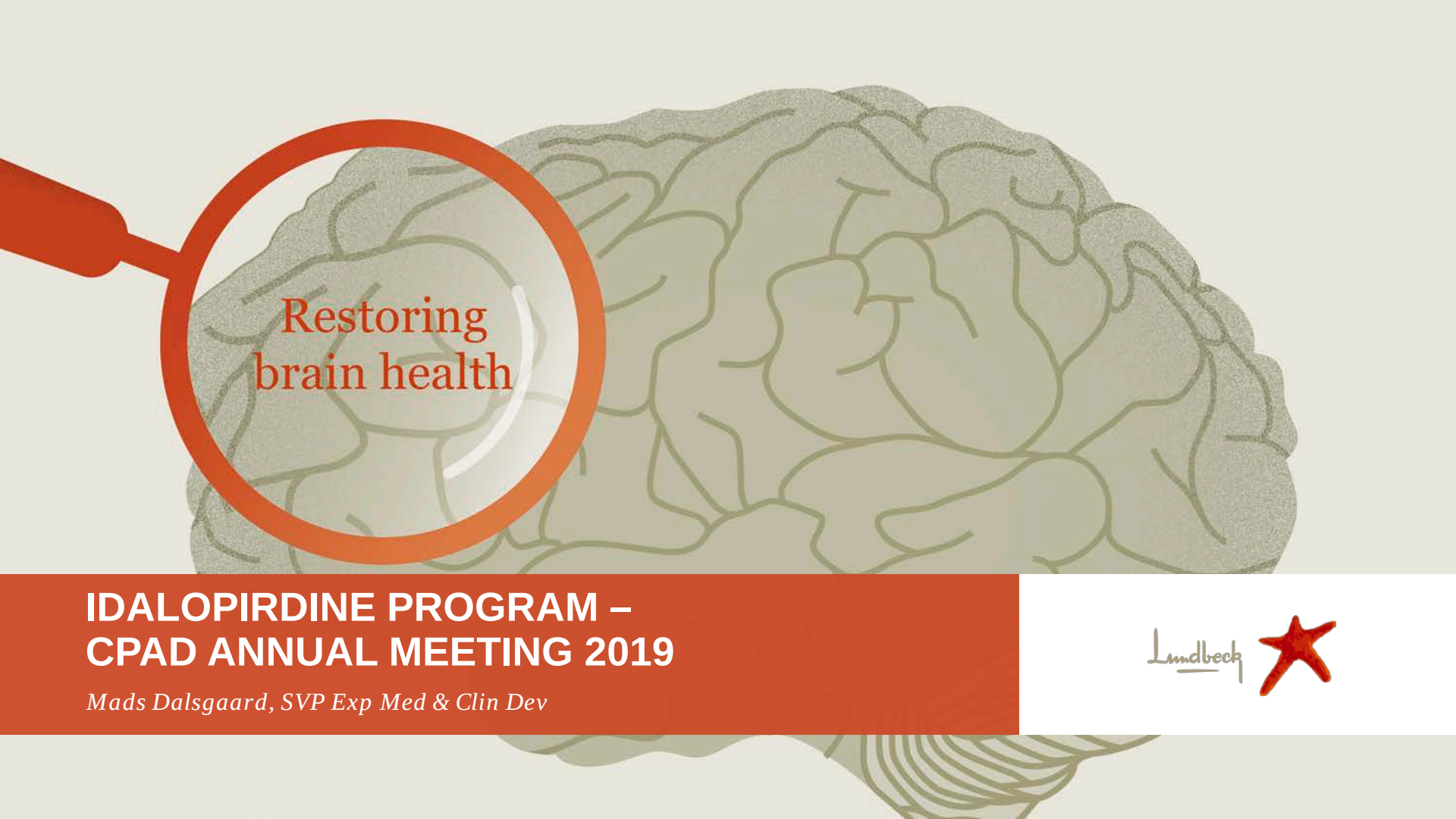


IDALOPIRDINE PROGRAM – CPAD ANNUAL MEETING 2019

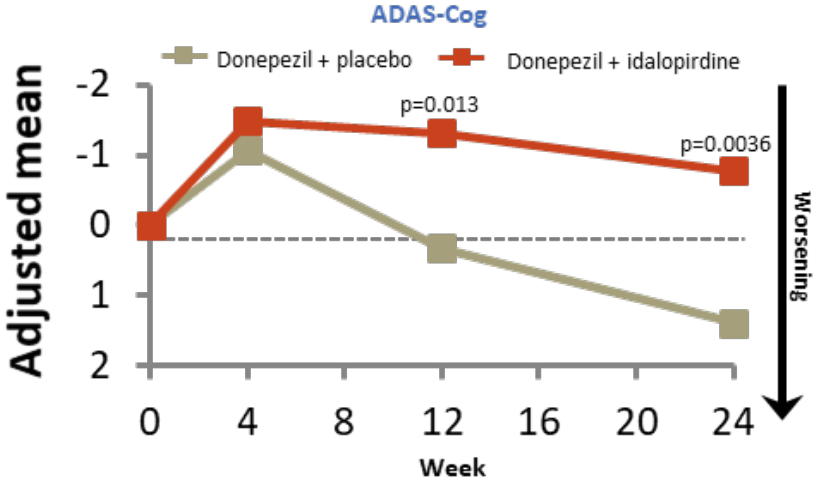
Mads Dalsgaard, SVP Exp Med & Clin Dev

Objectives

- Brief overview of the Idalopirdine trials and dataset
- Reflections on data-sharing process with CPAD

Proof-of-concept study of Idalopirdine

5-HT6 receptor antagonist



	MMRM analysis (primary)		ANCOVA OC	
Variable	Mean difference at Week 24 [95% CI]	P value	Mean difference	P value
ADAS-Cog	-2.18 [-3.64, -0.72]	0.0036	-2.41	0.0016
ADCS-ADL_{23}	1.72 [-0.48, 3.92]	0.12	2.39	0.046
ADCS-CGIC	-0.22 [-0.49, 0.05]	0.12	-0.26	0.062
NPI	-1.45 [-3.78, 0.88]	0.22	N/A	

ANCOVA=analysis of covariance; CI=confidence interval;
MMRM=mixed effects model for repeated measures; OC=observed case

Wilkinson et al. Lancet Neurol 2014;13(11):1092–1099;
Cummings et al. Neurobiol Aging 2016;39(Suppl 1):S2–S3; H. Lundbeck A/S. Data on file

Phase III program – overview and objectives

Overview

- Three 24-week, double-blind, placebo-controlled studies involving ~2,500 patients worldwide, and a 6–12 month, open-label extension study in ~1,500 patients[2]
- Objective to elucidate the efficacy and safety of idalopirdine (10–60 mg/day) in adults aged ≥50 years with:
  - Mild to moderate AD (MMSE 12–22), and
  - On stable background ChEI therapy with donepezil, galantamine, or rivastigamine[1,2]

Primary and key secondary objectives

- Change in cognition measured by ADAS-Cog and
- Global impression (ADCS-CGIC) or Activities of daily living (ADCS-ADL23)

Secondary objectives

- Safety and tolerability
- Other efficacy outcomes, including behavioral symptoms (NPI)

1. Wilkinson et al. Lancet Neurol 2014;13(11):1092–1099;
2. ClinicalTrials.gov study identifiers: NCT02006641; NCT01955161; NCT02006654; NCT02079246

Phase III program – Lundbeck & Otsuka

Study	Doses/ comparator	Background treatment	Treatment duration	Total population	Key efficacy endpoints
14861A RCT **STARSHINE**	30 mg/day 60 mg/day Placebo	Donepezil	24 weeks	932	ADAS-Cog, ADL, CGIC
14862A RCT **STARBEAM**	10 mg/day 30 mg/day Placebo	Donepezil	24 weeks	858	ADAS-Cog, ADL, CGIC
14863A RCT **STARBRIGHT**	60 (30) mg/day Placebo	Donepezil, rivastigmine, galantamine	24 weeks	734	ADAS-Cog, ADL, CGIC
14861B Open-label extension[a]	60 (30) mg/day	Donepezil	28 – 52 weeks[b]	1463	ADAS-Cog, ADL, CGIC

[A] Extension of 14861A, and 14862A

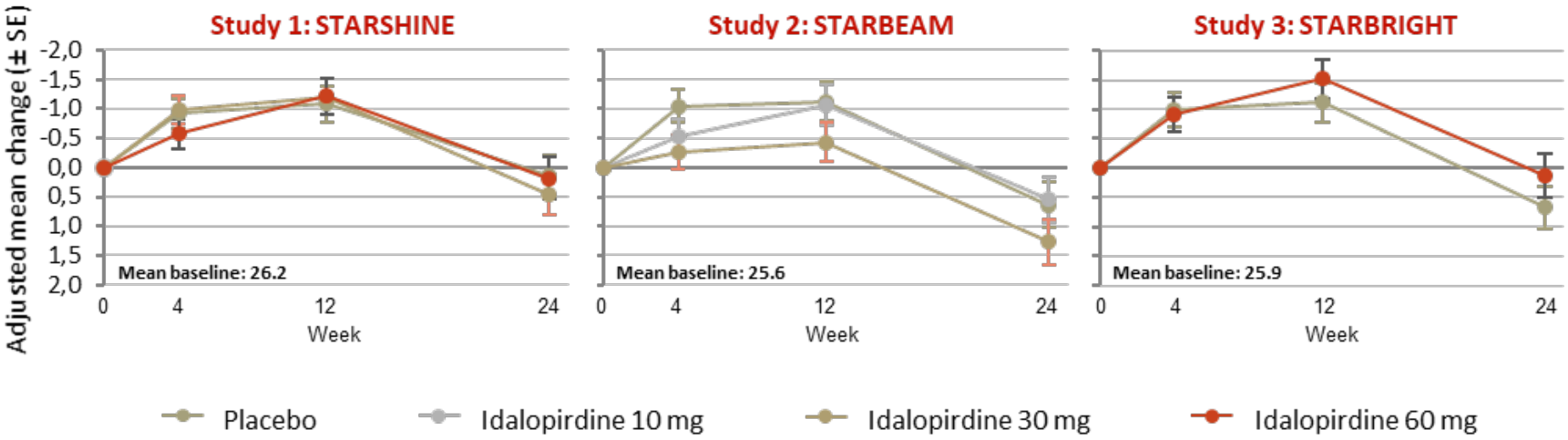
[B] 52 weeks applicable to 100 patients who initiate memantine after 28 weeks

ADAS-Cog=Alzheimer's Disease Assessment Scale, cognitive subscale; ADL_{23}=Activities of Daily Living, 23 item; CGIC=Clinical Global Impression of Change; ChEI=cholinesterase inhibitor; MMSE=Mini Mental State Examination

ClinicalTrials.gov study identifiers: NCT02006641, NCT01955161, NCT02006654, NCT02079246;

Primary endpoint – ADAS-Cog

ADAS-Cog

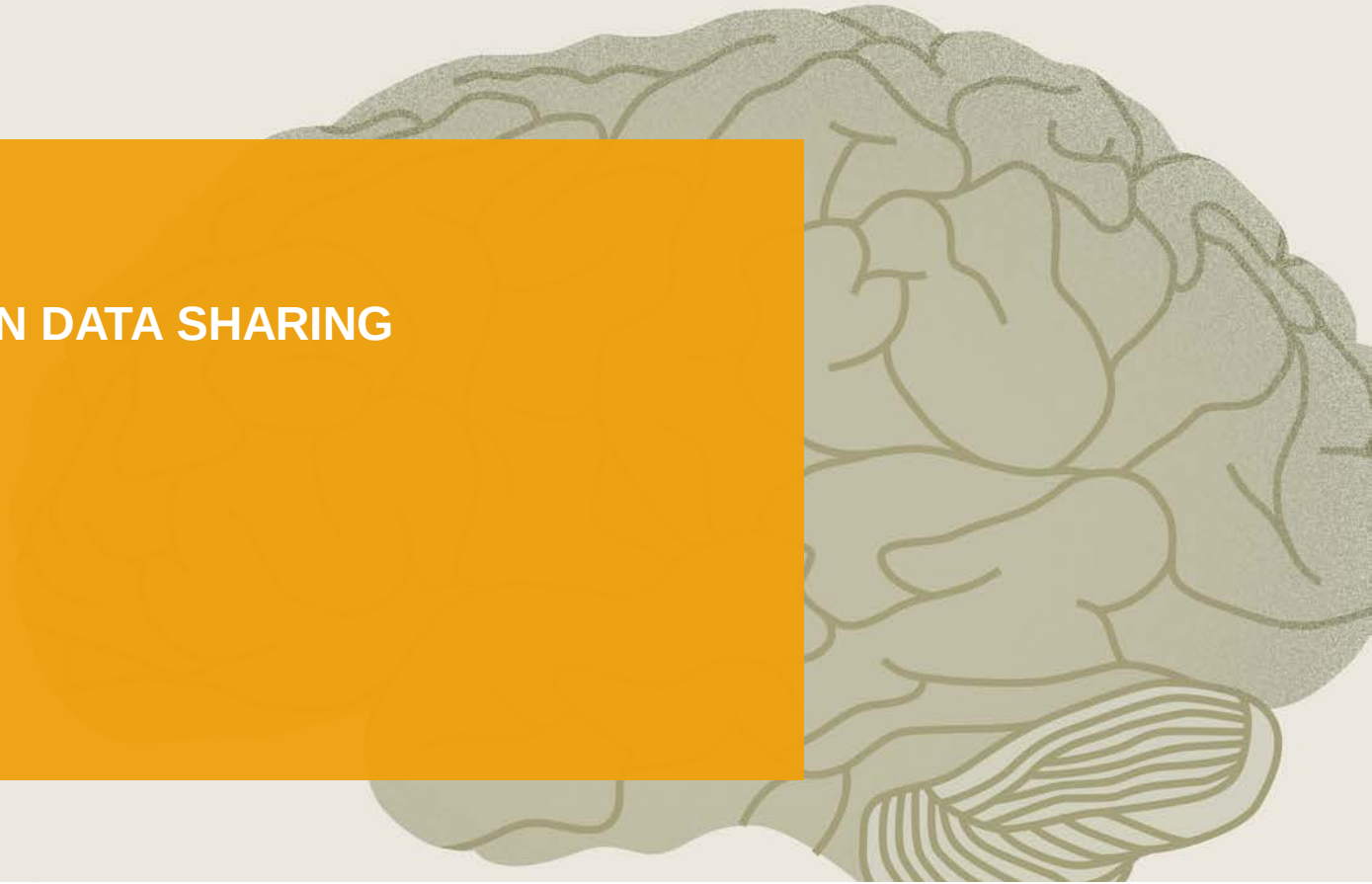


ADAS-Cog=Alzheimer's Disease Assessment Scale, cognitive subscale; ADCS-ADL$_{23}$=Alzheimer's Disease Cooperative Study – Activities of Daily Living, 23-item scale; ADCS-CGIC=Alzheimer's Disease Cooperative Study – Clinical Global Impression of Change; SE=standard error

Conclusion

- With 2,525 patients worldwide, one of the largest development programs completed in mild-moderate, symptomatic AD
- The Phase III program did not replicate ‘proof-of-concept’ efficacy results
- Idalopirdine 10–60 mg/day adjunctive to donepezil/ChEI therapy, while supporting a good safety and tolerability profile in the Phase III program, is overall not effective in alleviating clinical symptoms in mild–moderate AD

REFLECTIONS ON DATA SHARING



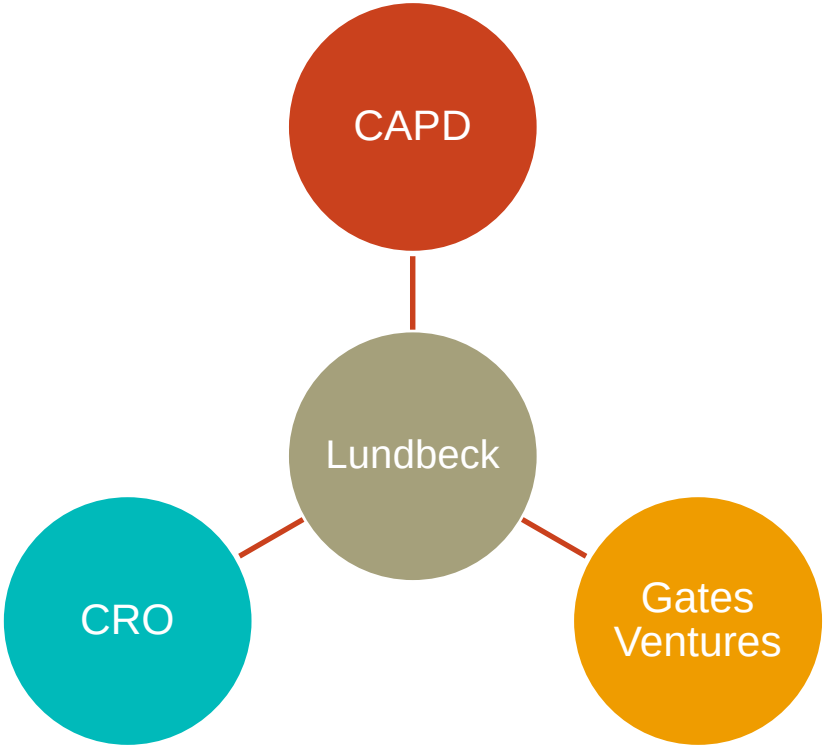
Experience with data sharing – internal “obstacles”

- Challenges related to IP and opportunities for developing into other areas, subgroups etc
- Freeing up resources – for data anonymization, preparation
- Coordination across multiple functions within company (Clinical Dev, Data Management, Biostatistics, Contracting etc.)

Prerequisites for data sharing

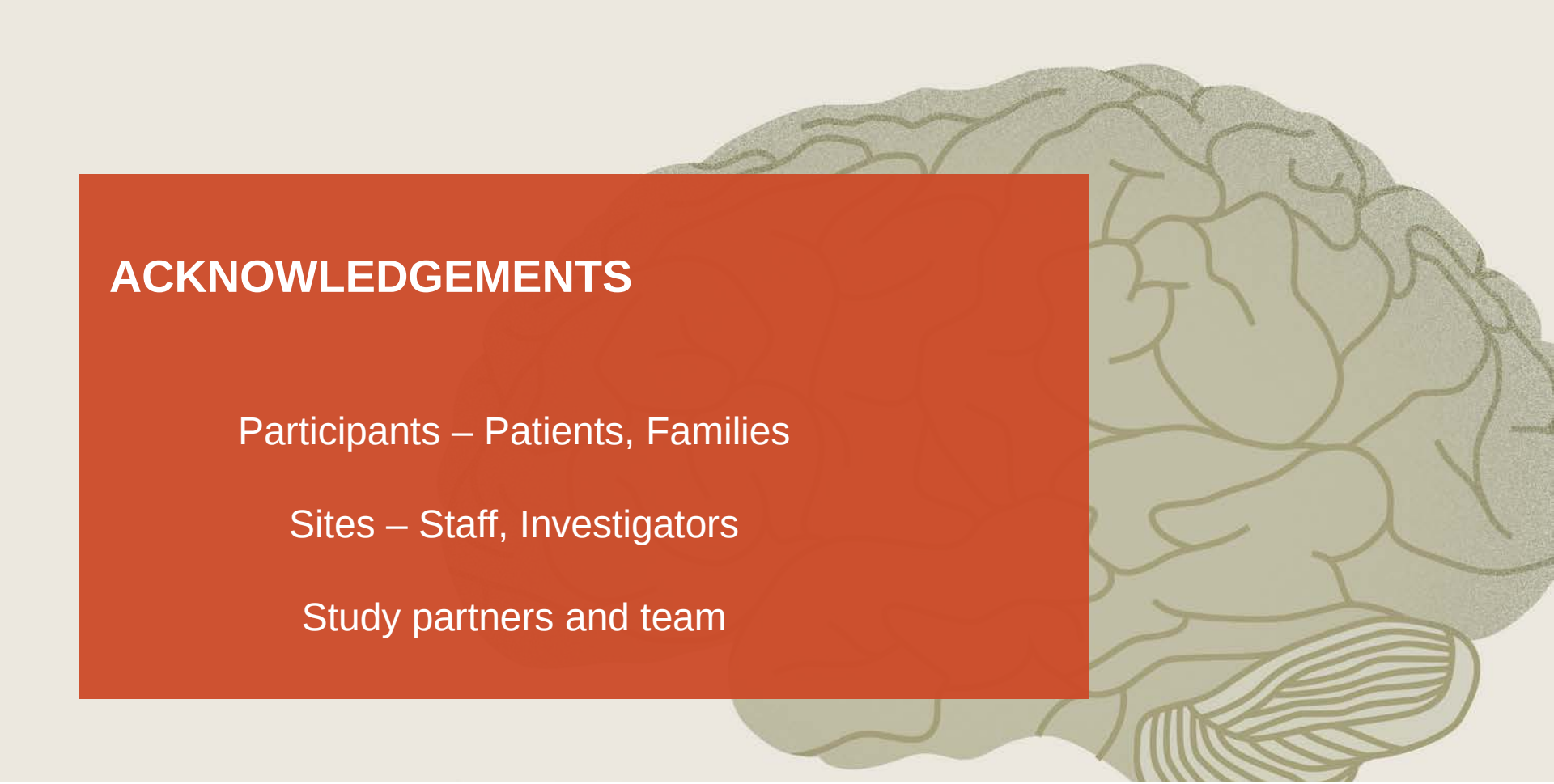
- Patient informed consent
- GDPR and anonymization
- Redacting documents

Collaboration with partners



Enablers

- High degree of willingness to make data available
- Contracting and agreement straight forward
- Good support from and dialogue with CPAD
- Not only the *right* thing – but the *only* thing to do



ACKNOWLEDGEMENTS

Participants – Patients, Families

Sites – Staff, Investigators

Study partners and team