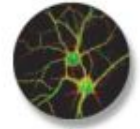


# Corporate Presentation

Bharatt Chowrira, CEO

January 2012



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# Addex Pharmaceuticals

- Addex is located in Geneva, Switzerland
- ADXN is traded on the SIX Swiss Stock Exchange
- 85 people / founded in 2002
- Focus: pioneering oral small molecule allosteric modulation-based drug discovery and development

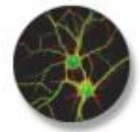


# key value drivers

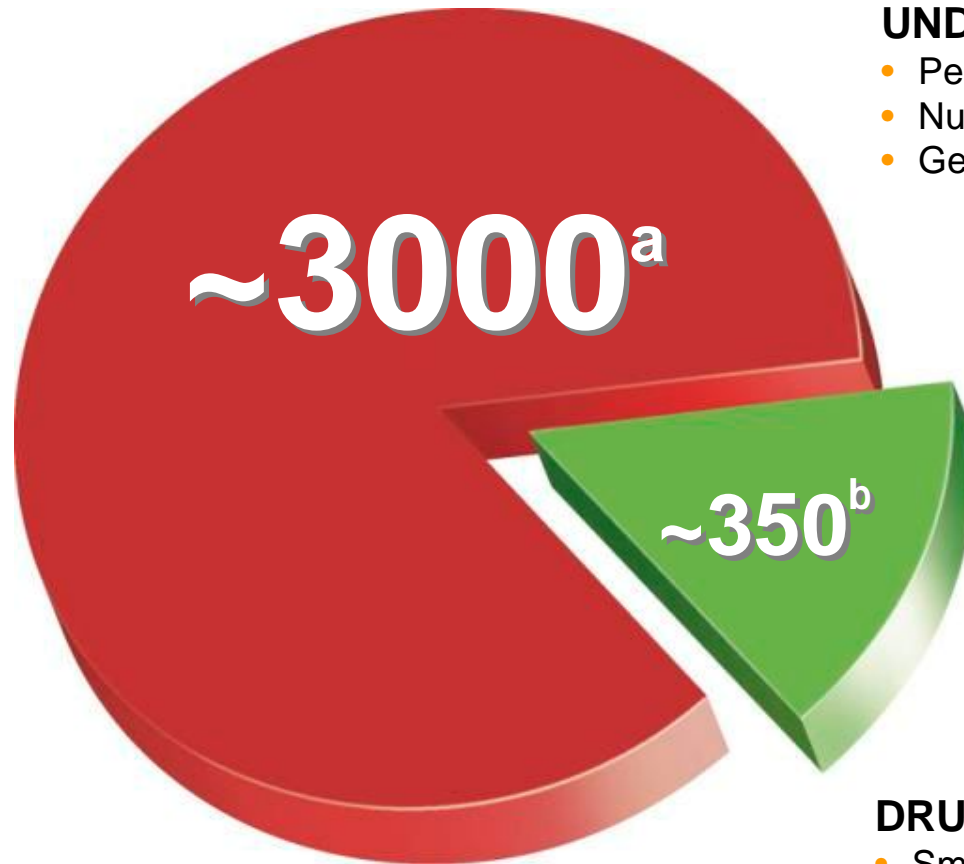
Leading allosteric drug discovery	<ul style="list-style-type: none"><li>• Proprietary 70,000 allosteric-biased small molecule library</li><li>• Proprietary HTS systems</li><li>• Deep allosteric know-how &amp; expertise</li></ul>
Validated emerging therapeutic class	<ul style="list-style-type: none"><li>• Proven mechanism, that has led to marketed products</li><li>• Significant investment from all major pharma</li><li>• Growing pipeline of allosteric modulators in the clinic</li></ul>
Robust pipeline	<ul style="list-style-type: none"><li>• 2 Phase II programs</li><li>• 8 preclinical programs</li><li>• Unmatched track record advancing allosteric modulators</li></ul>
Partnership with leading pharma	<ul style="list-style-type: none"><li>• Janssen Pharmaceuticals Inc. (JPI) for mGluR2 PAM in Phase II testing for schizophrenia</li></ul>
Dominant IP portfolio	<ul style="list-style-type: none"><li>• 13 issued patents</li><li>• 45 pending patents</li></ul>
Strong balance sheet	<ul style="list-style-type: none"><li>• CHF50 (US\$62 / €43) million at June 30, 2011</li><li>• No debt</li></ul>



# allosteric drug discovery



# drug discovery challenge



## UNDRUGGED TARGETS

- Peptides/biologics
- Nucleic acid based therapeutics
- Gene therapy/vaccines

## DRUGGED TARGETS

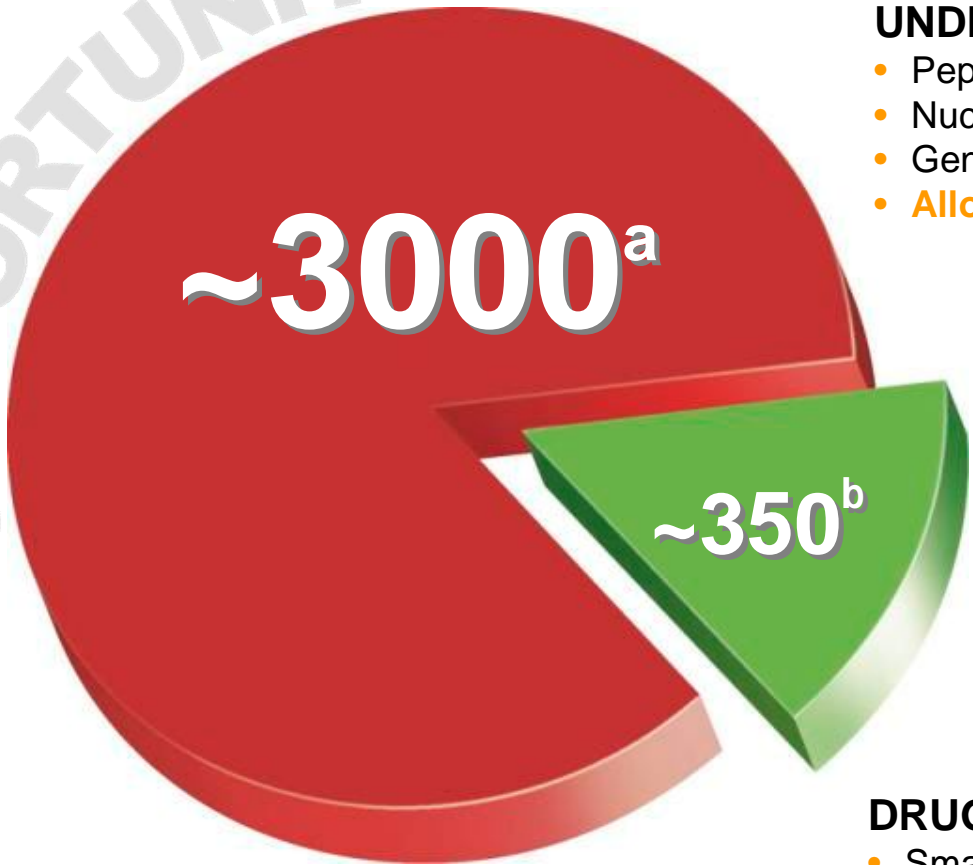
- Small molecules
- Peptides/biologics



<sup>a</sup>Overington et al. Nature Reviews Drug Discovery 5, 993–996 (December 2006)  
<sup>b</sup>Goh et al. PNAS 104 (21), 8685–8690, (May 22, 2007)

# drug discovery opportunity

OPPORTUNITY

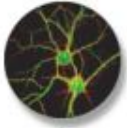


## UNDRUGGED TARGETS

- Peptides/biologics
- Nucleic acid based therapeutics
- Gene therapy/vaccines
- **Allosteric modulators**

## DRUGGED TARGETS

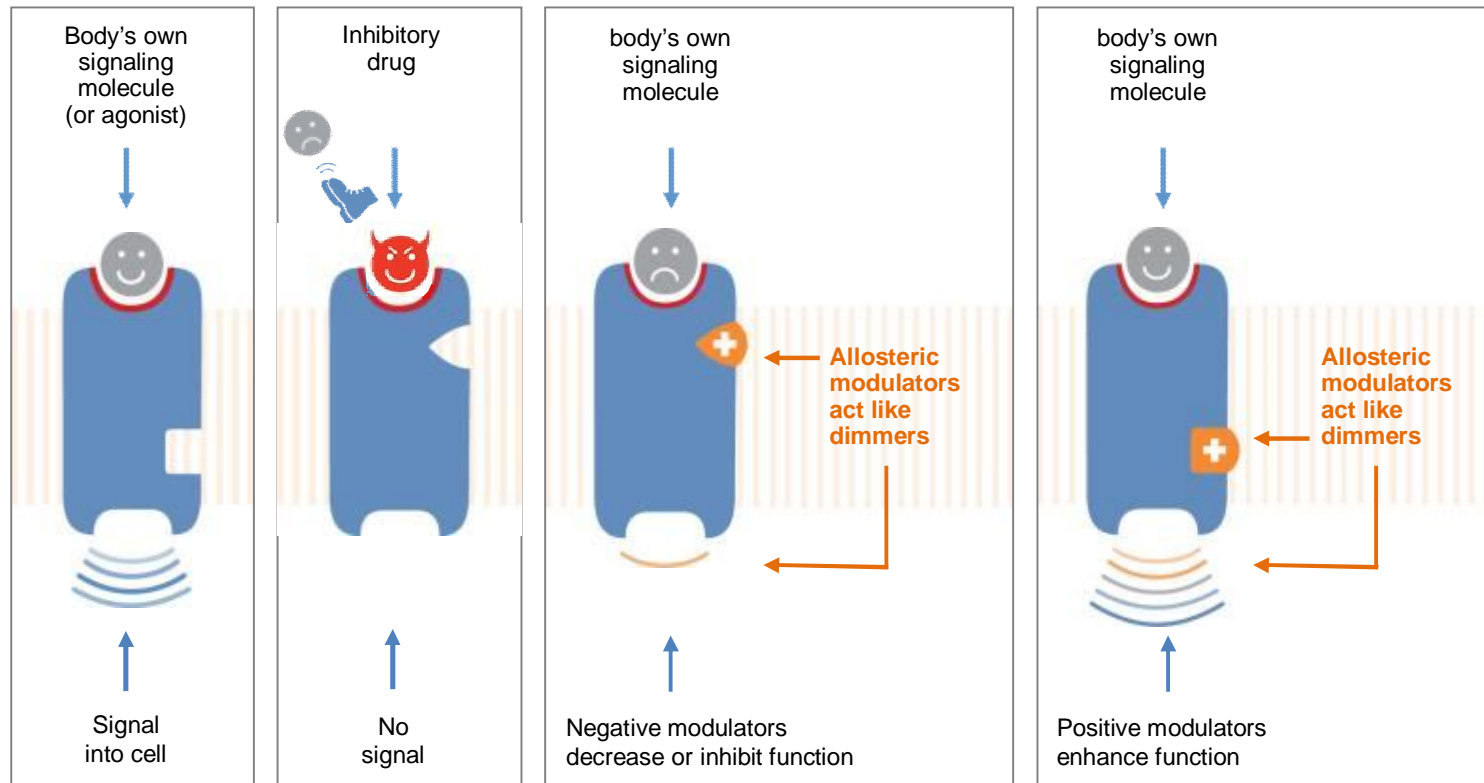
- Small molecules
- Peptides/biologics
- **Allosteric modulators**



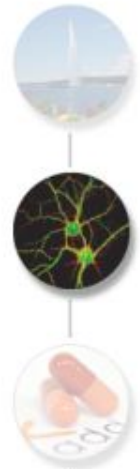
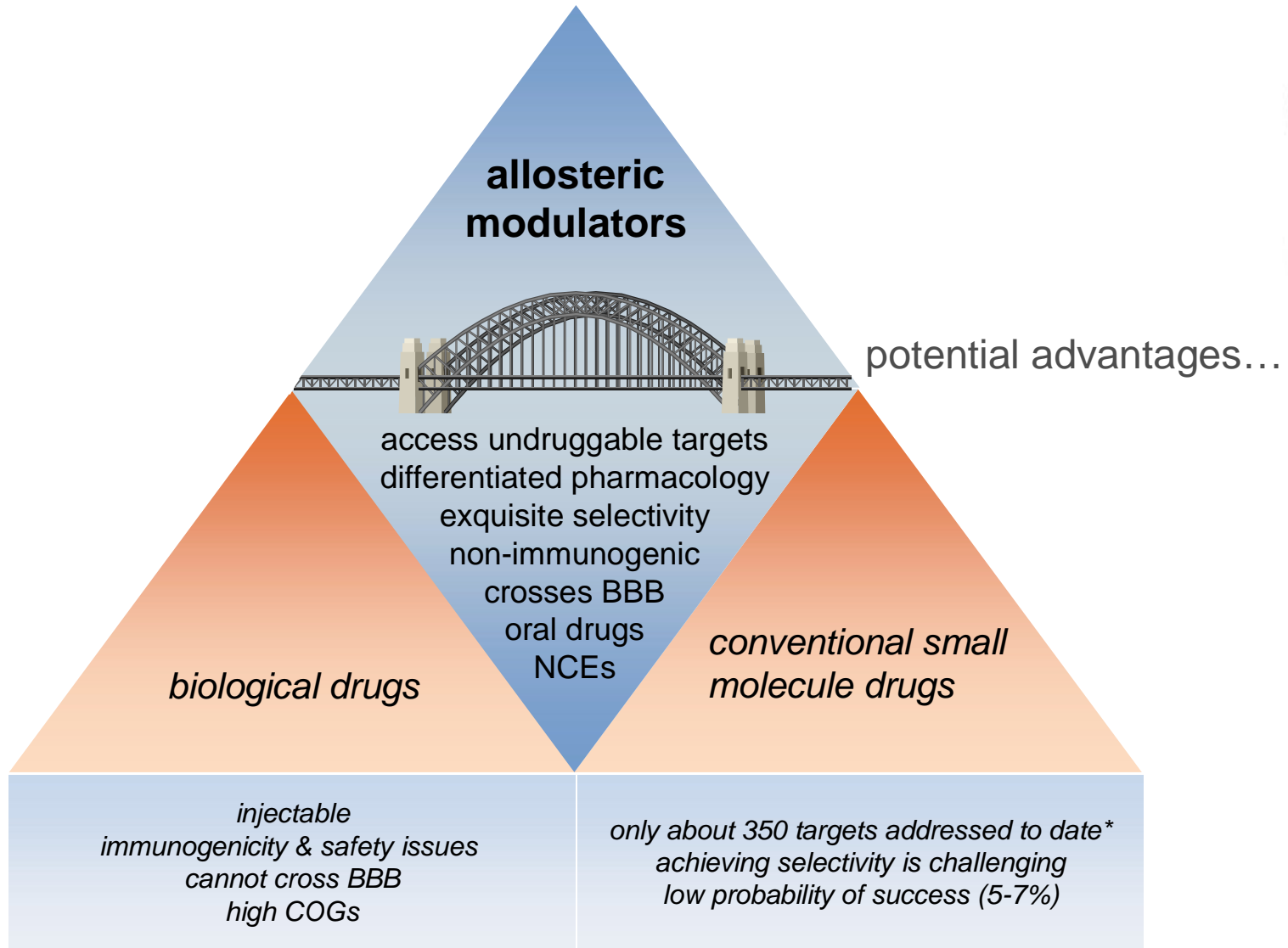
<sup>a</sup>Overington et al. Nature Reviews Drug Discovery 5, 993–996 (December 2006)  
<sup>b</sup>Goh et al. PNAS 104 (21), 8685–8690 (May 22, 2007)

# allosteric modulators (AMs) are different from conventional drugs

## allosteric modulation explained

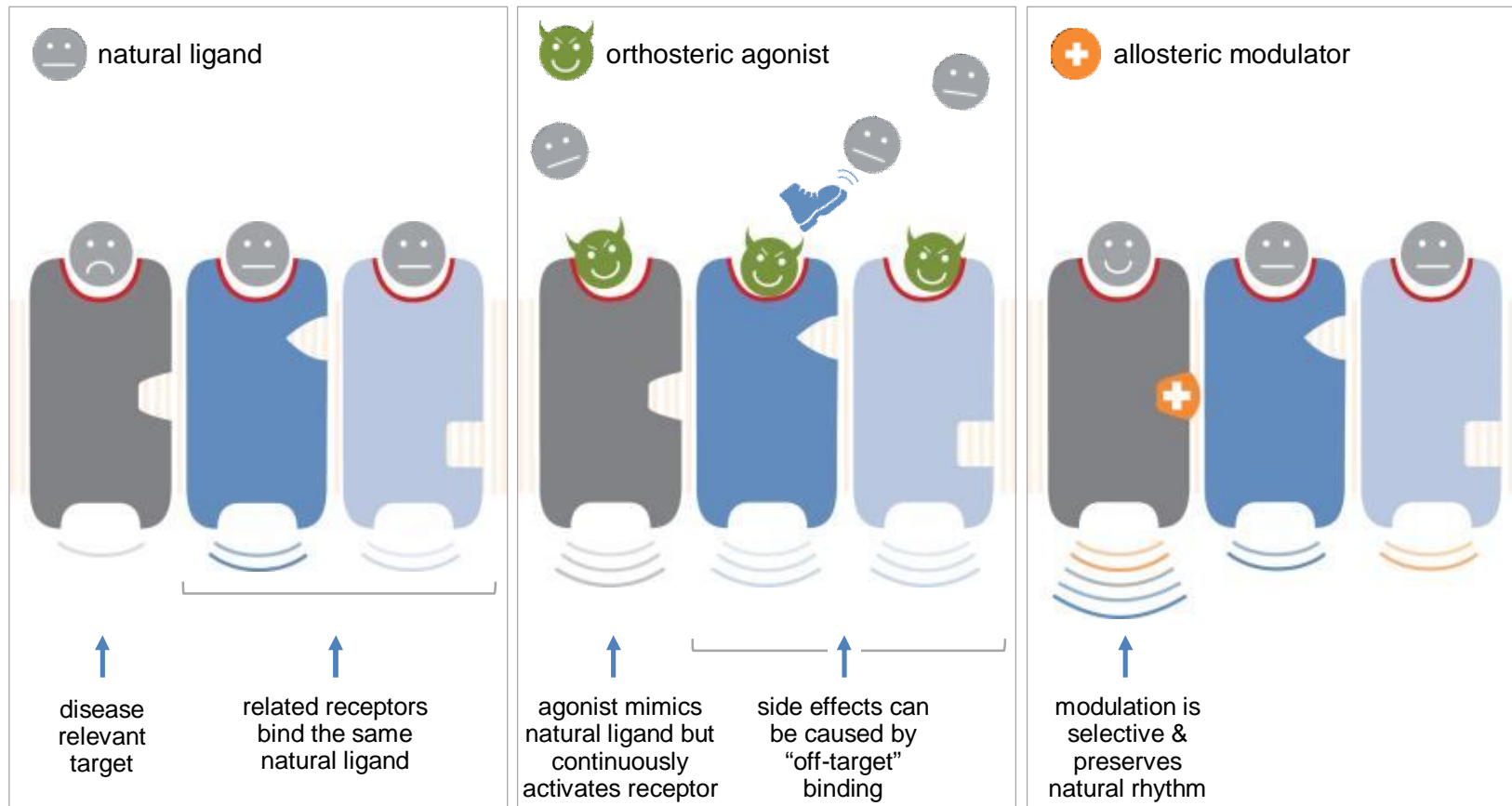
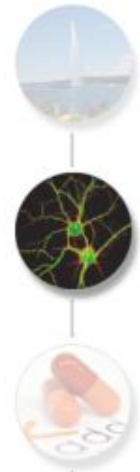


# allostery bridges the divide, offers best of both worlds



# why are allosteric modulators are uniquely suited for “undruggable” targets?

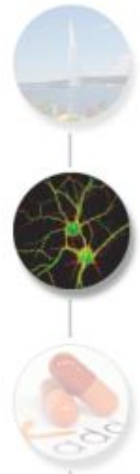
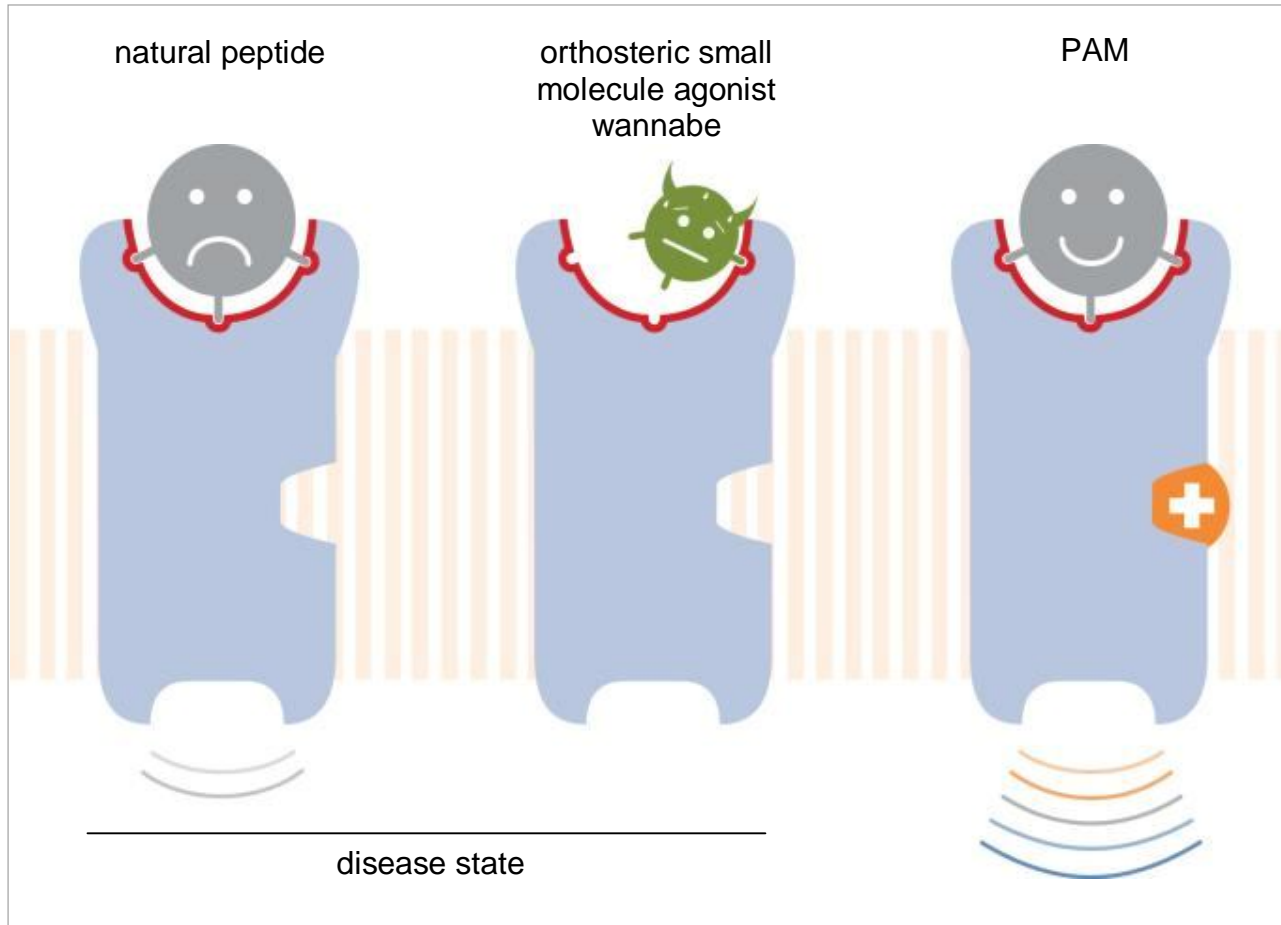
## selective receptor modulation



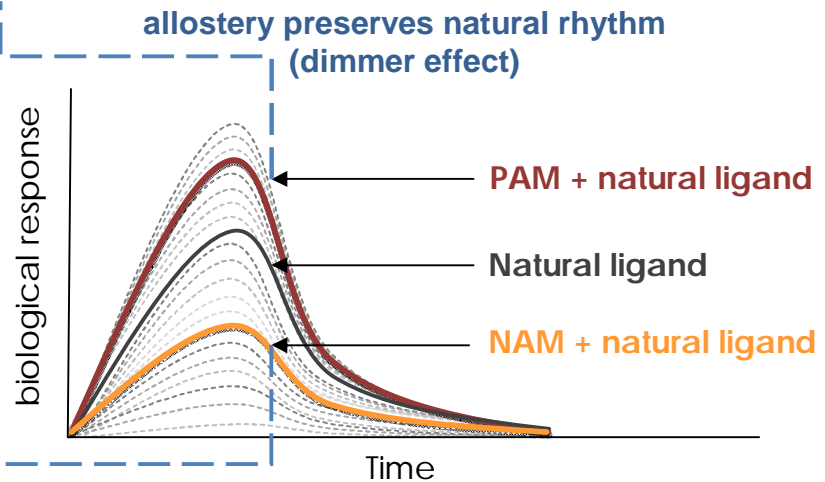
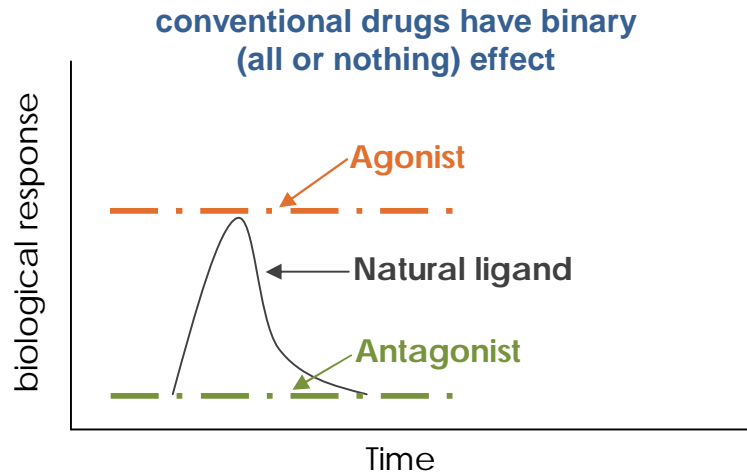
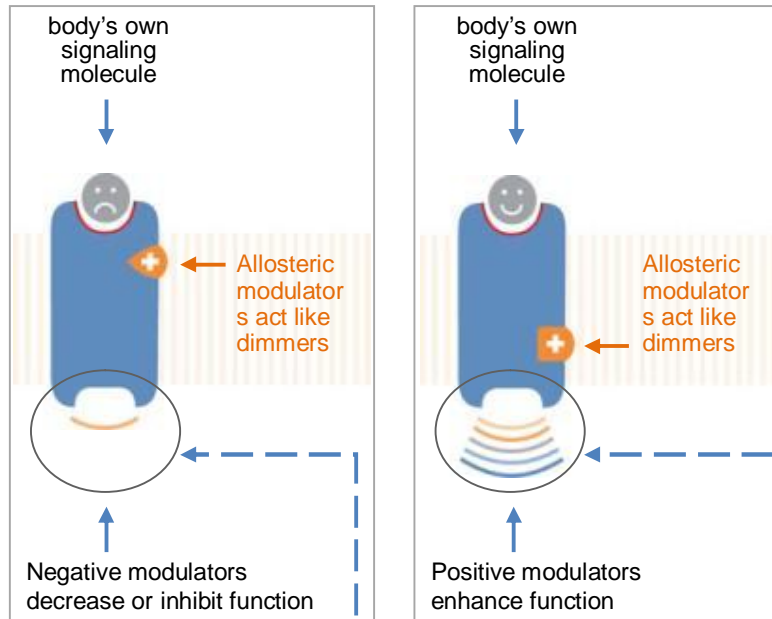
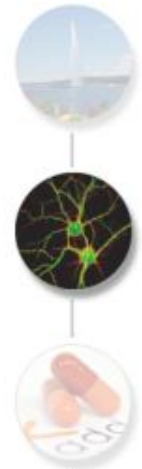
■ active sites are highly conserved across related family members; in contrast, allosteric sites are variable

# allostery can enable oral small molecules to replace injectable biologics

modulating receptors with large ligand binding sites (peptide receptors)



# allosteric modulators (AMs) do not perturb physiological rhythm of receptor function

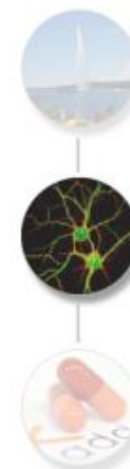


## the road less traveled...

- Potential of AMs to reinvigorate small molecule discovery is generally well recognized BUT AMs are hard to find using conventional routes
  - Traditional screening tools have yielded rare successes
  - Conventional libraries are biased towards orthosteric (“active site”) drugs



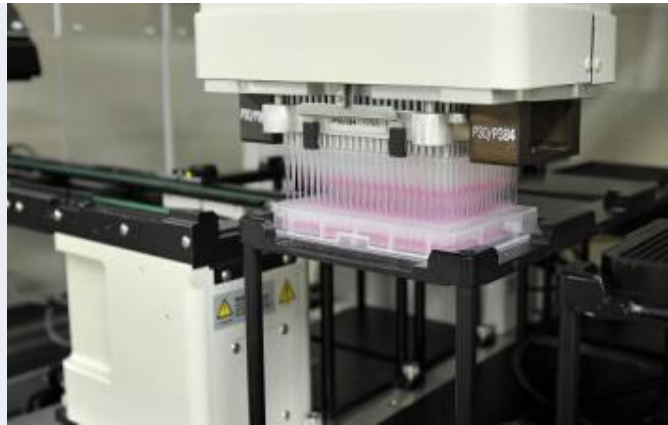
- High barrier to entry
  - Addex is the leader in allosteric discovery and development
    - Specific dedicated expertise & broad experience
    - Proprietary & unique chemistry and screening capabilities
  - Initial investment is significant
    - Addex infrastructure well-established



# the Addex advantage

## allostery-specific screening systems

- High-throughput
- Fewer false +’s
- Fewer false -’s

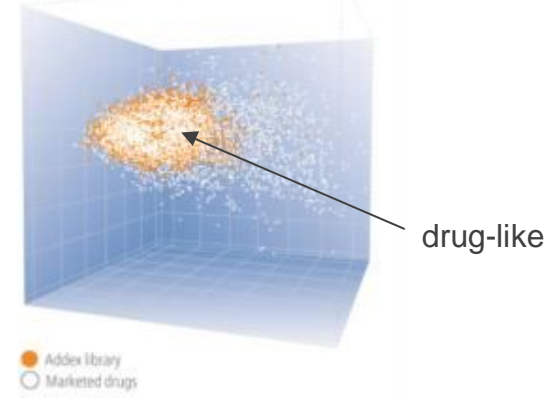


### Addex advantages

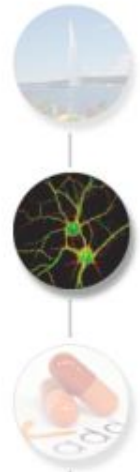
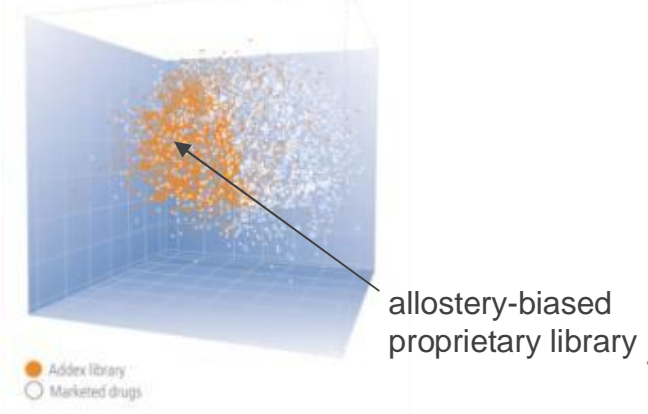
- Greater sensitivity & fidelity
  - Addex hit confirmation rate: 70-95%
  - Industry hit confirmation rate: 10-30%
- Seamless integration with development
- Strong IP protection

## allostery-biased library

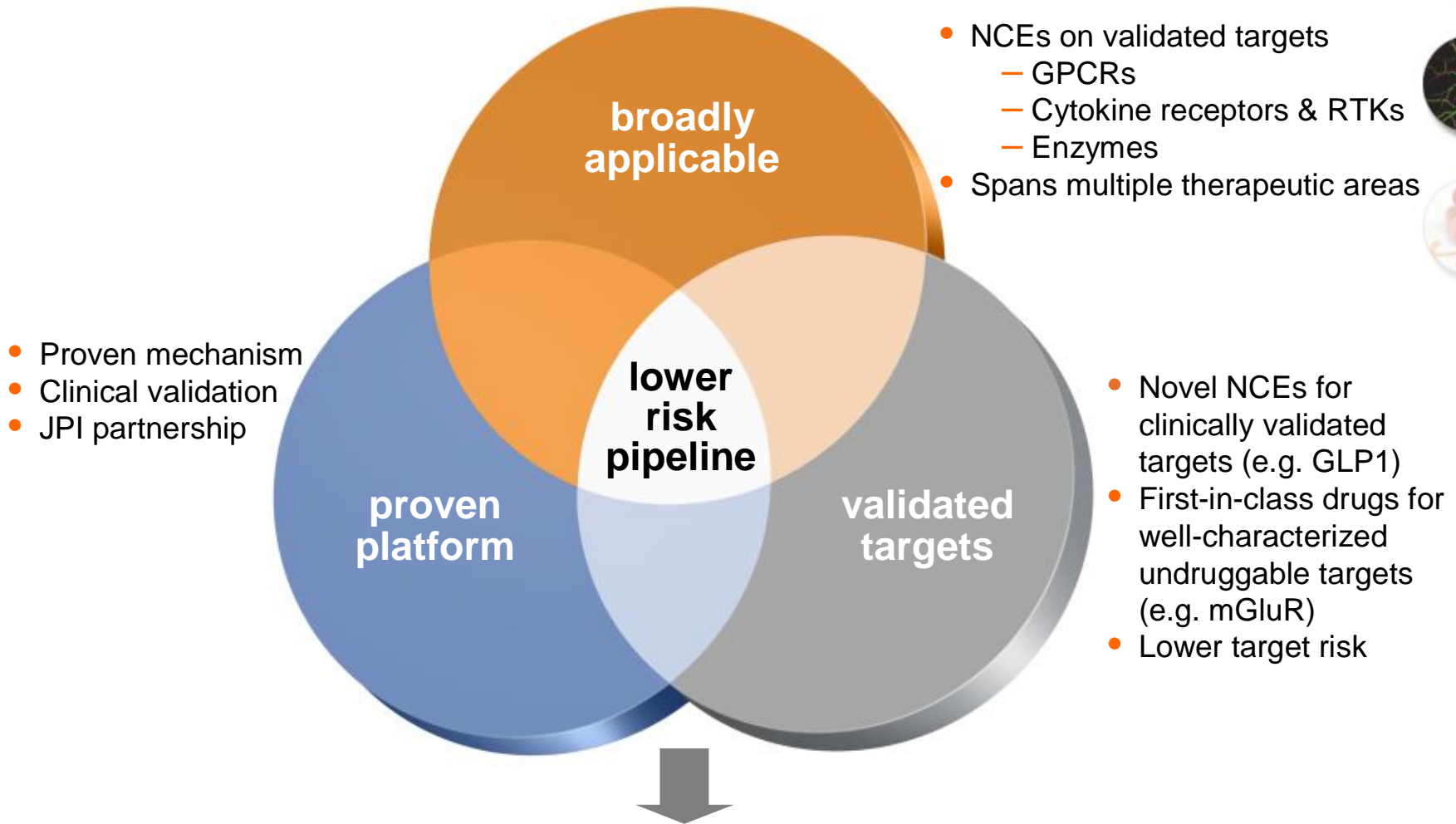
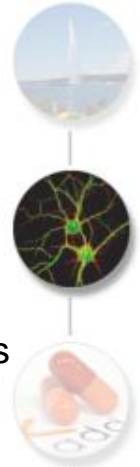
### physicochemical comparison



### structural comparison



# addex is uniquely positioned in the biopharma world

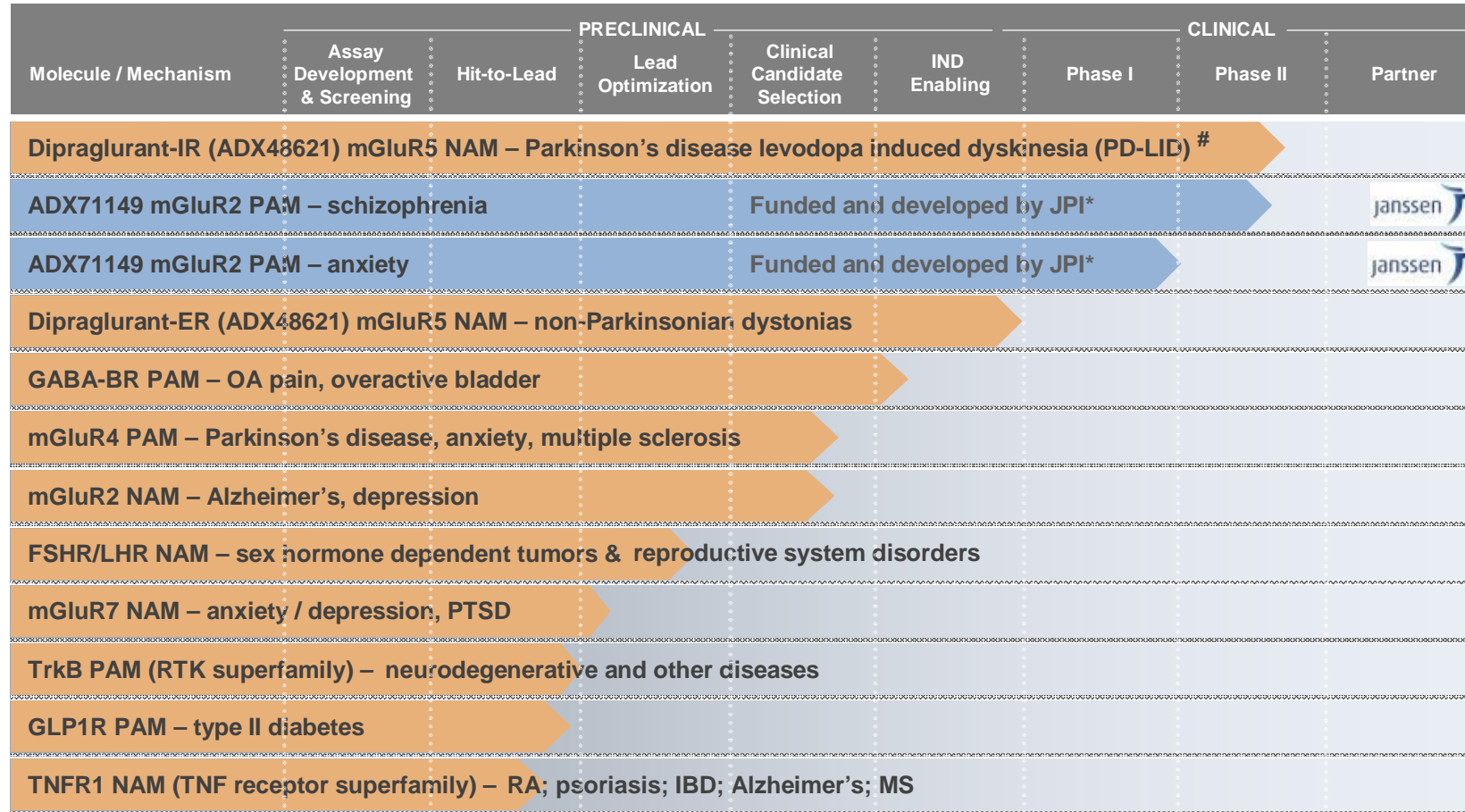


**Pipeline – robust and lower risk**

# products in development



# pipeline



NAM = negative allosteric modulator (inhibitor)  
 PAM = positive allosteric modulator (activator)

\*Janssen Pharmaceuticals Inc., formerly Ortho-McNeil-Janssen Pharmaceuticals Inc.

# partially funded by a grant from the Michael J. Fox Foundation for Parkinson's Research

Orange arrow: Wholly-owned by Addex  
 Blue arrow: Partnered



# programs

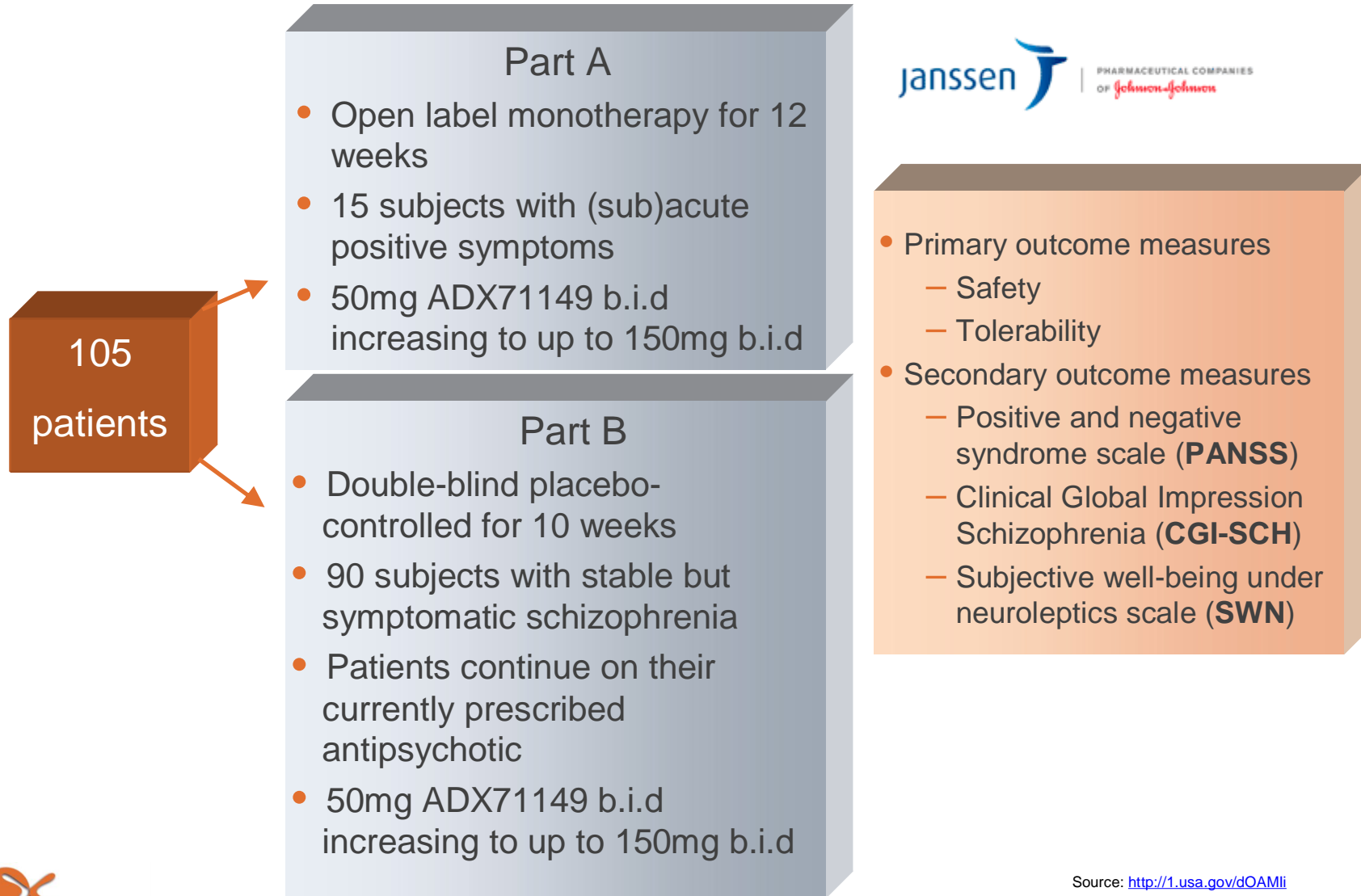


# schizophrenia

- Worldwide antipsychotic drug sales >\$16 billion
  - Antipsychotics are off patent
  - Atypical antipsychotics are going off patent now
- Typical and atypical antipsychotics inhibit dopamine D2 receptor
  - Address positive symptoms
- Significant unmet medical need in Schizophrenia
  - Negative symptoms like depression/anxiety & cognitive dysfunction are inadequately addressed
  - Non-dopaminergic drugs that do not cause prolactinemia (lactation); weight gain; extrapyramidal symptoms are needed
- mGluR2 activation is the first non-dopaminergic mechanism to show clinical efficacy in decades\*
  - Potential to provide a more desirable profile compared to D2 antagonists



# ADX71149 ongoing EU Phase IIa schizophrenia study



# dipraglurant (ADX48621) overview

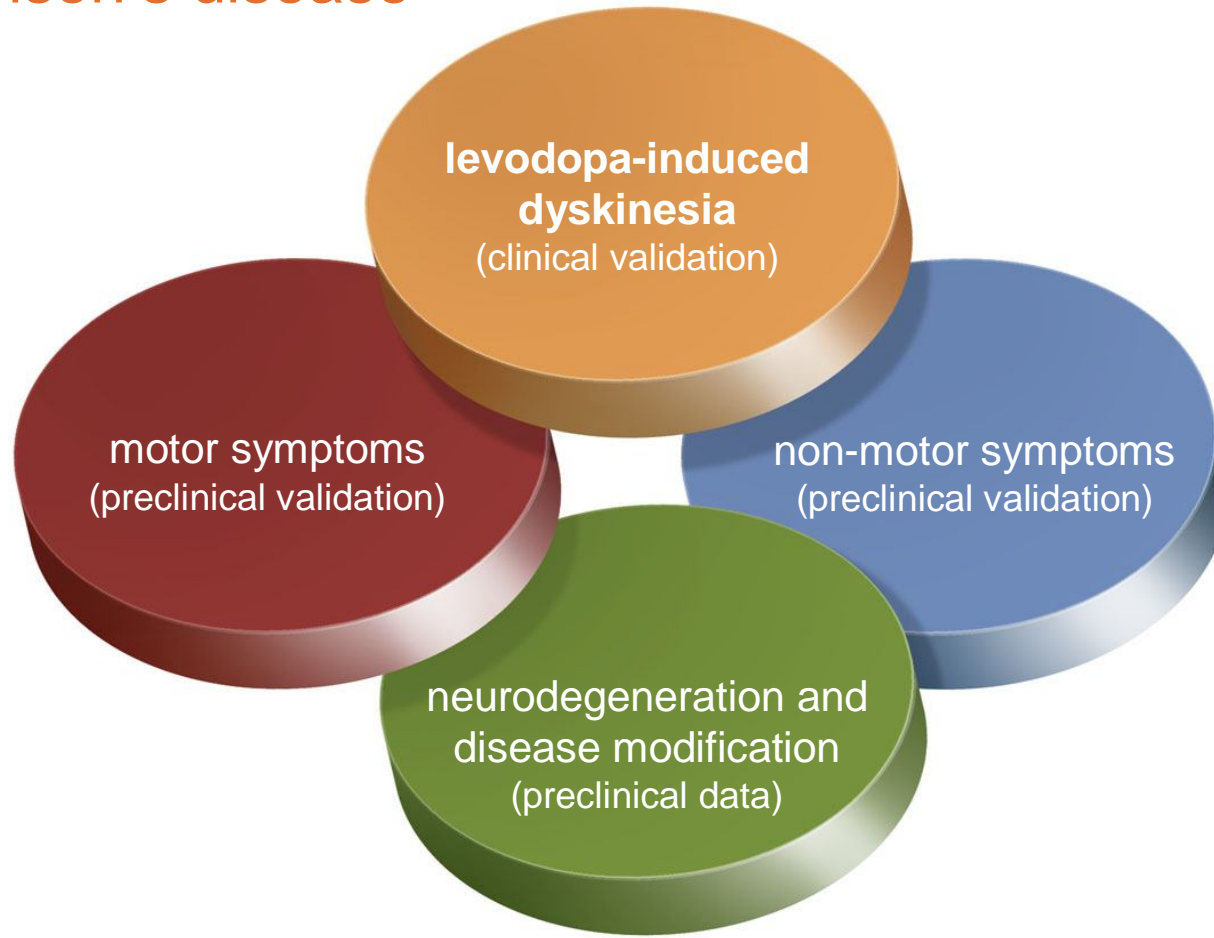
- Dipraglurant is an oral small molecule metabotropic glutamate receptor 5 (mGluR5) inhibitor (negative allosteric modulator - NAM) discovered at Addex
- mGluR5 inhibition has validation in multiple indications

Clinical validation for mGluR5 NAM	
<b>PD levodopa-induced dyskinesia (PD-LID)</b>	Acute migraine pain
Generalized anxiety disorder (GAD)	Gastroesophageal reflux disease (GERD)
Preclinical validation for mGluR5 NAM	
Parkinson's disease (PD) motor symptoms	Depression
Pain	Addiction

- Initial Phase I program of dipraglurant successful
  - Three studies: single & multiple ascending doses, gender/food effects
  - 132 subjects studied to date, including 30 older subjects
  - Dipraglurant – IR formulation developed and tested
  - Pharmacokinetics ideal for acute treatment of PD-LID
  - Safety & tolerability support further clinical study
- Dipraglurant-IR is being studied in a Phase IIa trial in 72 PD-LID patients
  - Top-line data end of 1Q12
  - Michael J. Fox Foundation awarded Addex \$900,000 for trial
- Dipraglurant-ER formulation development is complete
  - Preclinical testing indicate it has potential to be twice- or once-daily
  - ER form has potential for non-Parkinsonian dystonias and validated indications above
  - Phase I testing will be initiated in 2012



# dipraglurant has potential to manage multiple facets of Parkinson's disease



dipraglurant has potential to change PD treatment paradigm  
**levodopa-induced dyskinesia indication - most direct path to market**

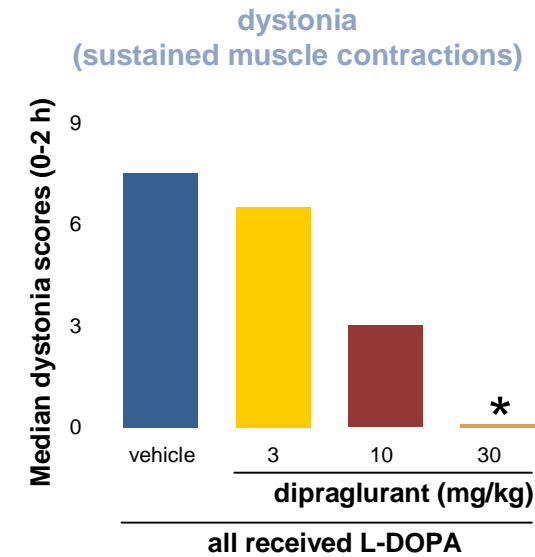
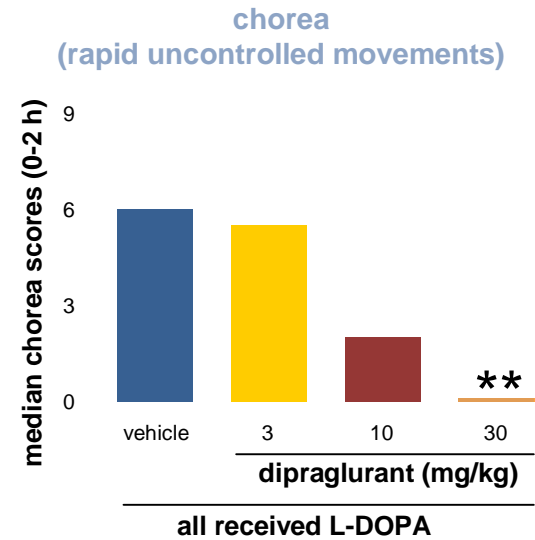
## why are we pursuing PD-LID for dipraglurant?

- PD-LID is a growing unmet medical need with no approved treatment
  - 50% of PD patients suffer from LID after five years of levodopa treatment
    - Incidence & severity of LID increases with use of levodopa
  - Clear path to market for this mechanism
    - PD-LID is recognized by FDA as a distinct indication with unmet medical need
    - Potential for rapid path to market (fewer patients, shorter trials than in PD)
  - Potential market size of over \$1 billion (Datamonitor analysis)
- Exceptional preclinical data with dipraglurant-IR in PD-LID models
- PK profile of IR formulation similar to that of levodopa
  - Therefore well-suited for acute treatment of LID
- PD-LID is a more direct path to market than PD
  - 3 month pivotal efficacy studies
  - 1 year open label for safety database



# dipraglurant (ADX48621) in PD-LID model

- Both components of dyskinesia, chorea and dystonia are exhibited in the Parkinsonian (MPTP-treated) macaques model of levodopa-induced dyskinesia (LID)
- Behavioral assessment began upon levodopa administration
  - trained observers performed video review
  - dyskinesia & PD scoring (10 min every 30 min for 4hrs)
- In this model of PD-LID, dipraglurant effectively reduced the severity of both components of dyskinesia, chorea and dystonia, without affecting the anti-Parkinson's efficacy of levodopa
- **Dipraglurant is the first compound ever reported to show efficacy for dystonia in this model**



# EU and US Phase 2A dipraglurant trial for PD-LID



72 patients

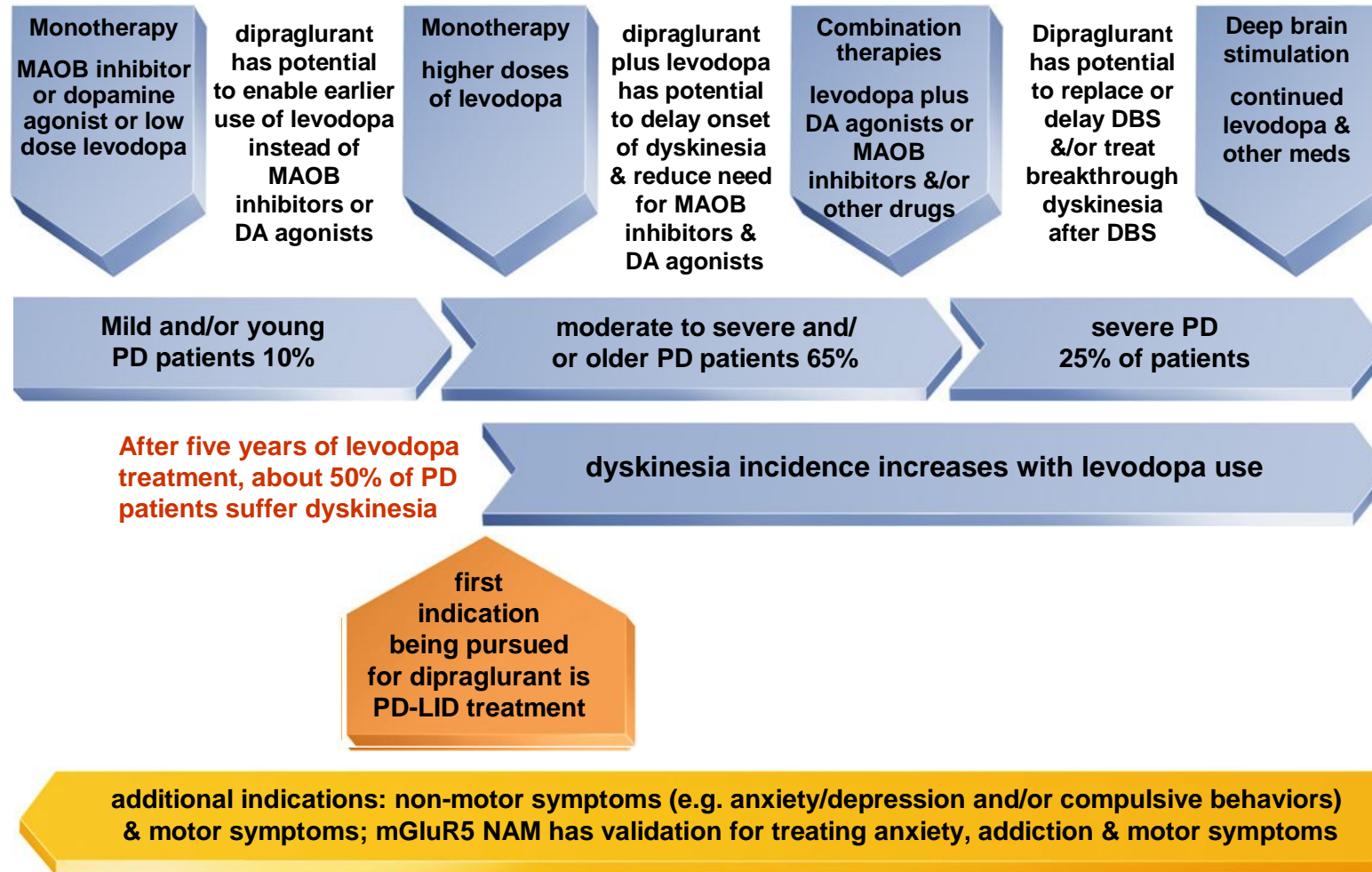
- Randomized, double-blind, placebo-controlled, multi-center trial
- Moderate to severe LID patients

- Dipraglurant taken with levodopa
- Dipraglurant titration from 50mg q.d. to 100mg t.i.d over 4 weeks
- Individual levodopa regimens remain constant for duration of study (300 -1500mg/day)

- **Primary objective:** safety & tolerability
- **Secondary objective:** exploratory efficacy
- **Objective evaluation in the clinic on day 1 and 14 & 28**
  - Trained observer scores LID severity using **mAIMS** – modified Abnormal Involuntary Movement Scale
- **Patient diaries of on & off time**
- **Unified Parkinson's Disease Rating Scale (UPDRS)**
- **Patient and clinician global impression of change (PGIC & CGIC)**
- **Evaluation of mood using Hospital Anxiety & Depression Scale (HADS)**

top-line data end of 1Q12

# dipraglurant-IR has potential to change PD treatment paradigm



## oral GABA-B receptor PAM

- Activation of gamma-aminobutyric acid subtype B (GABA-B) receptor is clinically & commercially validated
  - Generic GABA-B receptor agonist, baclofen, is marketed for spasticity & some spinal cord injuries and used for overactive bladder (OAB)
  - Orthosteric GABA-B receptor agonists showed clinical validation in gastroesophageal reflux disease (GERD)
- GABA-B receptor PAMs are differentiated from baclofen
  - Allosterism may reduce/eliminate development of tolerance
  - Allosterism may reduce other tolerability issues, like somnolence
- Addex GABA-B receptor PAMs have shown efficacy in multiple preclinical models including: pain, osteoarthritis pain and anxiety
- Target indications
  - Pain (e.g., Osteoarthritis Pain)
  - Overactive bladder (OAB)
- Clinical candidate selection 4Q11
- Regulatory filing for clinical testing 4Q12



## oral mGluR4 PAM

- mGluR4 PAM is one of the most exciting approaches for PD and MS
  - Disease-modifying potential\*
  - Non-dopaminergic
  - Potential for treatment of symptoms
- Addex has **first-in-class brain penetrant oral** small molecule mGluR4 PAM candidates
  - First oral nanomolar mGluR4 PAM to achieve preclinical PoC
  - Clinical candidate selection expected in 1H12



## oral GLP1R PAM

- GLP-1 peptide drugs are marketed for diabetes
  - Marketed drugs are injectable and have been reported to have side effects (immunogenicity, pancreatitis and injection site reactions)
  - Oral PAM mechanism has potential to offer superior product profile
- Addex has identified oral small molecule GLP1R PAM candidates
  - Addex lead series have drug-like properties
  - Addex GLP1R PAMs have demonstrated functional activity in relevant *in vitro* & *in vivo* models, including “diabetic” (db/db) mice oral glucose tolerance test



## oral TNFR1 NAM

- TNF pathway is targeted by five marketed biological drugs generating over \$16 billion in annual revenues
  - Marketed drugs are injectable and have been reported to have side effects (immunogenicity and injection site reactions)
  - Oral selective TNFR1 NAMs have potential to offer a superior product profile
- Addex is optimizing oral small molecule TNFR1 NAMs
  - Addex has developed proprietary, highly sensitive HTS screening & validation systems to identify small molecule allosteric modulators selectively targeting individual members of the **TNF receptor superfamily**
  - TNFR1 NAMs are likely to be brain penetrant – opening the possibility for development of additional indications, including neurological inflammation (Alzheimer's, multiple sclerosis, depression, etc)



## oral TrkB PAM

- Pharmacology of BDNF is well characterized
  - The natural ligands for TrkB receptor are BDNF and NT-4
  - TrkB (an RTK) has been intractable using conventional small molecule approaches & biologicals
  - Allosteric modulation offers a novel way to address this **undruggable** target
- TrkB PAM has broad potential for treating neurodegenerative diseases
  - Parkinson's, Alzheimer's & Huntington's diseases
- Addex has identified oral small molecule TrkB PAM candidates
  - Addex has developed proprietary, highly sensitive HTS screening & validation systems to identify small molecule allosteric modulators selectively targeting individual members of the **receptor tyrosine kinase (RTK) superfamily**
  - Potentially the first small molecules selective for TrkB
  - Lead optimization to begin in 1Q12

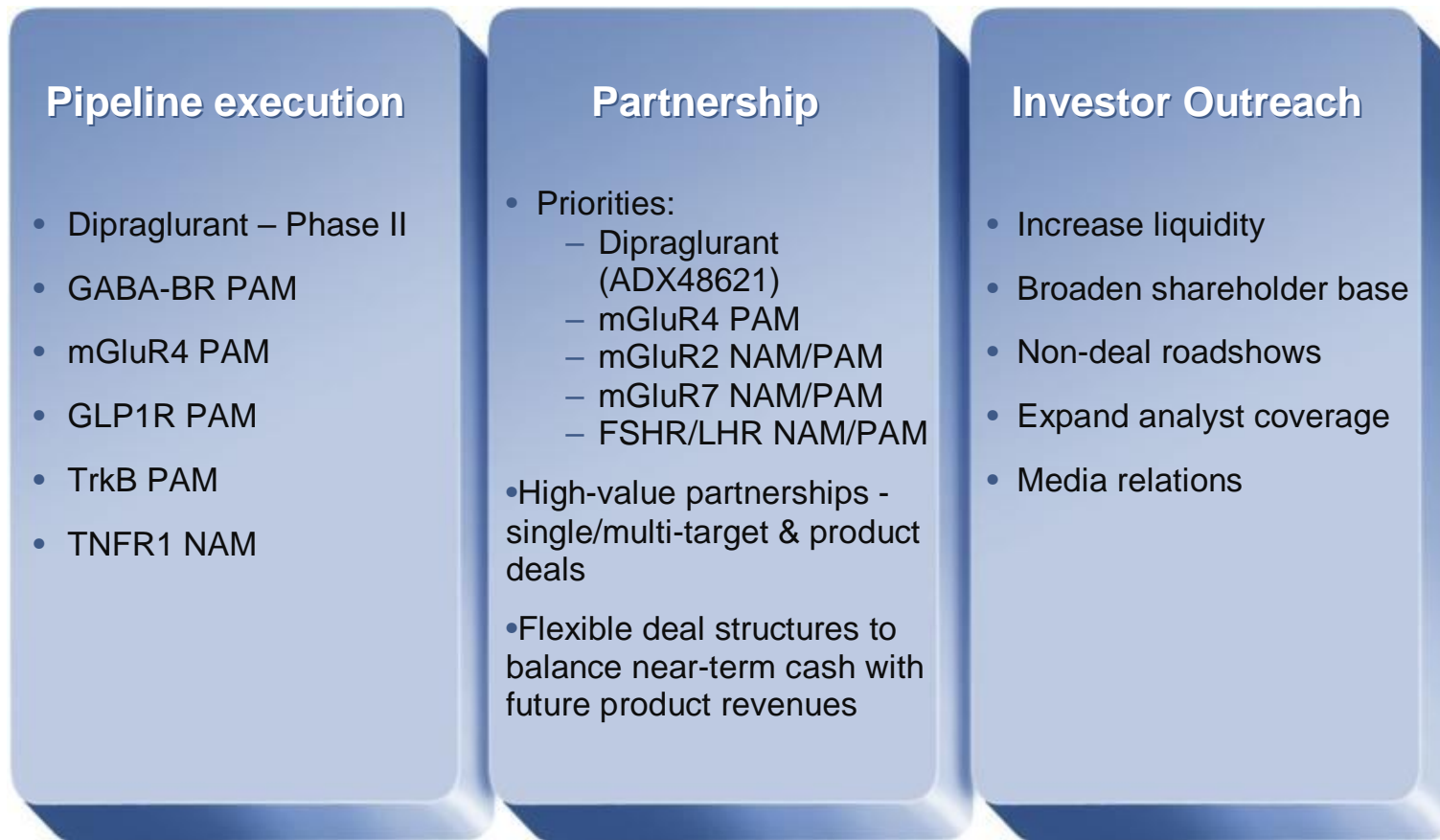


## major milestones for 2012

Milestone	Timing
Clinical candidate selection for GABAB-R PAM program	1Q12
Dipraglurant-IR mGluR5 NAM Phase IIa PD-LID data	End of 1Q12
ADX71149 mGluR2 PAM Phase IIa Schizophrenia data	ND
Start dipraglurant-ER Phase I testing	2012
Regulatory filing for clinical testing of at least one compound	4Q12



# three-pronged strategy for building value



← Increasing Shareholder Value →



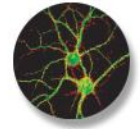
## financials and stock

- Cash through Q3 2013
  - CHF50.2 (US\$63 / €44) million in cash as of June 30, 2011
  - 2011 burn guidance CHF28-32 million
- Traded on SIX Swiss Exchange: ADXN (ISIN:CH0029850754)
- 7,835,878 shares outstanding
  - Biotechnology Value Fund holds 30%
- Five analysts covering:
  - Jefferies: Peter Welford and Philippa Gardner
  - Ladenburg Thalmann: Juan Sanchez
  - Helvea: Olav Zilian
  - Bank am Bellevue: Bruno Eschli
  - Edison: Robin Davison



# addex offers a unique opportunity for investors





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