



NOVEL PARTNERSHIPS TO TACKLE CNS DISEASES

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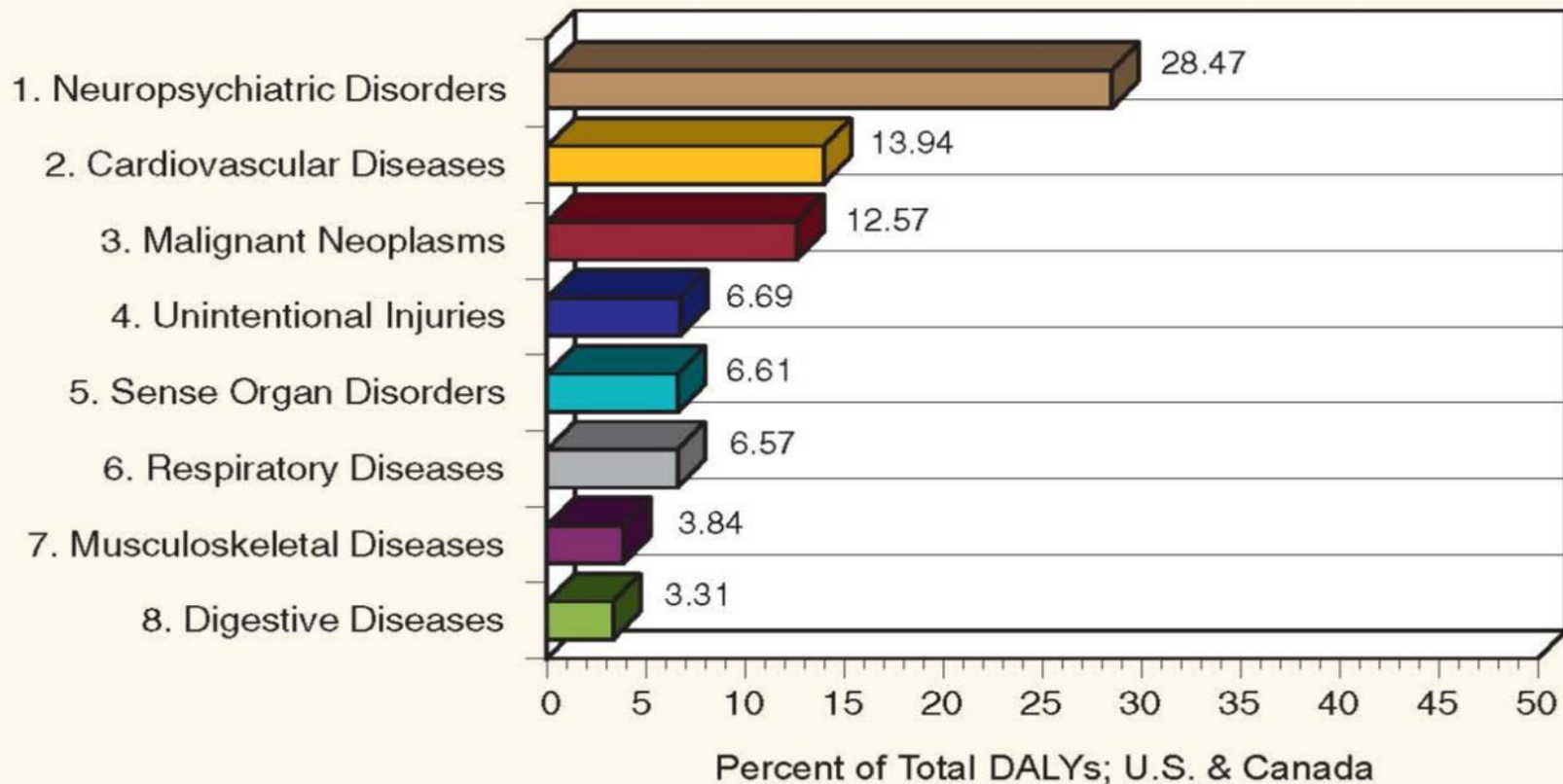
World CNS Summit

February 17th 2015

CNS DISEASES REMAIN A SIGNIFICANT HEALTH BURDEN



**Burden of Disease:
Lead Contributing Disease Categories to DALYs**

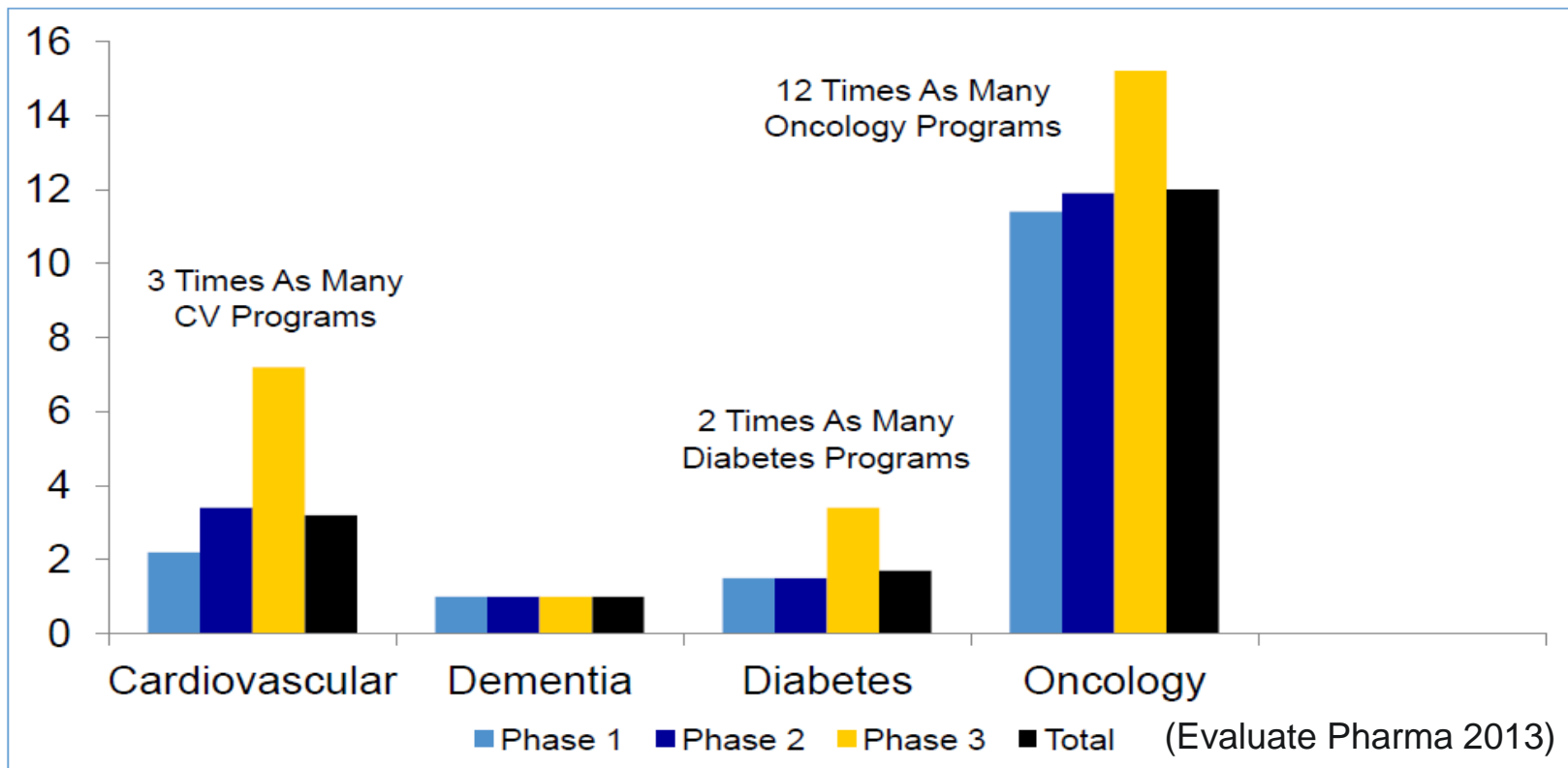


Data courtesy of WHO

INDUSTRY IS UNDERINVESTING IN NEUROSCIENCE R&D



Focus on Unmet Need in Dementia Relative Number of Drugs in Development (Index Dementia=1)



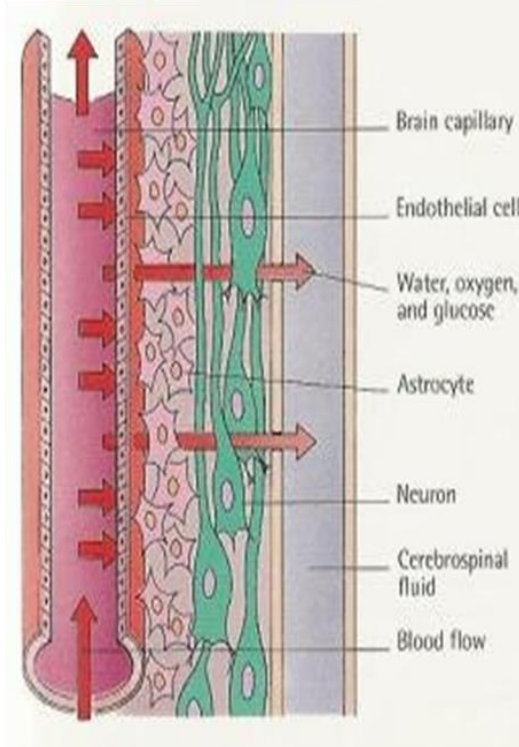
WILL MORE BIG PHARM COS RETURN TO CNS ?

R&D Cuts Curb Brain-Drug Pipeline

THE WALL STREET JOURNAL.

Development of new medicines for brain disorders could be threatened as major drug makers scale back research

March 27, 2011



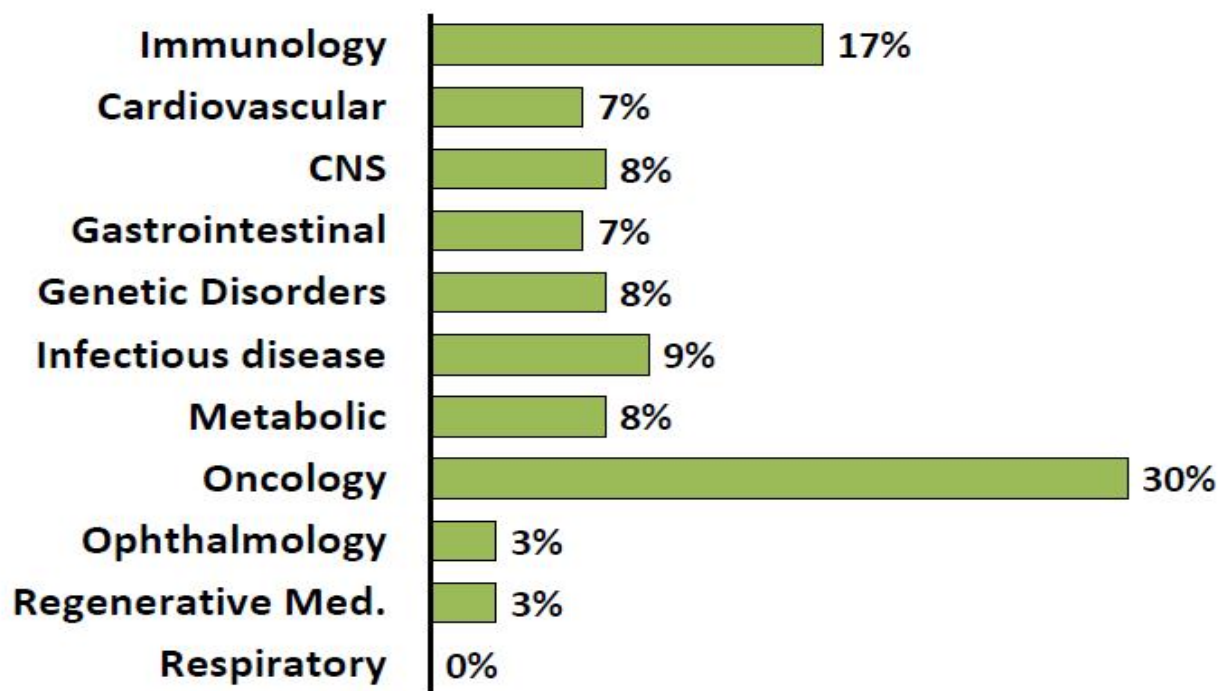
INVESTOR APPETITE FOR CNS LAGS OTHER AREAS



BioCEO & INVESTOR
CONFERENCE



Which therapeutic areas offer the best investment opportunities?



FDA APPROVALS FOR 2014 – 44 NEW DRUGS APPROVED! ... BUT ONLY 4 FOR CNS

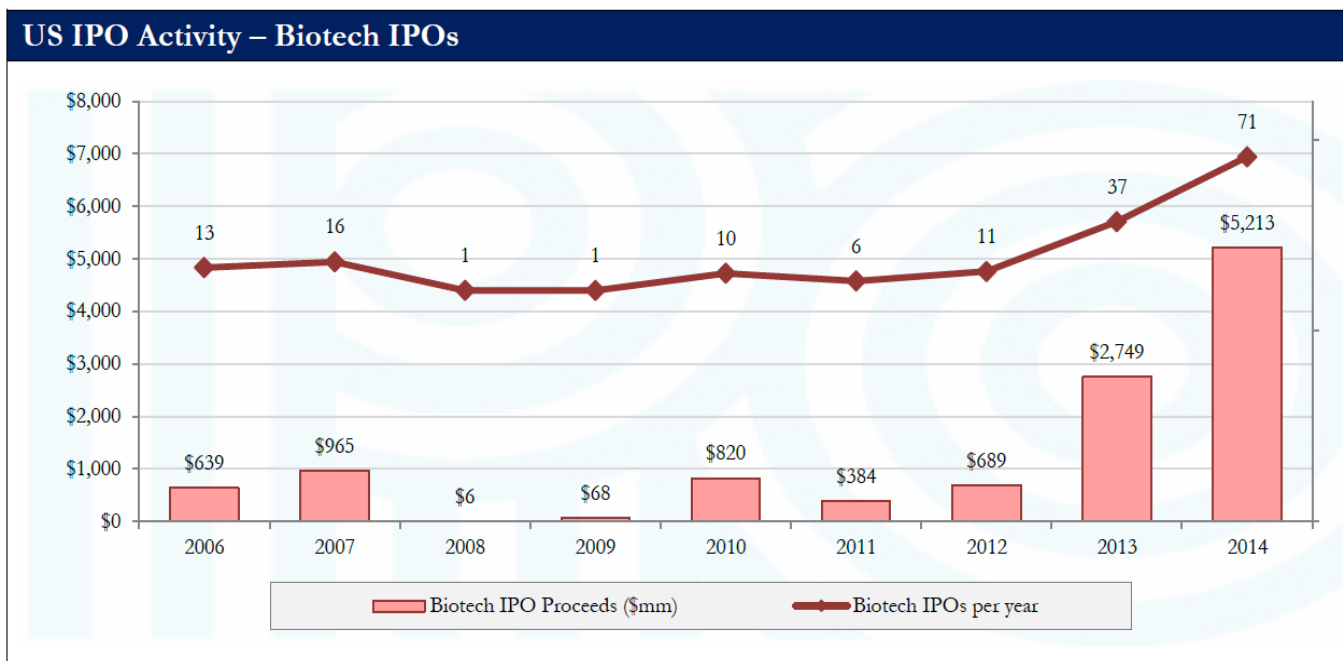


Therapeutic category	No of drugs approved	Percent of total	New modes of action
Infectious diseases	12	27%	4
Cancer	8	18%	4
Rare diseases	5	11%	4
Endocrine System	4	9%	0
Nervous System	4	9%	1
Hematology	4	9%	0
Respiratory	3	7%	2
Cardiovascular	1	2%	1
Digestive System	2	5%	0
Immune system	1	2%	1

Source: Calculated from FDA data

Brand	Company	Indication	MOA
Nothera	Chelsea	Orthostatic hypotension	synthetic norepinephrine
Plegridy	Biogen	Multiple Sclerosis (RRMS)	interferon beta-1a
Hetlioz	Vanda	Non-24 sleep wake disorder	melatonin receptor agonist
Belsomra	Merck	Insomnia	orexin receptor antagonist

IPOS FOR 2014 – 71 DEALS COMPLETED! ... BUT ONLY 5 FOR CNS



Source: Renaissance Capital. Includes IPOs with a market cap of at least \$50 million and excludes closed-end funds and SPACs. Data through 12/31/14.

Therapeutic Area	Number	Percent
Oncology	18	25%
Infectious diseases	12	17%
Rare/Orphan	11	15%
Diagnostics	6	8%
Biosimilars/Generics	6	8%
Immunology	5	7%
CNS	5	7%
Other	8	11%

PERCEPTION OF CNS IS THAT RISK IS HIGHLY STACKED



NON-CNS VS CNS – THE VITAL STATS



	Non-CNS	CNS
POS in Ph 3	66.0 %	46.0 %
POS overall	15.0 %	8.0 %
Ph 2 + 3 devt time	6.1 years	8.1 years
NDA to Approval time	1.2 years	1.9 years
Ave patient # in trials	300-500	10,000-60,000
Ave cost of devt	\$600M-1.0B	\$1.0B-\$5.0B

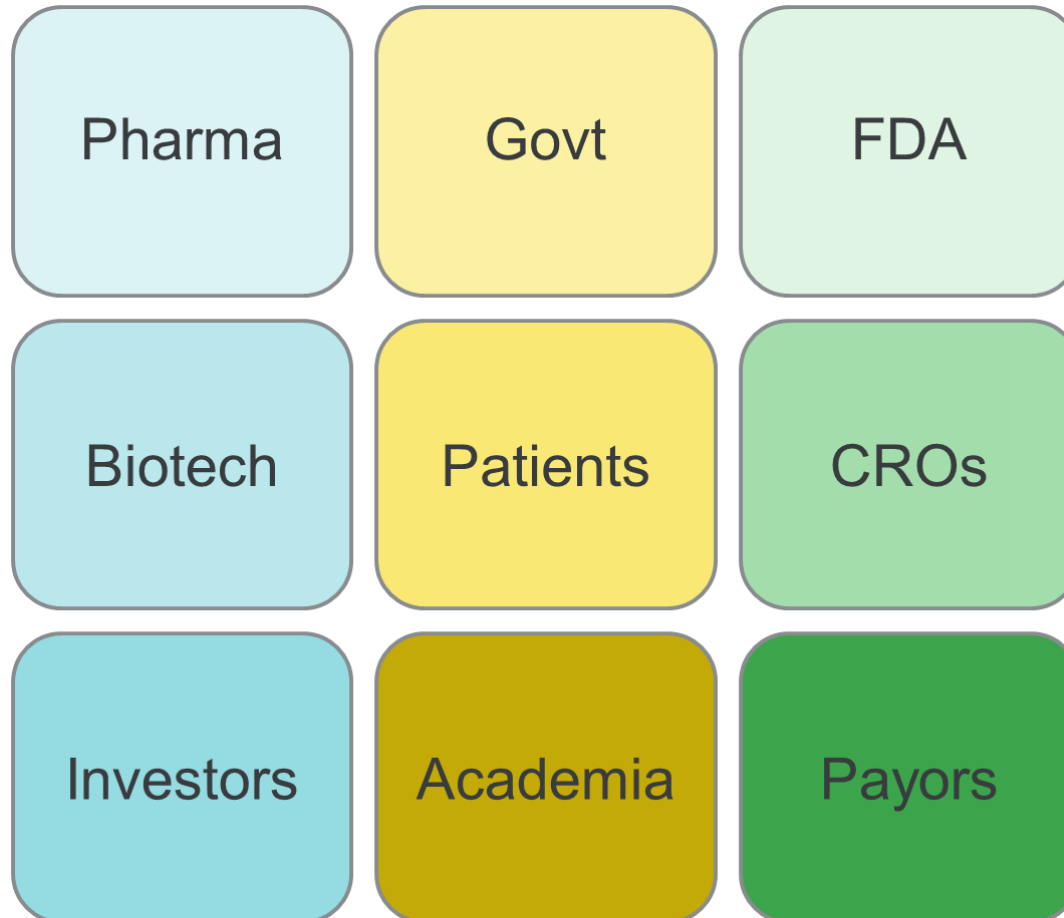
Source: Tufts Center for Drug Discovery & Development, 2012

INVESTORS DILEMMA – THE CNS ROI PROBLEM

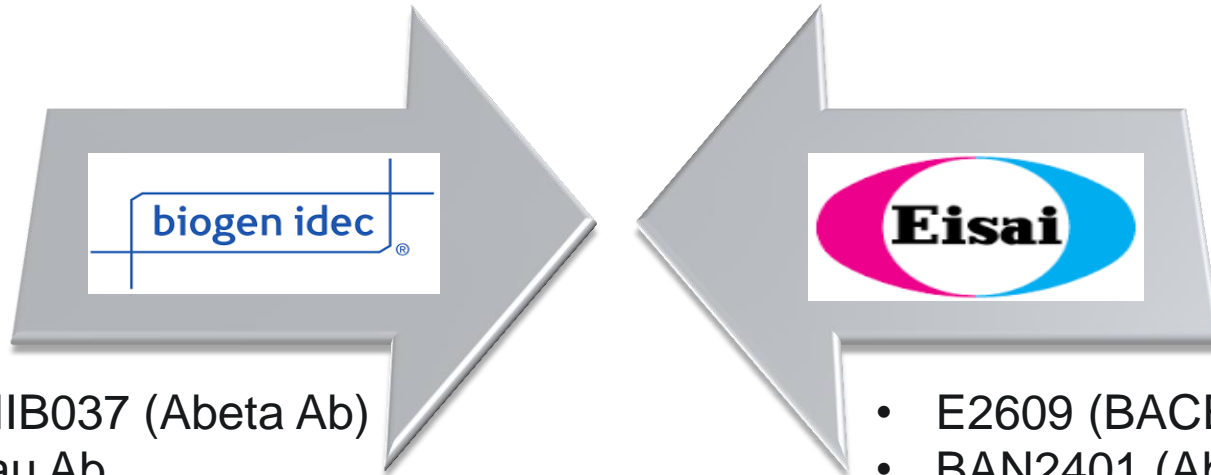


$$\text{Return on Investment (ROI)} = \frac{\text{Market Revenue Potential (\$)}}{\text{Invested Capital (\$)}} \times \text{Probability of Success (POS)}$$

PARTNERSHIPS AMONGST KEY STAKEHOLDERS



BIOGEN-EISAI – PHARMA/BIOTECH SHARE RISK IN AD



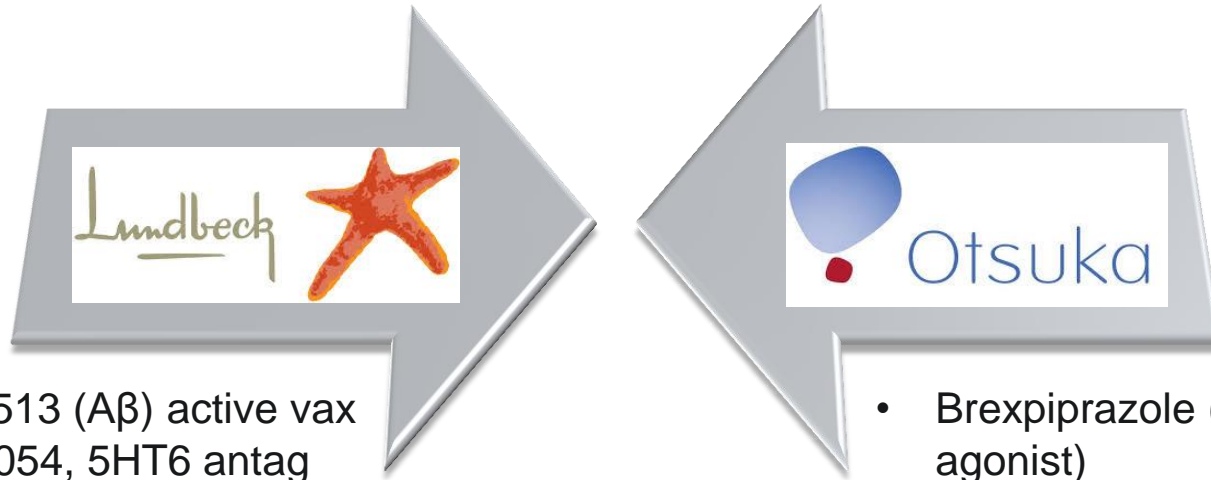
- BIIB037 (Abeta Ab)
- Tau Ab

- E2609 (BACE inhibitor)
- BAN2401 (Abeta Ab)

Biogen-Eisai collaborate on AD Therapeutics (March 2014)

Both companies will share the costs and potential profits, as well as co-promote the drug candidates should they eventually win approval from regulators.

LUNDBECK-OTSUKA – PHARMA/BIOTECH SHARE RISK IN AD



- Lu AF20513 (A β) active vax
- Lu AE58054, 5HT6 antag

- Brexpiprazole (D2 partial agonist)

Lundbeck-Otsuka expand collaboration in AD (2013)

In a series of separate partnerships Lundbeck/Otsuka combined several AD assets. Both companies will share the costs and potential profits, as well as co-promote the drug candidates should they eventually win approval from regulators.

OTHER RECENT EXAMPLES OF RISK SHARING IN AD



- **Lilly/TPG/Quintiles (July 2008):** Lilly announced an agreement with TPG-Axon Capital and Quintiles under which they will pay up to \$325 million in development funding for its two lead Alzheimer's disease compounds, a gamma secretase inhibitor and an A-beta antibody, each ready to begin Ph3 testing. TPG and Quintiles receive future milestones and royalties.
- **JNJ/Elan (July 2009):** J&J's purchase of Elan's Alzheimer's immunotherapy program for \$1.0B via a stock purchase plan that gives JNJ approximately 25% of future profits of bapinuzemab. JNJ is also required to provide an additional \$500M in development costs.
- **AstraZeneca and Lilly (September 2014):** Parties announce alliance to develop and commercialise BACE inhibitor AZD3293 for Alzheimer's disease. Lilly will pay AZ up to \$500 million in development and regulatory milestone payments. The companies will share all future costs equally for the development and commercialisation of AZD3293, as well as net global revenues post-launch.

ALZHEIMER'S DISEASE NEUROIMAGING INITIATIVE (ADNI)

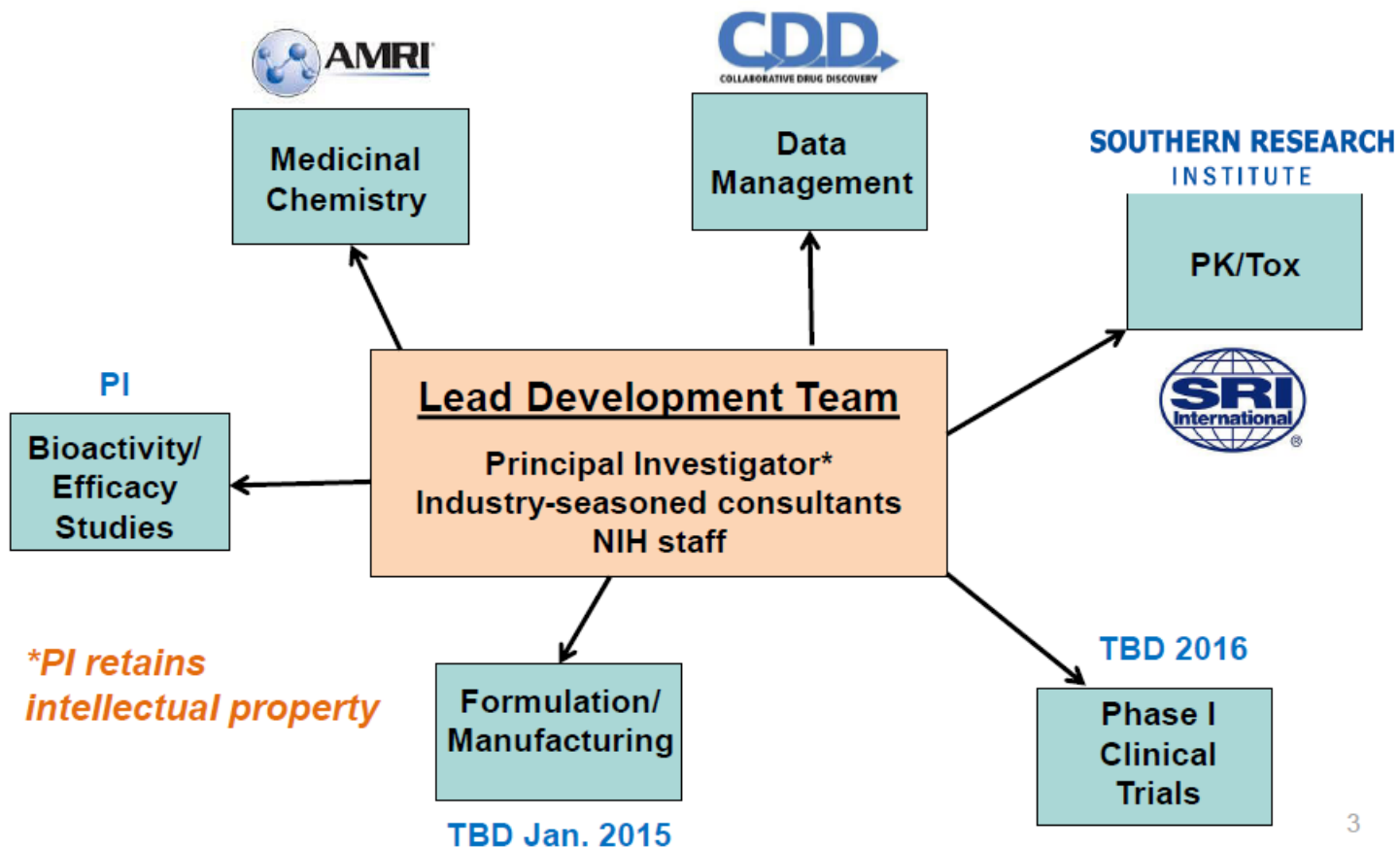


PUBLIC-PRIVATE PARTNERSHIPS FOR AD TRIALS



- **DIAN** - Dominantly Inherited Alzheimer Network (DIAN). DIAN is an international research partnership studying autosomal dominant forms of AD (PS1, PS2, and APP mutations). Funded by a multiple-year research grant from the National Institute on Aging. chosen two investigational monoclonal antibodies (solanzemab-Lilly and gantenerumab-Roche) for clinical trials that will try to prevent dementia in people who are on the path to Alzheimer's disease due to an inherited autosomal-dominant mutation.
- **A4** - Anti-amyloid Treatment in Asymptomatic Alzheimer's Disease (A4) prevention clinical trial. This is the first time investigators will test an A β -clearing drug (solanzemab-Lilly) in older people thought to be in the pre-symptomatic stage of Alzheimer's. The trial will enroll 1,000 people 70 and older with evidence of amyloid in their brains, but who do not show clinical symptoms of the disease.
- **Alzheimer's Prevention Initiative Autosomal Dominant Alzheimer's Disease Treatment Trial.** Genentech, Banner Alzheimer's Institute, and the NIH will together spend \$96 million to test Genentech's crenezumab, a mAb that binds A β , in people certain to develop early Alzheimer's disease owing to autosomal dominant gene mutations (PS1).

NINDS BLUEPRINT NEUROTHERAPEUTICS



SMA FOUNDATION – PTC THERAPEUTICS – ROCHE



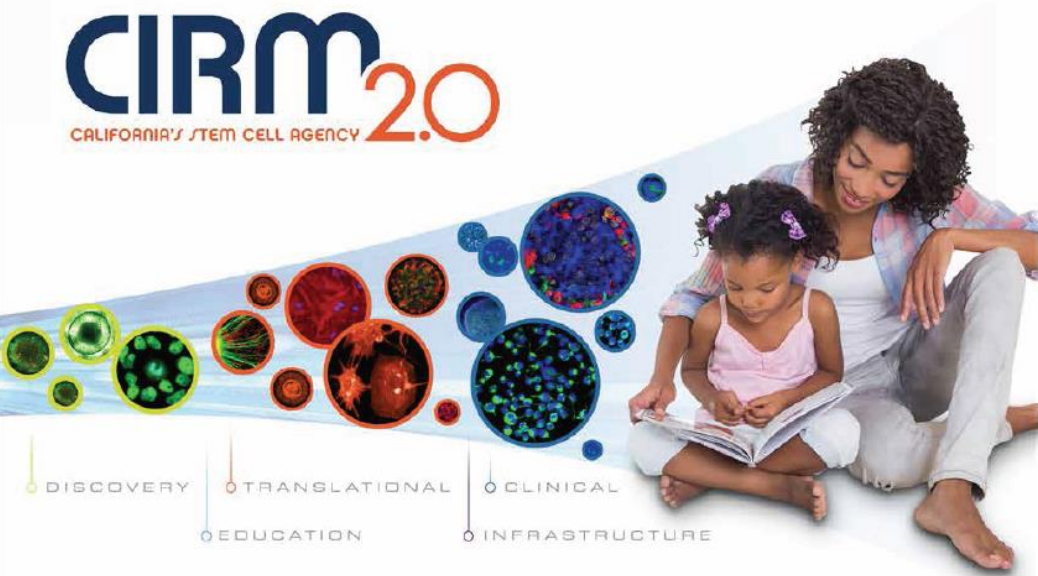
- \$13.3M to PTC to fund SMA exon skipping small molecule program
- SMA foundation to receive future single digit royalties
- \$30M to PTC from Roche to fund SMA discovery program
- 2 year FTE funding
- Milestones up to \$325M
- Royalties on sales
- Exclusive right to develop and commercialize SMA program world wide

ABLEXIS – CONSORTIA TO FINANCE DISCOVERY TOOLS



- VCs finance Ablexis with a \$13M Series A
- Pharma(s) pay \$XM consortia entrance fee
- Ablexis delivers Ab platform to meet pre-specified specs by certain date
- Pharma(s) pay \$YM milestone payment upon delivery of Ab platform

CIRM – PROVIDING INCENTIVES FOR STEM CELL THERAPY



- Currently with >\$3B in funding for over 300 projects
- Focus primarily on cell therapy
- Requires California base
- Cost sharing mechanisms available for private industry

Applicant Type	Pre-Clinical	Phase 1	Phase 2	Phase 3*	Supplement
Non-Profit	None	None	40%	50%	40%
For-Profit	20%	30%	40%	50%	40%

*CIRM contribution not to exceed \$20 million

PHARMA-PAYOR/PROVIDER ALLIANCES



13G Johnson & Johnson (J&J) — AOK and Care4s

Nationwide network for integrated outpatient care for schizophrenia patients in Lower Saxony region of Germany:

- ▶ Case managers and nurses build the team on site.
- ▶ Structured treatment path with psycho-educational or drug adherence and shared decision-making initiatives are in place.
- ▶ Patients and relatives are active in the decision process.

Merck — M2Gen

Merck's for-profit collaboration with H. Lee Moffitt Cancer Center aims to improve cancer care with personalized treatments.

Moffitt's M2Gen database of genetic data derived from tumor tissue samples and clinical information from 85,000 patients allows researchers to match molecular signatures of patients' cancers with treatments.

AstraZeneca — Healthcore

AstraZeneca and HealthCore (WellPoint's health outcomes based subsidiary) are conducting retrospective and prospective studies to determine effective and economical treatments for chronic diseases.

Fresenius — Aetna

A patient-centric care coordination program is improving clinical outcomes and reducing costs by slowing the progression of chronic kidney disease in members and facilitating gentler, less costly transitions to dialysis or pre-transplant care. The program is enhancing coordination of care among specialists, primary care providers and nurses.

Merck — Camden Coalition of Healthcare Providers

Merck Foundation committed \$15 million in 2009–2013 to fund the Alliance to Reduce Disparities in Diabetes, a public/private partnership encouraging *evidence-based collaborative approaches* to improve care and reduce care disparities in low-income, underserved populations.

Abbott — Anthem BCBS, UHC*, Humana, Cincinnati doctors**

Cincinnati Patient-Centered Medical Home (PCMH) Pilot and Co-Pilot Project is organized under the Aligning Forces for Quality (AF4Q) initiative.

The project is sponsored by Health Improvement Collaborative of Greater Cincinnati and funded by Anthem BCBS, Humana, Abbott, UHC* and various physician practices.

Sanofi-Aventis — Baltimore County Dept. of Aging, John A. Hartford Fdn and NCOA

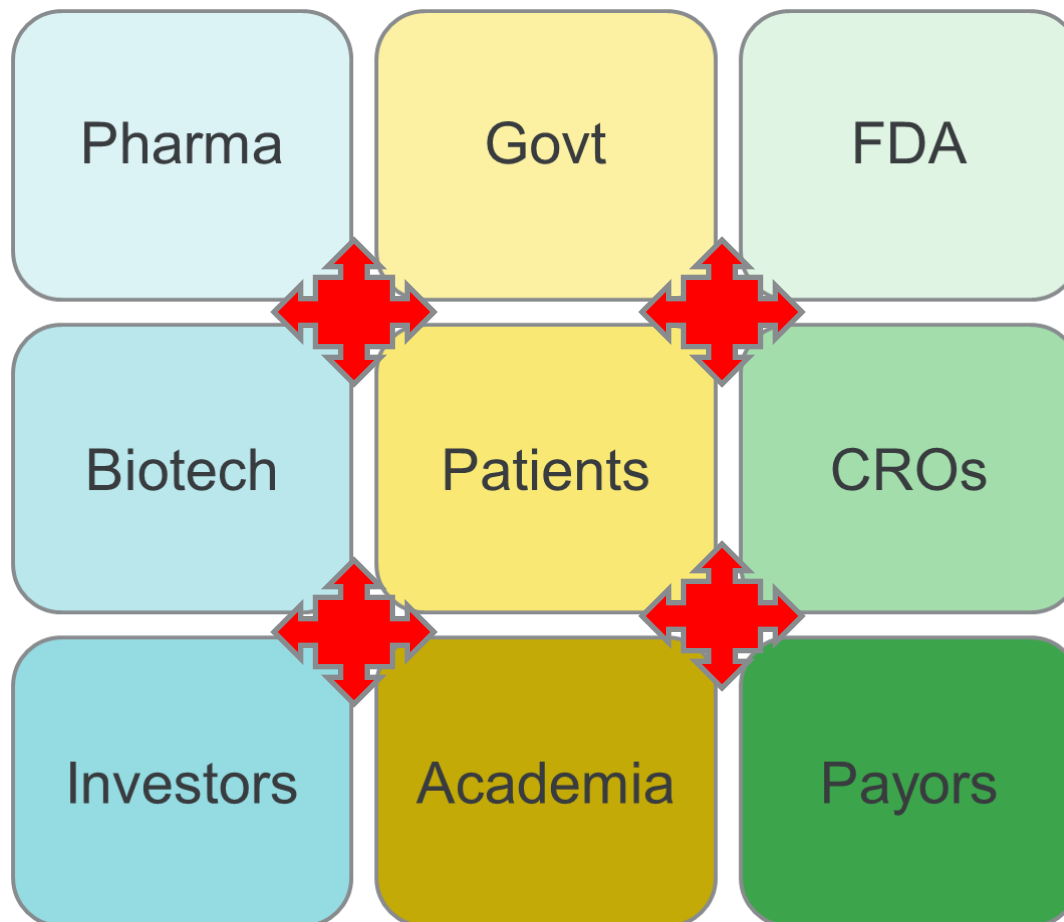
Sanofi-Aventis, the Baltimore County Department of Aging, the John A. Hartford Foundation and the National Council on Aging (NCOA) launched a pilot program to help physicians connect older patients with diabetes to evidence-based education and wellness support.

Lilly — Anthem BCBS and five other Indiana-based Health Care Provider (HCPs)

The alliance aims to achieve better outcomes for diabetes patients. Policyholders of Anthem BCBS who have diabetes, but have performed their testing, will receive reminder phone calls.

*UHC=United Healthcare; **BCBS=BlueCross BlueShield Association

PARTNERSHIPS AMONGST KEY STAKEHOLDERS ...CRITICAL TO TACKLE CNS DISEASES



 THANK YOU