National Institute of Neurological Disorders and Stroke

Can a Public-Private Partnership Engineer Preclinical Testing Platforms with Better Predictive Validity?

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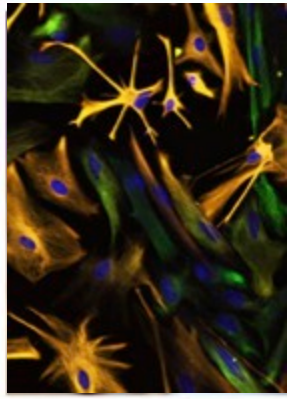
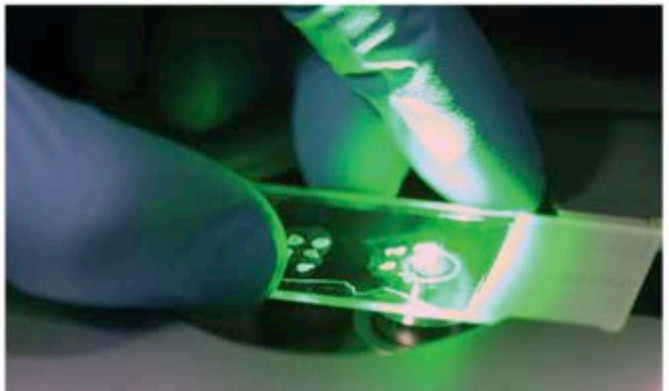
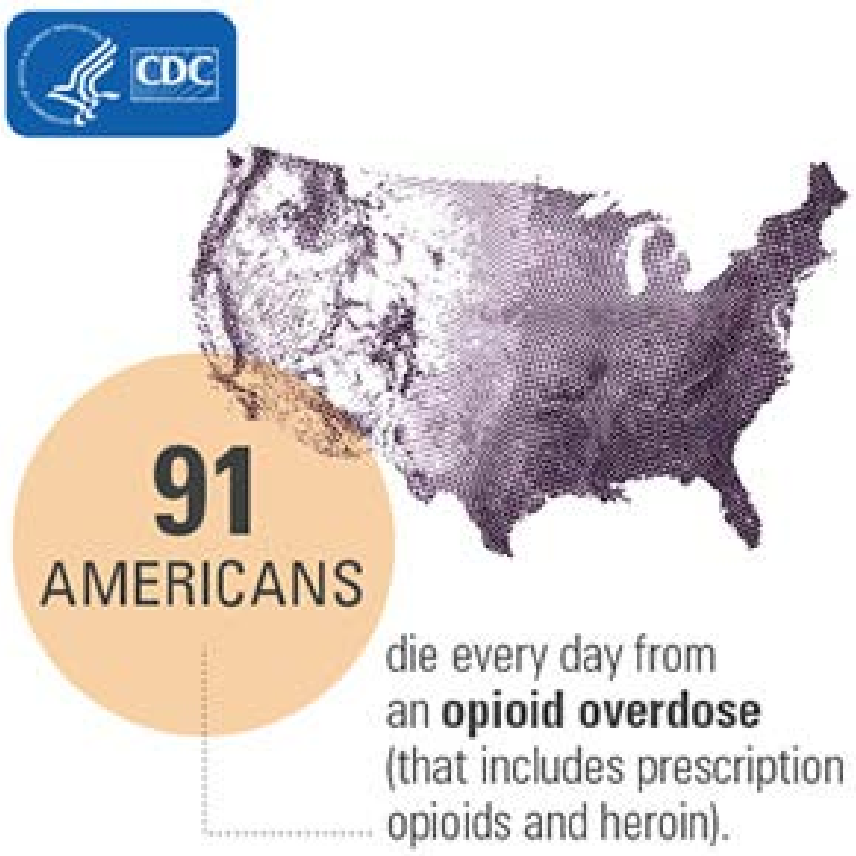




The Opioid Epidemic - Grand Challenge



- Opioids overdoses claim the lives of 91 Americans every day – one every 16 minutes *(CDC, epub. December 16, 2016)*
- "America currently lacks "safe, effective, non-addictive strategies" to combat the opioid epidemic" *Dr. Francis Collins, at the National Rx Drug Abuse & Heroin Summit, Atlanta* ***April 4, 2017***
- Dr. Francis Collins announced a public-private partnership to develop solutions to the opioid crisis. *Dr. Francis Collins interview by Julia Lurie, Mother Jones Magazine,* ***May 20, 2017***

Proposed Preclinical Testing Program

A Program that catalyzes the discovery and characterization of non-addicting modalities for the treatment of pain

1. Establish a preclinical screening program to help identify non-addicting analgesics (small molecules, biologics or devices) to combat acute and/or chronic pain

2. Provide in-kind access for the research community to test and characterize promising non-addicting leads

Advantages of the Preclinical Testing Program

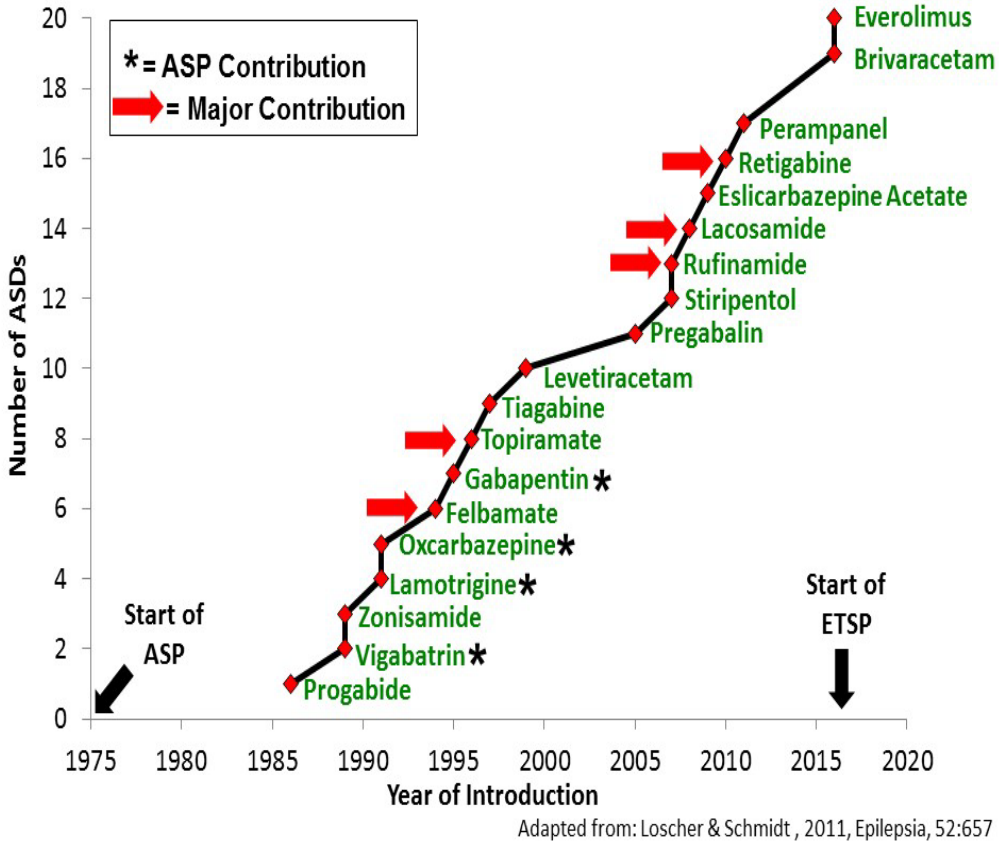
1. Incentivize academic & industry research communities to pursue discovery of non-addicting therapies

2. Facilitate a one-stop resource to interrogate existing and novel pain relief modalities without the upfront economic burden or expertise required for screening

3. Generate high quality data in pain models to support business partnerships or applications to NIH translational programs

A Proven Platform to Spur Innovative Therapies

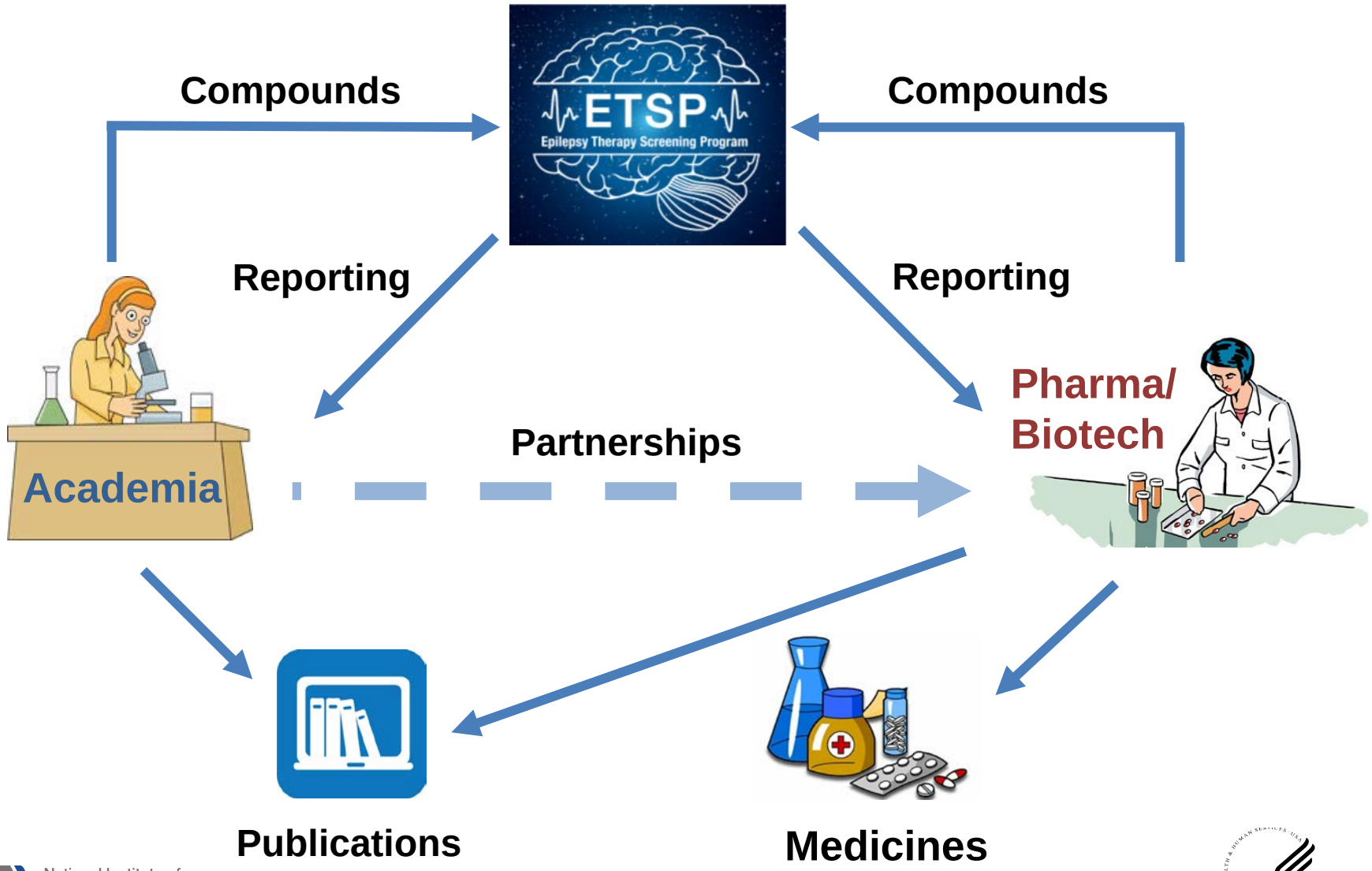
- Concept based on successful NINDS-funded Anticonvulsant Screening Program (ASP*)
- Rigorous testing of submitted compounds in a battery of preclinical seizure models
- Significant contribution to advancement of 9 therapeutics to the market for treatment of seizures in epilepsy



Adapted from: Loscher & Schmidt , 2011, Epilepsia, 52:657

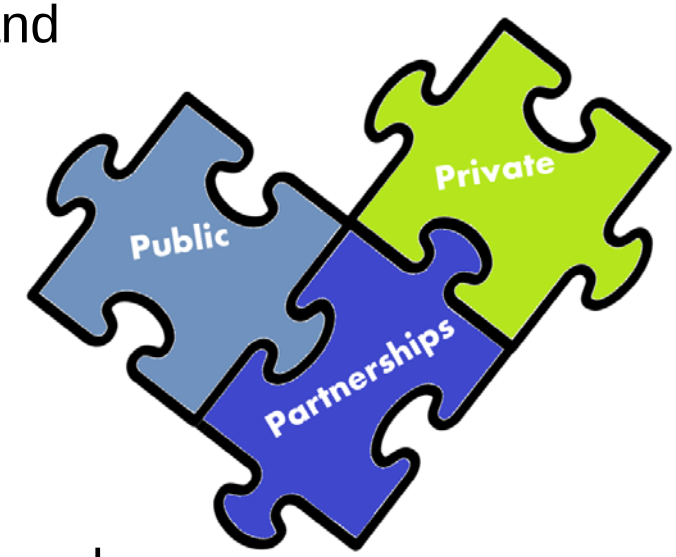
*Currently known as the "Epilepsy Therapy Screening Program" (ETSP)

Epilepsy Therapy Screening Program (ETSP)



“ETSP-Like” Testing Platform: Concept to Reality

1. Harness collective expertise and resources:
   - Develop testing funnels, protocols, and reporting structures
2. Deploy NIH existing infrastructure
   - Sample handling
   - Testing
   - Data Storage & Reporting
3. Make the resources available to the research community
4. Create rigorous data sets
5. Connect partners to effectively move projects from discovery to development



Key Elements to Build into Testing Program

1) Balance of robust assays configured into streamlined flowcharts with milestones

2) Model refinement/development to address gaps

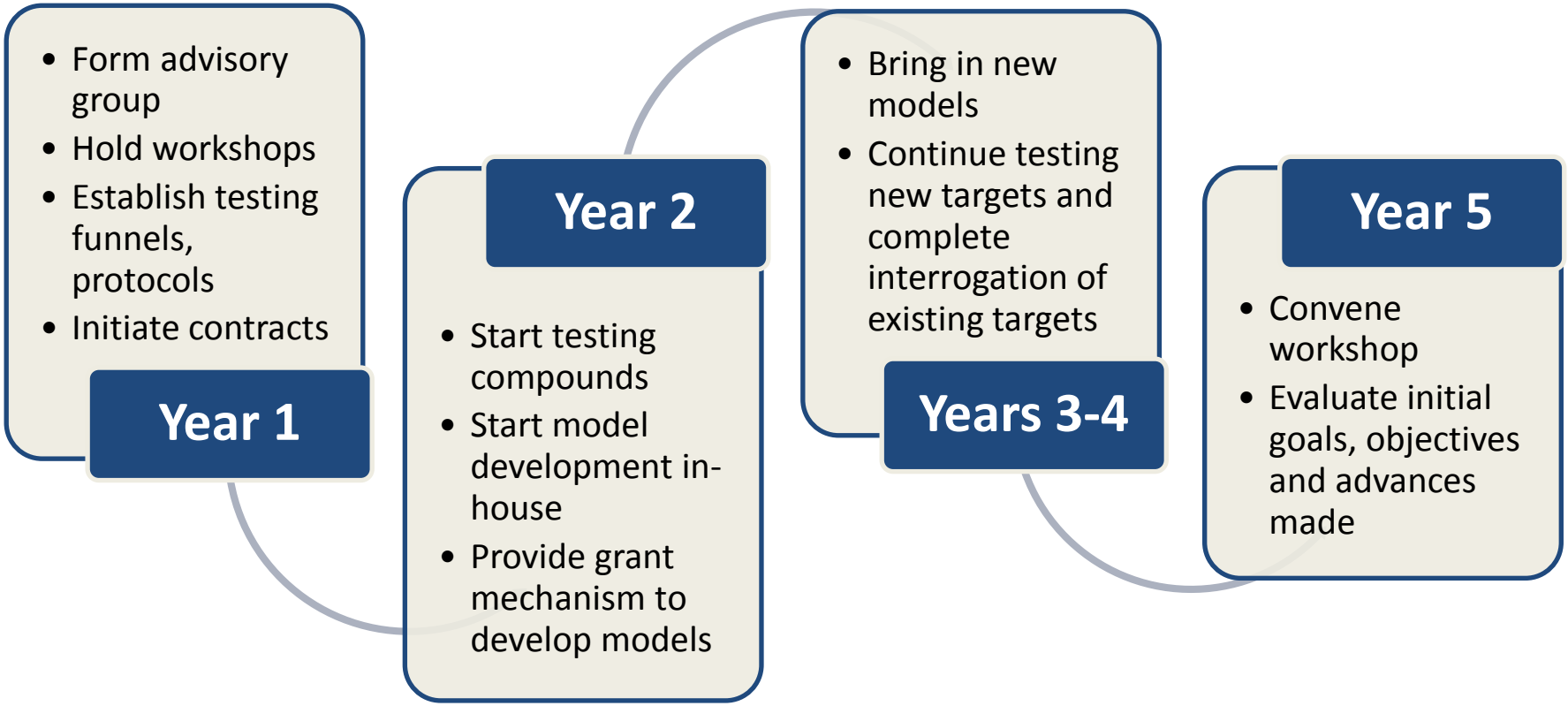
3) Flexibility to adapt to various pain indications and flexible decision making process with input from partners

4) Qualified staff to manage the screening program

5) Commitment to data sharing (publications, publicly accessible website)

→ A PPP could add considerable value beyond the ETSP model by accessing collective capabilities, scale, and resources

Five Year Proposed Plan



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Access to capabilities, scale & resources of a PPP could:

- Enable the design of a rigorous, centralized, flexible screening engine for generating robust data
- Provide a rapid, "apples to apples" evaluation of early stage targets/modalities to find the most promising leads
- Position the ecosystem so that drug developers can rapidly embark on translating discoveries into drugs

→ Contribute to Francis Collins' bold objective to "cut in half" the time to develop non-addicting analgesics

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