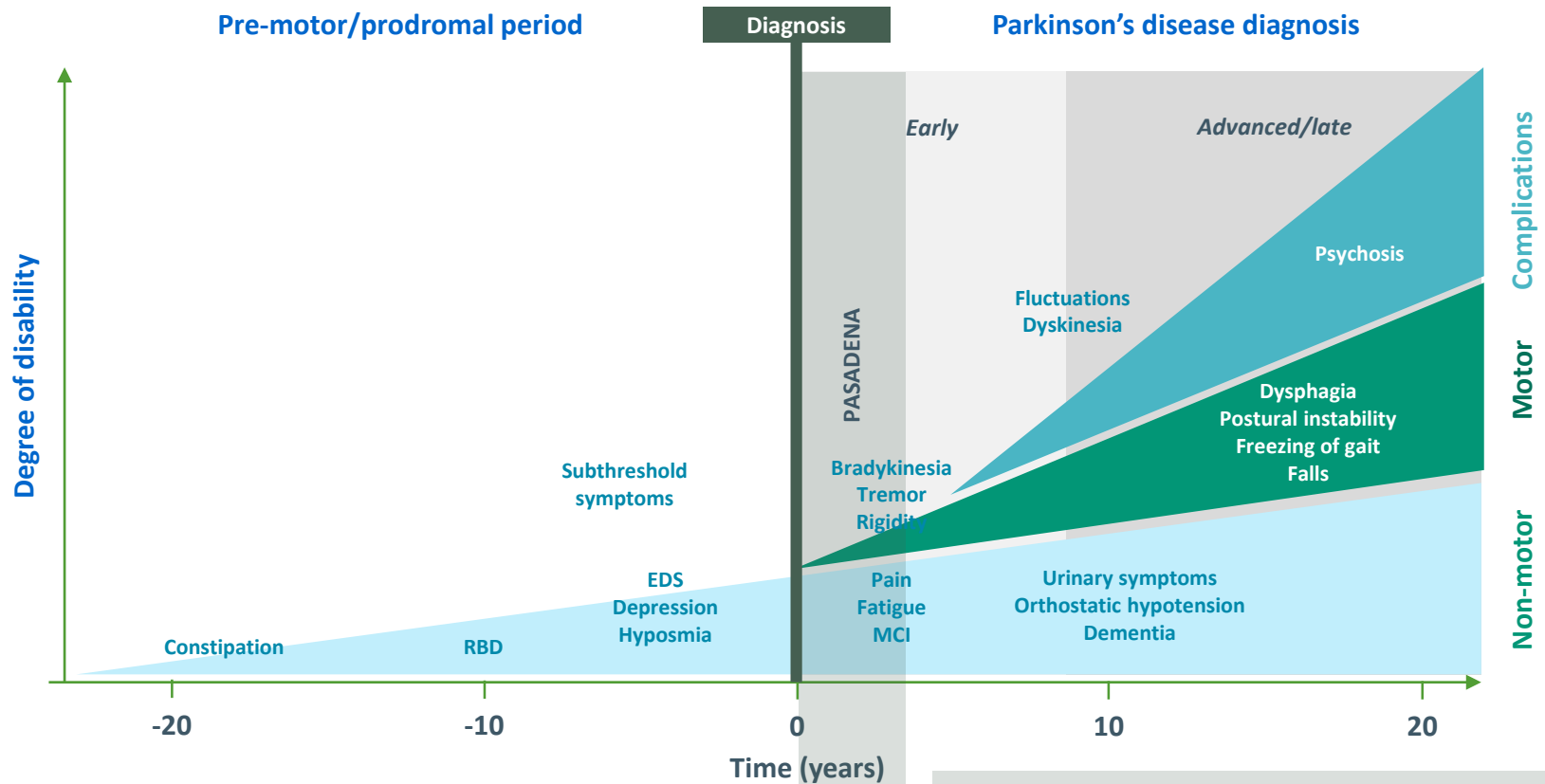
- First report of an anti- $\alpha$ -synuclein antibody immunotherapy in patients with PD
- Rapid dose- and time-dependent mean **reductions in free serum alpha-synuclein levels of up to 97%**
- Similar decreases in free  $\alpha$ -synuclein after first and last infusions Jankovic J et al. *Mov Disord.* 2017;32 (suppl 2):S 560.

„Neue Therapieoptionen bei Parkinson“

UnivProf. Dr. med. Claudia Trenkwalder

Kassel, 15. April 2019

# Patient Population for the Phase 2 PASADENA Study



Kalia LV, Lang AE. *Lancet*. 2015;386:896-912.

Patients with early Parkinson's disease (Hoehn & Yahr I-II)  
Untreated/MAO-B inhibitor treated

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# Zukunft

- PASADENA Studie (Roche) hat begonnen deutschlandweit, Rekrutierung bis ca. Ende 2018
- Weitere Studie mit passiven alpha-synuclein-Antikörper von Biogen startet 2019
- Experimentelle Forschung zu aktiven Immunisierung bereitet neue Studien vor

## Helpen Sie mit, forschen Sie mit uns!

- Frühes Auftreten von Traum-Schlafverhaltensstörungen  
gefördert von der M.J. Fox Stiftung

**Ansprechpartner:** „Früherkennung Parkinson -Ambulanz“  
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Oder:

**Parkinson-Zentrum Göttingen/Kassel**  
UMG, Anmeldung Parkinson-Ambulanz



# Vielen Dank für Ihre Aufmerksamkeit!



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