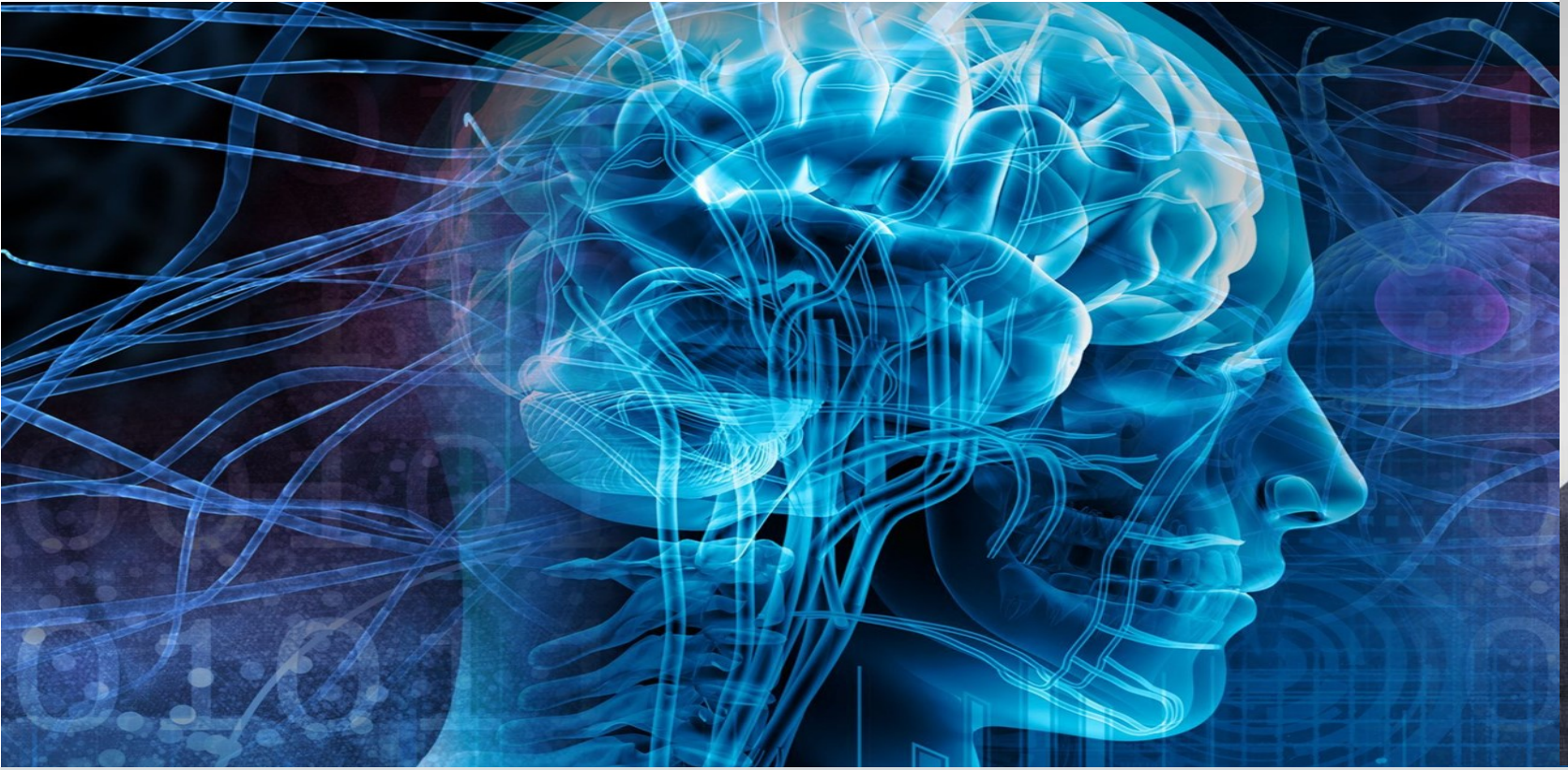


Welcome and Consortium Overview

October 27, 2020

Sudhir Sivakumaran, Executive Director, CPAD

Critical Path for Alzheimer's Disease (CPAD)

Vision: Develop a disease progression model across the entire continuum of Alzheimer disease (AD) – from the earliest stages to severe AD – to optimize trial design & execution, reduce trial costs & time, and reduce patient burden.

- ✓ A neutral, nonprofit, pre-competitive consortium.
- ✓ Integration and transformation of patient-level data into generalizable and actionable knowledge to advance new drug development tools.

Advanced Data Management

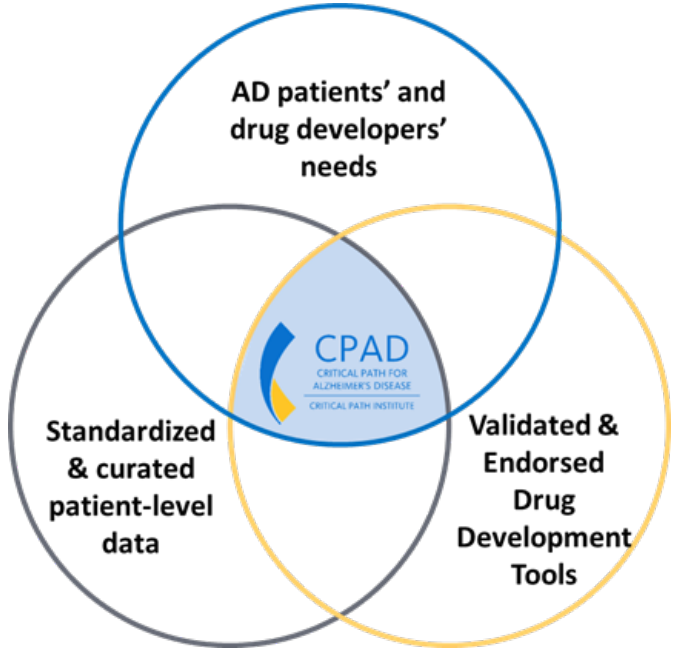
Extant technical expertise and infrastructure to obtain, integrate and make accessible high-quality patient-level datasets suitable for queries and analyses

Advanced Analytics to Generate Solutions

Data-based ability to generate a disease progression model across the entire continuum of Alzheimer's disease (AD) – from earliest stages to severe AD

Focus on Drug Development

Potential to dramatically accelerate the evolution of the scientific understanding of AD, reduce clinical trial costs, and thereby expedite drug development



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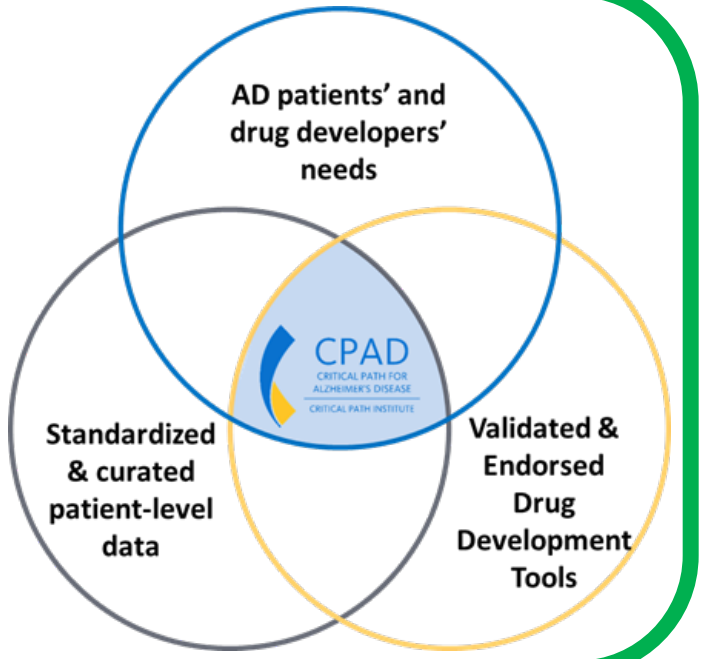
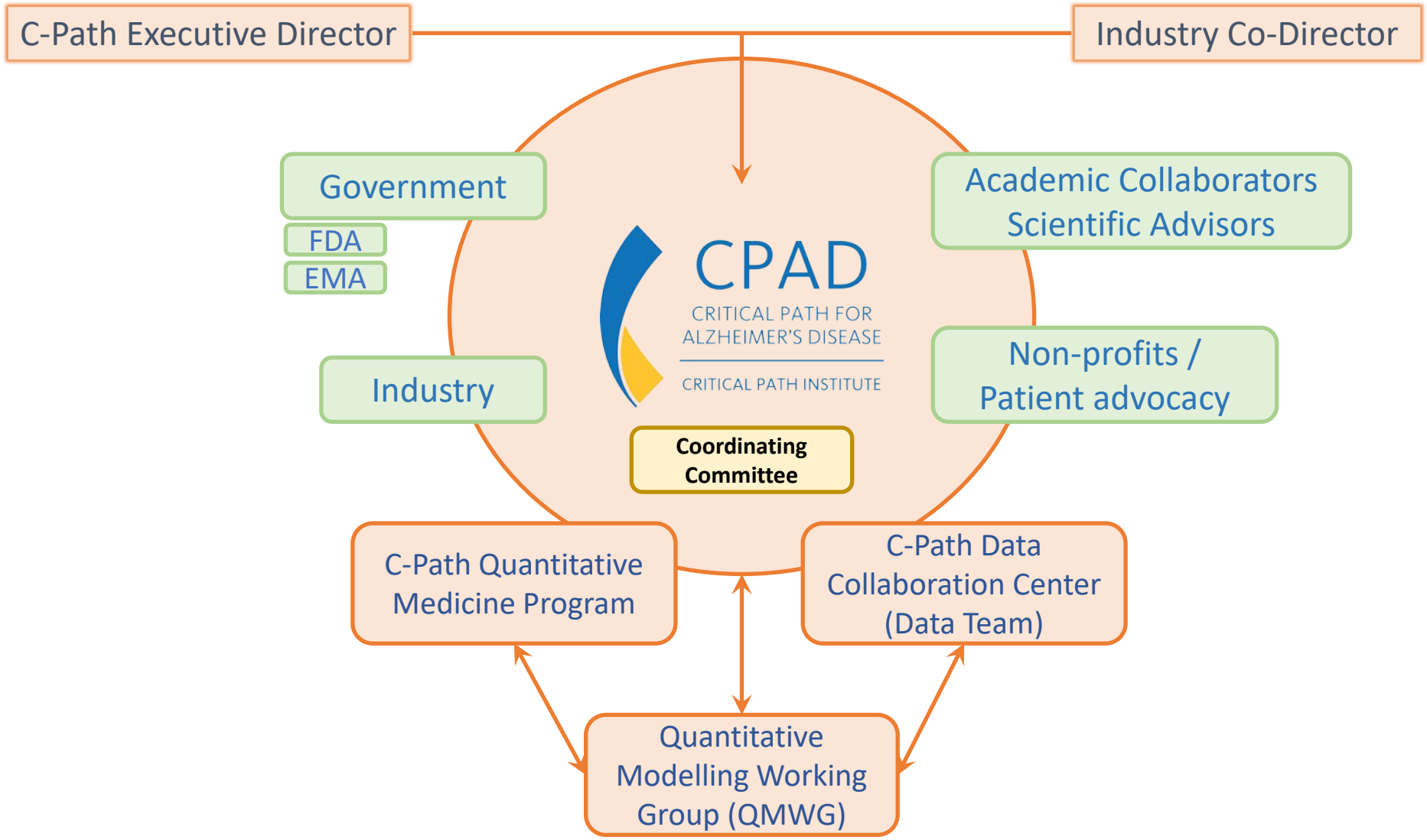
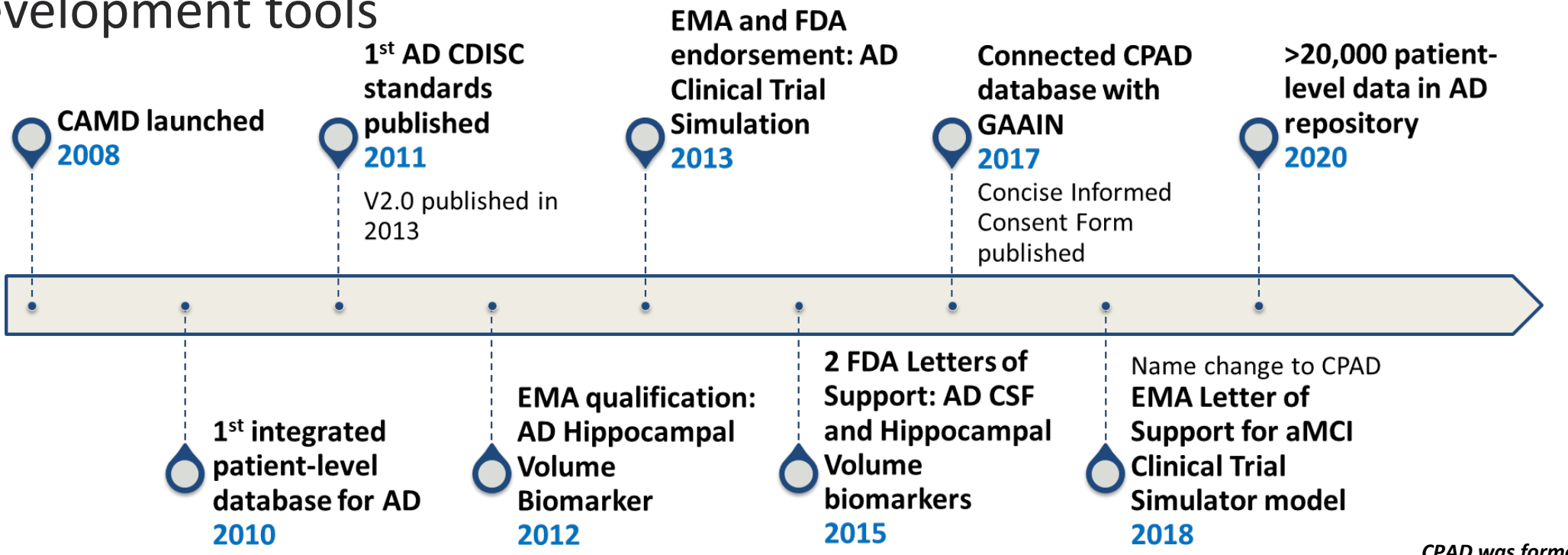


CPAD Governance



Scientific and Regulatory Expertise

- Enable iterative EMA/FDA/PMDA participation in developing new methods to assess the safety and efficacy of medical products
- Official regulatory endorsement of novel methodologies and drug development tools



CPAD was formerly called CAMD

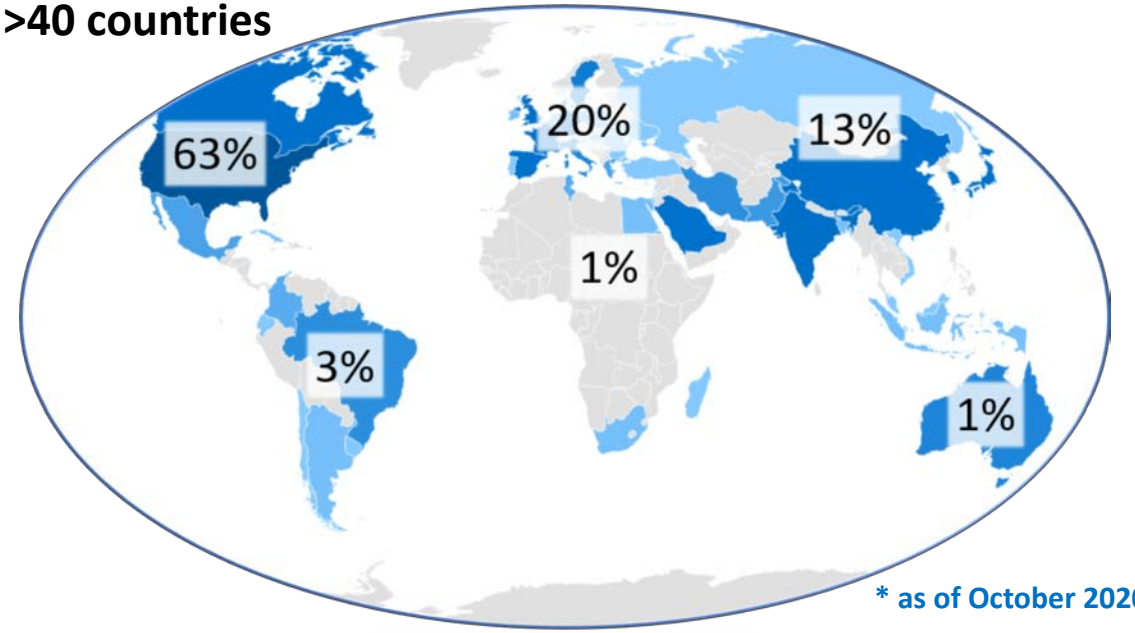
Consortium Stats

- **41 AD studies with 20,549 individual anonymized patient records and more than 420,000 covariate measurements**

(shared by Abbott Laboratories, AstraZeneca, Bellus Health, Eisai, Forest Laboratories, GlaxoSmithKline, Lundbeck, Johnson & Johnson, Novartis, Pfizer, Sanofi, Servier, Takeda, vTv Therapeutics, Washington University (DIAN) and ADCS)

456* approved applicants from >150 distinct institutions from >40 countries

- **Pharmaceutical Industry**
- **Government Agencies**
- **Non-profit Organizations**
- **Academia**
- **Independent Researchers**



*** as of October 2020**

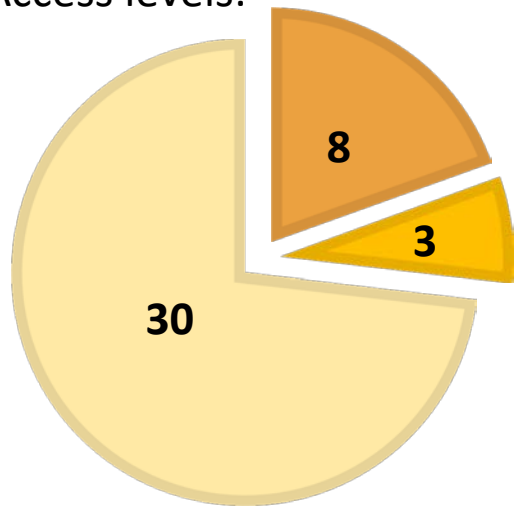
- **19 Members**

Studies Integrated Into the CPAD Data Repository

Name	Contributors	# of Subjects
ABT89	Abbott	102
SIROC	AstraZeneca	164
EFC24	Sanofi	719
EFC46	Sanofi	644
COX2	Pfizer	140
GSK670	GSK	494
GSK672	GSK	500
GSK640	GSK	166
LEADE	Pfizer	326
DON2	Pfizer	146
E402	Eisai	57
E412	Eisai	821
P302	Pfizer	162
P311	Pfizer	105
P304	Pfizer	274
DON1	Pfizer	144
FMD12	Forest Labs	216
FMD10	Forest Labs	202
E315	Eisai	167
E401	Eisai	137
ANM	King's College	279
GAL11	J&J	492
HC	ADCS	601
E231	Eisai	105
E312	Eisai	217
CL2005	Servier	53
CL2009	Servier	23
CL2011	Servier	179
CL2012	Servier	200
ADNIGO	ADCS	621
ADNI	ADCS	1431
ADNI2	ADCS	1694
ADNI3	ADCS	1114
INNTST	Innogenetics	373
INDDEX	Novartis	394
MEGA	Eisai	2055
WUCSF	Washington Univ.	507
WUMRI	Washington Univ.	144
NEURCH	Bellus Health	679
STDFST	vTv	208
TOMM	Takeda	3494
TOTAL	**41 studies**	**20549**

CPAD Data Repository

Access levels:



Please email questions to ykarten@c-path.org

Industry Data Sharing Initiative – Prioritized AD Trials

Sponsor	Trial	Treatment	Stage	ApoE	Imaging	Fluid	Subjects
Takeda	*TOMMORROW*	Pioglitazone	Cognitively Unimpaired	Y	vMRI		3,494
Janssen / Pfizer	*ApoE4 Carrier/Non-Carrier*	Bapineuzumab	Mild to Moderate	Y	vMRI, Aβ-PET	Aβ, t-tau, p-tau	1,331/1,121
Novartis / Amgen	*GENERATION S1 / S2*	Umibecestat	Cognitively Unimpaired	Y	vMRI, PET (Aβ, tau)	Aβ, t-tau, p-tau	480/1,145
Eli Lilly	*EXPEDITION1, 2 and 3*	Solanezumab	Mild to Moderate	Y	vMRI, Aβ-PET	Aβ	1,000/1,040/2,129
Eli Lilly / AstraZeneca	*AMARANTH / DAYBREAK-ALZ*	Lanabecestat	MCI	Y	vMRI, PET (Aβ, tau)	Aβ, t-tau, p-tau	2218/1722
Biogen	*EMERGE / ENGAGE*	Aducanumab	MCI, Mild	Y	vMRI, PET (Aβ, tau)	t-tau, p-tau	1,638/1,647
Eisai / Biogen	*MissionAD1 / AD2*	Elenbecestat	MCI, Mild		vMRI, PET (Aβ, tau)	Aβ, t-tau, p-tau	950/950
Eisai / Biogen	*NCT01767311*	BAN2401	MCI, Mild	Y	vMRI, Aβ-PET	Aβ, t-tau, p-tau	800
Eisai / Biogen	*Clarity AD*	BAN2401	MCI	Y	vMRI, PET (Aβ, tau)	Aβ, t-tau, p-tau, NfL	1,566
Roche	*CREAD/CREAD 2*	Crenezumab	Prodromal to Mild	Y	vMRI, PET (Aβ, tau)	Aβ, t-tau, p-tau	813/806
Roche	*GRADUATE 1 / 2*	Gantenerumab	Prodromal or Mild		vMRI, PET (Aβ, tau)	Aβ, t-tau, p-tau	814/760
Merck	*EPOCH/APECS*	Verubecestat	Mild to Moderate	Y	vMRI, Aβ-PET		2,211/1,454

Data in-house	DCA executed Pending data transfer	DCA execution in progress	Contact initiated w/ data contributor Strong support for data sharing *	Contact initiated Discussions on hold

MCI = Mild Cognitive Impairment, DCA = Data Contribution Agreement

* data sharing discussions to continue once their internal milestones are reached and/or when ongoing studies are completed.

Industry Data Sharing Initiative – Successes

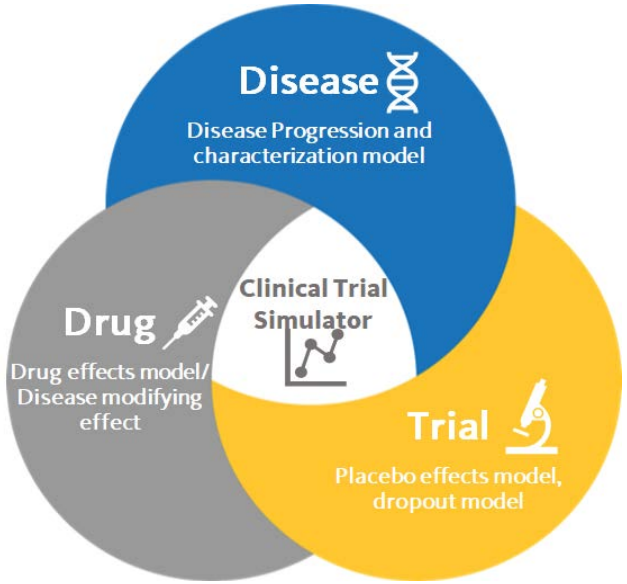
Sponsor	Trial/Study	Treatment	Rationale	Subjects
H. Lundbeck A/S	Lu AE58054	Idalopirdine	moderate AD	**278**
H. Lundbeck A/S /Otsuka	STARSHINE	Idalopirdine	mild to moderate AD; APOE4	**933**
H. Lundbeck A/S	STAR Ext.	Idalopirdine		**1,463**
H. Lundbeck A/S /Otsuka	STARBEAM	Idalopirdine		**858**
H. Lundbeck A/S /Otsuka	STARBRIGHT	Idalopirdine		**734**
Washington University/NIA	DIAN-obs	n/a	mutation carriers and non-carriers; Aβ- and FDG-PET; vMRI; fluid BM (Aβ40, Aβ42, t-tau, p-tau)	**700**

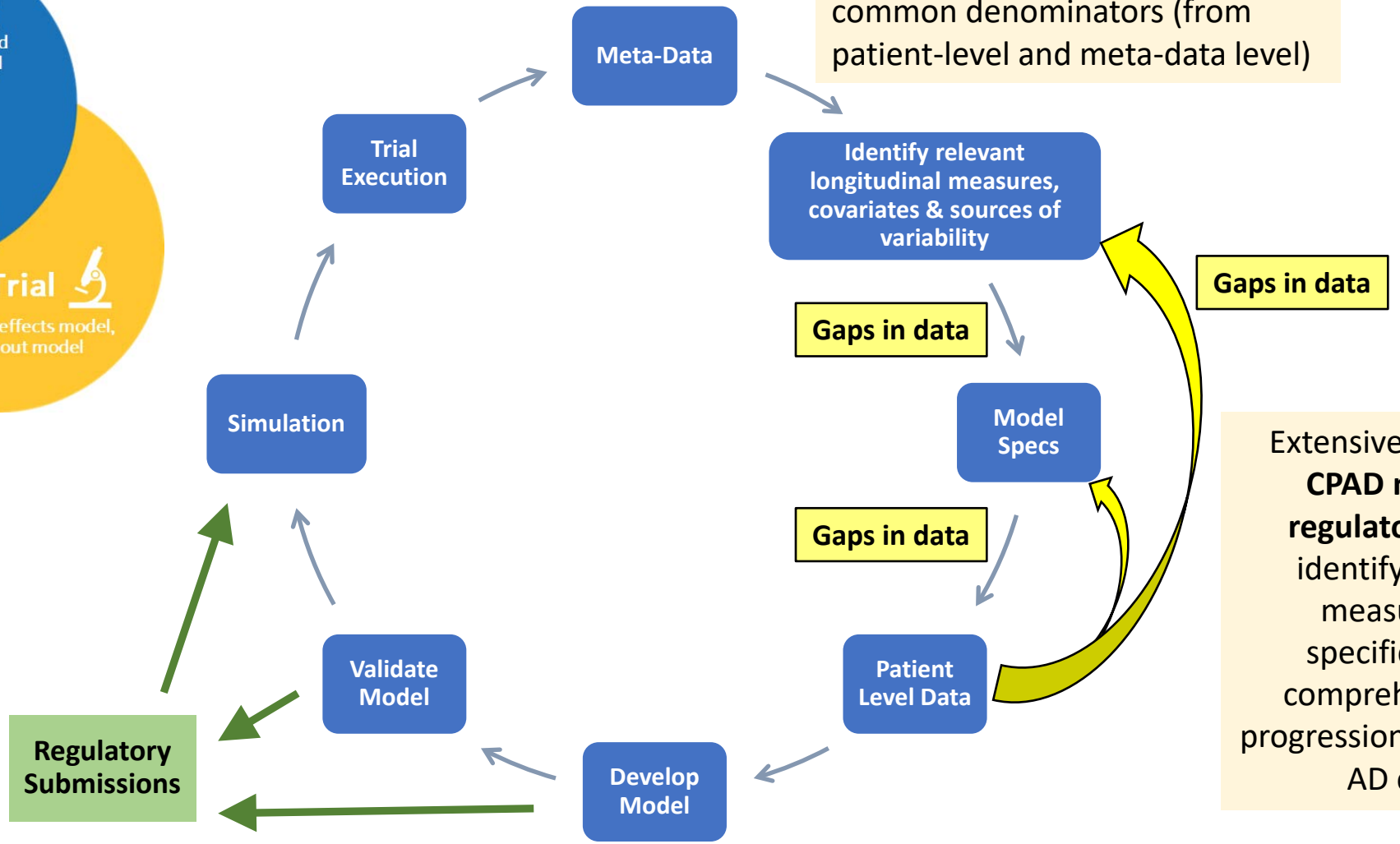
Other trials and studies

Sponsor	Trial/Study	Treatment	Rationale	Subjects
Eli Lilly and others	A4 $	Solanezumab	APOE4, Aβ- and tau-PET; vMRI; fluid BM (Aβ, t-tau, p-tau)	**6945** *
CSIRO and others	AIBL $	n/a	APOE4, Aβ-PET; vMRI	**862**
Skane University Hospital/Lund University	BioFINDER #	n/a	APOE4, FDG-, Aβ- and tau-PET; vMRI; fluid BM (Aβ, t-tau, p-tau)	**900**

** Screening data only. $ Downloaded from LONI. # Contact initiated; future dataset*

CPAD – Quantitative Strategy and Objectives

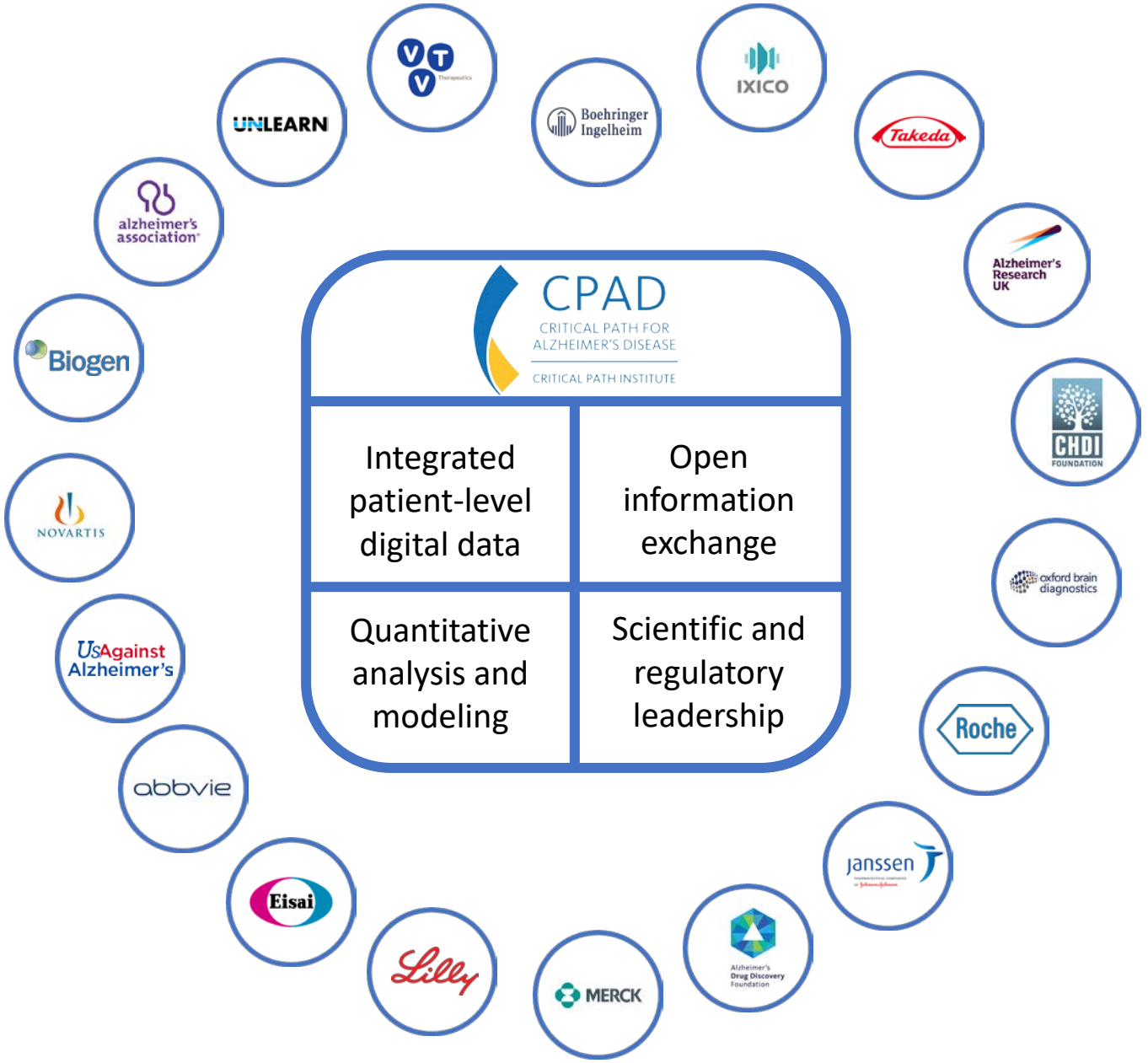




Dataset exploration to identify common denominators (from patient-level and meta-data level)

Extensive discussion with **CPAD members** and **regulatory agencies** to identify variables and measures for core specifications of the comprehensive disease progression model across the AD continuum

Adapted from Josh Cosman



Adapted from Josh Cosman

CPAD IS UNIQUELY FOCUSED ON DEVELOPMENT IN A TRULY NEUTRAL PRE-COMPETITIVE ENVIRONMENT WITH ESTABLISHED SUPPORT OF BOTH INDUSTRY AND REGULATORS

Adapted from Josh Cosman

2020 Annual Meeting & Regulatory Science Workshop

- Scientific dialogue to guide the strategic development of comprehensive disease progression models spanning the AD continuum by utilizing advanced quantitative modeling methodology, such as nonlinear mixed effects approaches, artificial intelligence and machine learning.

- Achieve consensus on gaining actionable information from fluid and imaging biomarker data for use in quantitative analysis and disease progression modeling, for the purpose of developing regulatory-endorsed model-informed quantitative Drug Development Tools in Alzheimer's Disease.

2020 Annual Meeting & Regulatory Science Workshop

- Theme and Objective
  - Increased Data Sharing
  - Integration of biomarkers into quantitative modeling
  - Regulatory-grade quantitative drug development solutions
- Expert speakers and panelists
  - CSF, plasma and imaging biomarkers
  - Challenges and opportunities

Due to confidential, unpublished information that will be discussed:

Please, no recording or screenshots of the presentations.