Staying on the Critical Path

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Senior Vice President, Research and Development

March 6, 2013
Workshop
CIRM Grantee Meeting
Avoiding “bumps” in the pathway
Objectives are to increase understanding of preclinical and manufacturing activities...

- Increase understanding of the preclinical studies and manufacturing activities on the development pathway to develop a product for patients
- Provide opportunity to share lessons learned on the development pathway between previously- and newly-funded grantees
- Raise awareness about ways to engage in collaborative interactions for clinical trials with the UK

Overview of product development pathway, identify the timeline for activities e.g., analytical, process, preclinical, clinical, regulatory, quality, along with questions to ask along the way, and where to get help. A mix of didactic talks and interactive exercises

Overall goal is to enable interested Grantees to more effectively stay on the critical path to develop a product.
Today’s speakers and agenda include…

2:00 Setting the context, sharing lessons learned
Ellen G. Feigal, MD, Senior Vice President, R&D, CIRM

2:15 Designing preclinical studies to optimize first-in-human
Joy Cavagnaro, PhD, DABT, RAC, President, Access BIO
Q and A

3:00 Manufacturing and regulatory issues on development pathway
Keith Wells, PhD, Senior Consultant, Biologics Consulting Group
Q and A

3:45 Case Studies, Q and A  Drs. Cavagnaro/Wells

4:30 Clinical trials – Opportunities for California researchers to collaborate with the UK
Christopher Bravery, PhD, Director, Consulting Advanced Biologicals, Ltd; Matthew Hallsworth, PhD, Head of Communications, Nat’l Institute for Health Research Office of Clinical Research Infrastructure; Natalie Mount, PhD, Chief Clinical Officer, Cell Therapy Catapult; Nicholas Hooper, Head of Science and Innovation, British Consulate-General and Kathryn Brown, Regional Director
Mission
“To support and advance stem cell research and regenerative medicine under the highest ethical and medical standards for the discovery and development of cures, therapies, diagnostics, and research technologies to relieve human suffering from chronic disease and injury”

Explore (2004-2010)
- Fund broad number of diseases and projects
- Establish foundation for leadership in stem cell research

Focus (2011-2016)
- Prioritize projects and investments
- Drive clinical trials for patients to generate preliminary evidence of therapeutic benefit
- Develop partnerships

Deliver (2016+)
- Facilitate commercialization of therapies
- Advance therapies to patients
- Enable business model for stem cell-based therapies
Over 560 research and facilities awards to over 60 institutes and companies

12 new institutes and centers of regenerative medicine

Over 1200 major scientific papers published

Over 130 new major stem cell researchers in California

77 translational/development programs
  – 51 Early Translation programs, 24 Disease Teams, 2 Strategic Partnership programs

$1.7 B awarded
CIRM’s core programs provide a pathway spanning scientific advances to therapies.

Basic Research → Candidate Discovery Research → Preclinical Research → Preclinical Dev. → Phase 1 Clinical Research → Phase 2 Clinical Research

Select Development Candidate → File IND

Training

Basic Research

Tools & Technologies

Early Translational Research

Disease Teams

Strategic Partnerships
CIRM Disease Teams Initiative: Target End Goals

<table>
<thead>
<tr>
<th>RFA (Year Awarded by ICOC)</th>
<th># of INDs</th>
<th>$(MM)$ towards IND</th>
<th># of Early Stage Clinical Trials</th>
<th>$(MM)$ towards Early Stage Clinical Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease Team I (2009)</td>
<td>14</td>
<td>$228.0</td>
<td>0</td>
<td>$0</td>
</tr>
<tr>
<td>Disease Team II (2012)</td>
<td>3</td>
<td>$60.0</td>
<td>8</td>
<td>$148.1</td>
</tr>
<tr>
<td><strong>TOTALS</strong></td>
<td><strong>17</strong></td>
<td><strong>$288.0</strong></td>
<td><strong>8</strong></td>
<td><strong>$148.1</strong></td>
</tr>
</tbody>
</table>
25 Disease Teams comprise $436.1 MM

Pie slices are labeled as follows:

- **Blood Disorders**: $77.2, 4
- **Bone Disorders**: $29.2, 2
- **Cardiovascular Disorders**: $59.5, 4
- **Endocrine Disorders**: $20.0, 1
- **Eye Disorders**: $23.0, 1
- **Hematologic Cancers**: $33.2, 2
- **HIV/AIDS**: $34.6, 2
- **Neurodegenerative Disorders**: $11.7, 1
- **Skin Disorder**: $40.0, 2
- **Solid Cancers**: $67.7, 4
- **Neurologic Injuries**: $40.0, 2
- **Solid Cancers**: $17.7, 1
- **Solid Cancers**: $77.2, 4
- **Solid Cancers**: $25.1, 2
- **Solid Cancers**: $40.0, 2
- **Solid Cancers**: $23.0, 1
- **Solid Cancers**: $33.2, 2
Therapeutic modalities are broad

Cell Therapy
Gene-Modified Cell Therapy
Small Molecule/mAb/Protein
Cell Therapy Combination Product
Gene-Modified Cell Therapy Combination Product

Therapeutic modality of CIRM translational portfolio current as of October, 2012
13 DTI – 5 allogeneic, 4 autologous (1 iPS), 2 Mab, 2 small molecules
11 DTII – 7 allogeneic, 2 autologous, 1 Mab, 1 small molecule
2 SPI – 1 allogeneic, 1 autologous
Summary of DT highlights

• Over half of the DT1s successfully advanced through their pre-IND meeting with FDA, towards an approvable IND
• 1 clinical trial to start in 2013, expect 1 to 2 more in 2013
• Anticipate 5 clinical trials by end of 2014
• 5 have collaborative funding partners; 1 has collaboration with disease foundation; 2 have companies as PI or co-PI; 2 have founded companies
• 21 invention disclosures, 24 active/pending patent applications
• 18 scientific publications
Driven by science and evidence needed on regulatory pathway

- Prior to award
  - mutually agreed upon Go, no go and progress milestones, success criteria
- During the conduct of research
  - Interactive ongoing discussions between CIRM scientists and funded research team
  - Updates on interval progress on bi-annual to quarterly basis and overall annual progress updates
  - Clinical development advisor meetings yearly/ key milestones (DT1s have been assessed in 2011 at 12-18 month milestone, now at 24-30 month milestone)
- CIRM/FDA webinars, educational roundtables, conferences, seminars
We have expert advisors to listen....
And to try and position you for success...
Take home points from Target Product Profile Grantee Workshop 2011

- Successful drug development and commercialization should be label-driven, question-based
- TPP is developed by the sponsor to drive product development – start with the end in mind
- TPP is a living document and will change over time as data accumulates
- Criteria must be prespecified and measurable for optimal and minimal threshold (acceptable target differentiation for market advantage)
- Facilitates the efficiency of sponsor-FDA interactions and communications and helps to maintain focus on the labeling goals
- Helps address issues early in the process thereby preventing late-stage failures & decreasing total drug development time
Knowing where you’d like to go is key in product development.

IGNORANCE
It’s Amazing How Much Easier it is for a Team to Work Together When No One Has Any Idea Where They’re Going.
We hope this workshop will be informative and help guide your project.
CIRM templates to guide your product development; other websites you may find useful


• CIRM Major Milestones Template
• CIRM Clinical Protocol Synopsis Template
• CIRM Manufacturing Plan Synopsis Template
• CIRM Target Product Profile (TPP) Template
  – CIRM workshop on preparing a TPP:
    http://youtu.be/QK_zPmarkws
• Communications with the FDA on the Development Pathway for a Cell-based Therapy: Why, What, When and How? Stem Cells Translational Medicine Vol 1, #11, November 2012
  • www.fda.gov
  • www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation
  • www.fda.gov/ohrms/dockets/ac
  • drugs@fda.gov
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