Translational Science: From the Bench to the Clinic (and beyond)

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Developing products to prevent/treat human disease is a resource intensive activity


• Actual costs depend on many factors.

• Decisions to fund/proceed still made on case by case basis, in a transparent manner.

• Initial goal is to identify and manage risks
Transition from Research to Development – what is needed?

• Lead compound identified
• *In vitro*/in vivo efficacy - Proof of concept in relevant animal model
• Methods for making/testing API
• Ideas for clinical use – Target Product Profile
• Product development plan
Funding Translational Activities

• Early funding from non-profits is critical to the creation of new therapies
• Attracting funding from government and non-government sources depends on generation of early data
• We fund high risk, high reward activities that would not occur otherwise – failure is an option and is OK
FFB Science Pipeline and Funding Mechanisms

Exploratory A

Pathway Analysis
- Target identification
  - Discovery of disease mechanism
  - Discovery of disease related genes, proteins, intermediates and metabolites
  - High throughput screening-gene discovery
  - Vector development
  - Gene identification
  - Target cell identification
  - Stem cell technology
  - Stem cell differentiation
  - Mental Transplantation Technology

Target Validation
- Functional analysis of genes
  - Clinical structure-function correlation
  - Animal models
  - Cell-based models

Lead Identification
- High throughput screening
  - Identification of target molecules
  - Characterization of lead candidates
  - Assay development
  - Evaluation of in vivo efficacy

Candidate Optimization
- Medicinal chemistry, lead optimization
  - Preliminary safety, biodistribution, and PK

Pre-Clinical
- IND enabling studies
  - GLP raw material synthesis
  - Formulations, Stability, Tox

Clinical
- Safety in humans
  - Proof of biological effect in human

Exploratory B

Investments approved by CRI board
- In-house funds
- W-G TRAP funds
- Priority driven

Funding Mechanisms

Individual and Center Grants
- Career Development Awards
- Technology Specific Awards

Wynn-Gund Early Translational Research Acceleration Program
- Technology Specific Awards
Lessons learned from funding TS programs to date

- Translation to clinical studies is slow and costly – educate investigators
- Lack of clarity on how to get to clinic
  - Lack of understanding of quality, regulatory issues
  - When/how to engage/manage CRO
  - Missing key aspects in early development (formulation, etc.)
  - Disconnect between theoretical therapy and clinical practice
- Projects where we provided independent consulting did better
- Oversight of integrated activities requires active project management
- Funding translational activities without supplying expertise leads to waste of scarce resources
Investigators need

• CMC Support
• Pharm/Tox support
• Regulatory Support
• Project management support
• Clinical support
Gund Harrington Initiative

• The primary goal of the Gund Harrington Initiative is to identify promising therapies that can benefit from acceleration and provide:
  • Funding
  • Experienced commercial project management
  • Access to senior pharma expertise (no cost)
• The overall effort seeks to create a comprehensive package to facilitate raising funds for further development
Tools for Management of Translational Activities

• No one approach works for all diseases, products
Does your development path look like this?

- Low-Moderate $
- Moderate training/expertise required
- Streamlined path with explicit rules (well worn path)
- Low risk of failure, multiple entries possible
OR this?

- Moderate $$
- Training/expertise required
- Multiple different obstacles
- No one approach works for all
- High risk of failure, but not fatal

• Moderate – high $
• Extremely high level and diversity of training/
• expertise required
• Long and arduous
• High risk of failure, potentially fatal
Strategies to Reduce Risk

• GAP analysis to identify and mitigate risks
• Product development planning (TPP, PDP)
• Learn from others’ mistakes and manage expectations of team members
• Invest in expertise (regulatory, CMC) as early as possible
• Outsource carefully, with appropriate oversight (compliance audit, quality review by sponsor).
Target Product Profile

• “Beginning with the goal in mind.” The TPP is a useful tool for planning research and development activities throughout development.

• Identifies characteristics of marketed product

• Living document that changes as new information is obtained

• Can help all stakeholders focus on consensus goals and also understand the end results of the development efforts.

• FDA Guidance:

TPP Attributes

• Indications and Usage
• Dosage and Administration
• Dosage Forms and Strengths
• Contraindications
• Warnings and Precautions
• Adverse Reactions
• Drug Interactions
• Use in Specific Populations
• Drug Abuse and Dependence
• Overdosage
• Description
• Clinical Pharmacology
• Nonclinical Toxicology
• Clinical Studies
• References
• How Supplied/Storage and Handling
• Patient Counseling Information
• Endpoints for clinical evaluation
Product Development Planning

• A PDP is a tool for assessing and planning development path (road map)
• Include assessment of expertise residing in investigator laboratory
• Intellectual Property assessment
• Feasibility – can product be manufactured GMP
• Living document with iterative review (milestone based) to maximize utility
• NOT one size fits all
• Can be used by investigators to obtain funding, by funders to establish pipeline priorities and future funding needs
Components of PDP

• Background – disease, treatments, market landscape
• Overview of development to date
• Gap analysis
• Risk mitigation approaches
• Plans for development with cost and timeline – the “package”
Have PDP, Time to Start a Company?

• G-H partners such as FFB’s CRI, HDI’s BioMotiv, and commercial funding partners (such as Takeda) may support or co-partner development.

• Venture philanthropy model to fund commercialization of novel therapies

• Matchmaking with other pharma partners serves the mission just as well as direct investment
Investments Made Since 2008

• ACT
• AGTC
• Genable
• Mitochem
• ReNeuron
• Sparing Vision
• Spark
Strategies for leveraging investments in product development

• Invest in platforms that apply to multiple indications or solve issues that apply to >1

• Sharing of information – “lessons learned” in forums such as HRA

• Working together to bring common issues to light and resolve them, e.g. workshops
Questions after the meeting

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