



Past. Present. Future.



Conference – SMA Community

- Invested over \$2.5 Million to bring community together every year.
- Networking – Families and Researchers:
 - Opening, Lunches, Banquet, Carnival, Panels.
- Informal sharing is just as important.
- Workshops - Care:
 - Standard of Care – Breathing, Feeding, Movement, Illness.



Families of SMA *Research Support Hope*

DRUG DISCOVERY AND DEVELOPMENT
TRANSLATIONAL RESEARCH PROGRAM

SUMMER 2009

COMPASS

A Publication Dedicated To Research Updates

FSMA Quinazoline Program Update: Preparations Now Underway for a pre-IND Meeting with the FDA.

By Jill Jenks, Ph.D., Research Director FSMA

In June 2009, the IND-enabling safety studies were completed for the FSMA-derived Quinazoline program. This is the program previously worked on by Vertex Pharmaceuticals and JACDEC geneticists, and fully funded by Families of SMA.

The next step for this program is to request a pre-IND meeting with the FDA, and to prepare the required data package. Families of SMA will be working over the next several months with toxicology and regulatory experts to prepare for this meeting.

This meeting will be an exciting milestone for the project, and an essential step in the path towards human clinical trials of the drug candidate. During the pre-IND meeting, the FDA carefully reviews the existing data on the drug candidate, providing essential feedback on the feasibility of human clinical trials, and specific information on any additional experiments that may be required by the FDA for the Investigational New Drug (IND) Application.



3-D cryo-electron tomography reveals the conformational flexibility of the human drug binding site of Sup1 (PDB ID: 3U99). (Jenks & Mendez)

Drug Development Process



All investigation for drug candidates needed to file an IND Application must first be done in the mouse.

An IND application essentially seeks permission to begin human safety testing of a particular drug therapy. Its submission and pre-IND meeting will occur in September of 2009.

An IND filing would be the submission of almost 10 years of pre-clinical drug development work, which started at the earliest stage of drug discovery in mouse development. This project has successfully progressed through each stage of the pre-clinical process shown in the figure above.

Many groups have collaborated with us to reach this point, including Vertex Pharmaceuticals, JACDEC geneticists, Intelligen (Life Technologies), Perichem, the Douglas lab at Ohio State University, the Robinson lab at Northwestern University, the Williams lab at Rutgers University, the Chang lab at Columbia University and the SMA Project at MGH.

Families of SMA has invested over \$1.1 Million in this particular program to discover and develop a new drug treatment specifically designed for SMA.

Families of SMA Therapeutic Pipeline

FSMA is funding three distinct drug discovery programs:

- 1) Quinazoline to treat SMND expression.
- 2) Teracipilone at Vertex Pharmaceuticals to correct SMND splicing.
- 3) Motor neuron replacement program at California West Cell and VCI.

These three programs represent an investment of over \$10 Million so far to our pursuit to build a SMA drug pipeline.

FSMA plans to continue to invest and further expand the pipeline of drug programs. This pipeline will enable us to move multiple drugs forward at the same time. When one drug candidate drops out of consideration, another one will always be there. In addition, it allows us to tackle the treatment of SMA with several distinct approaches. Diversifying our approach increases the chance of success.



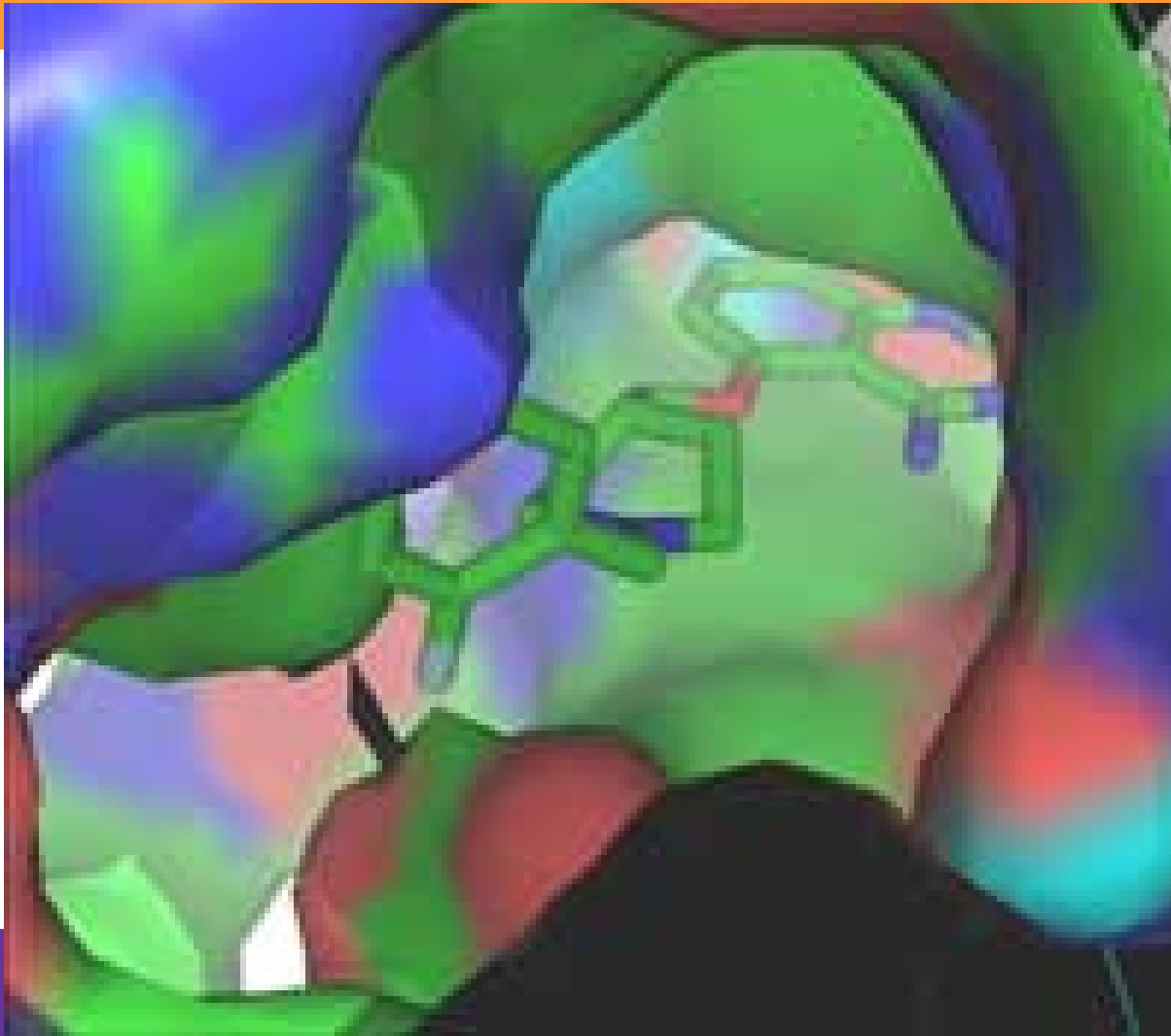
IND – Investigational New Drug: Regulatory



IND: Final Step Before Clinical Trials for New Drugs!



X-ray crystallography reveals the nano-sized drug binding site of DcpS.



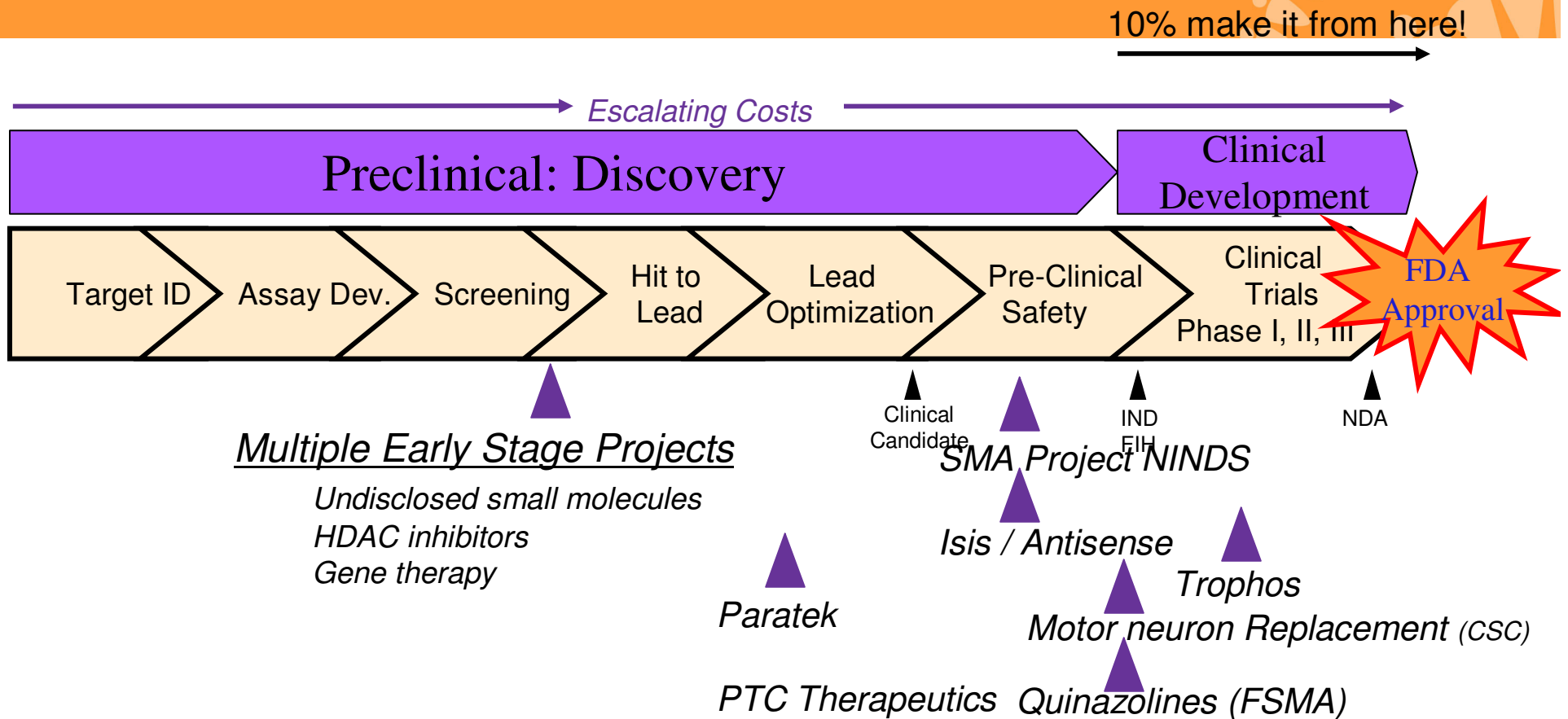
Drug Discovery Translational Research

- Failure is the rule – 90% Fail.
- Our Goal:
 - Build a pipeline of SMA drugs.
 - A new drug candidate is available if another fails.
 - Diversity of approaches increases success.

Families of SMA Therapeutic Pipeline

- FSMA is currently funding 3 distinct drug discovery programs:
 - Quinazolines.
 - Tetracyclines at Paratek Pharmaceuticals.
 - Motor neuron replacement at CSS and UCI.
- **These three programs represent an investment of over \$16 Million so far to build a SMA drug pipeline.**

SMA Community Drug Pipeline



IND = Investigation New Drug Application needed for FIH
 FIH = First in Human
 NDA = New Drug Application for FDA approval

SMA Community

Orphan Disease:

- Everything starts with the community.
- Small market – too risky for companies (and government) to get involved at start.

- Over time, if successful, will see transition:
 - plus Government,
 - plus Companies.