Driving Standards for Regenerative Medicine Treatments in California: A Perspective from CIRM

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California Institute for Regenerative Medicine

CIRM Background
Our Mission
Accelerate Stem Cell Treatments
To Patients with Unmet medical needs.

2004
CIRM created by Patient Advocates and California Stakeholders-Proposition 71

$3B
Committed to CIRM Mission

1000 (200 UNDER ACTIVE MANAGEMENT)
Cutting Edge Research & Transformative Programs funded

56 CLINICAL TRIALS
First in human, cell & gene medicine, some ready for final marketing approval

>1200 PATIENTS
Patients enrolled in CIRM Funded Clinical Trials
56 Clinical Trials: To Tackle Over 35 Different Unmet Medical Needs

Huntington’s Disease
Kidney Failure
Lung Cancer
Melanoma
Multiple Myeloma
Bone Disease
Immune Deficiencies
Sickle Cell
Metastatic Cancer
Paralysis
Stroke
Diabetes

Presentation Outline

- State of the Field:
  Overview of regenerative medicine treatments making their way to patient

- Risks to Patients of Unregulated Treatments:
  Harms resulting from unproven stem cell treatments

- Standards:
  Regulated, Reputable and Reliable

- A Path Forward:
  Considerations for patient protection
State of the Field Globally

1,069 Clinical Trials Underway Worldwide by End of Q2 2019

Number of Clinical Trials Utilizing Specific RM/AT Technology: Q2 2019

<table>
<thead>
<tr>
<th>Gene Therapy</th>
<th>Gene-Modified Cell Therapy</th>
<th>Cell Therapy</th>
<th>Tissue Engineering</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total: 366</td>
<td>Total: 410</td>
<td>Total: 249</td>
<td>Total: 44</td>
</tr>
<tr>
<td>Ph. I: 117</td>
<td>Ph. I: 187</td>
<td>Ph. I: 49</td>
<td>Ph. I: 5</td>
</tr>
<tr>
<td>Ph. II: 219</td>
<td>Ph. II: 207</td>
<td>Ph. II: 168</td>
<td>Ph. II: 23</td>
</tr>
<tr>
<td>Ph. III: 30</td>
<td>Ph. III: 16</td>
<td>Ph. III:32</td>
<td>Ph. III: 16</td>
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</tbody>
</table>

Source: https://alliancerm.org

Unregulated Treatments Pose Risks

FDA warns StemGenex Biologic Laboratories LLC of illegally marketing an unapproved cellular product

Defendants lacked scientific evidence that their "amniotic stem cell therapy" could treat or cure serious diseases, including Parkinson's, macular degeneration, cerebral palsy, and autism
Characteristics and Scope of Training of Clinicians Participating in the US Direct-to-Consumer Marketplace for Unproven Stem Cell Interventions

Table 1. Professional Backgrounds of Physicians and Nonphysicians Providing Stem Cell Interventions in California, Florida, and Texas

<table>
<thead>
<tr>
<th>Profession</th>
<th>Individuals, N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physicians</td>
<td>330 (91.6)</td>
</tr>
<tr>
<td>Medical degree (eg, MBBS) from non-US schools</td>
<td>7 (2.1)</td>
</tr>
<tr>
<td>Total physicians</td>
<td>401 (66.0)*</td>
</tr>
<tr>
<td>Nonphysicians</td>
<td></td>
</tr>
<tr>
<td>Physician assistants</td>
<td>55 (0.3)</td>
</tr>
<tr>
<td>Nurses</td>
<td>34 (5.6)</td>
</tr>
<tr>
<td>Complementary and alternative medicine practitioners</td>
<td>32 (5.3)</td>
</tr>
<tr>
<td>Podiatrists</td>
<td>29 (4.8)</td>
</tr>
<tr>
<td>Physical therapists</td>
<td>18 (3.0)</td>
</tr>
<tr>
<td>Other*</td>
<td>15 (2.5)</td>
</tr>
<tr>
<td>Scientists with a master’s degree or doctorate in philosophy</td>
<td>10 (1.6)</td>
</tr>
<tr>
<td>Unclear qualifications</td>
<td>10 (1.6)</td>
</tr>
<tr>
<td>Dentists</td>
<td>6 (1.0)</td>
</tr>
<tr>
<td>Total nonphysician clinicians</td>
<td>207 (34.0)</td>
</tr>
<tr>
<td>Total clinicians</td>
<td>608 (100)</td>
</tr>
</tbody>
</table>

*Mean age of 55 years (range, 32-95 years). Mean licensed years of practice of 25 years (range, 2-40 years).

- 351 companies at 570 clinics with the largest concentration in CA, FL & TX (Cell Stem Cell 2016, Turner & Knoepfler)
- 166 companies, 608 clinicians (66% physicians) in these 3 states in Jan. 2018
- 5 companies staffed exclusively by podiatrists, 2 by naturopaths, 1 by dentists and 1 by practitioners of unclear qualifications
- Of 157 companies with a physician, 52% had 1 physician with formal training to match conditions claimed to treat
- 77% of orthopedic-focused practices had 1 or more physicians with appropriate specialty training
- Only 19% of companies marketing stem cells for nonorthopedic indications had physicians practicing within their scope
- In 2018, the FSMB reported that 17 of 51 boards investigated complains and 8 took disciplinary actions related to physicians performing unlicensed stem cell procedures

Standards for the Delivery of Regenerative Medicine
Regulated Reputable Reliable

Qualified Doctors, Nurses and Technicians
FDA-authorized and Independent IRB Oversight
Leading Medical Centers with Field Expertise
Patient Centered Care with follow-up
What do we Have in Place Today?

- Clinicaltrials.gov – a trial registry being misused by unregulated clinics
- California Senate Bill 512 Dr. Hernandez (2017)- disclosure to patients that they are receiving unregulated putative “stem cell” therapy
- 2017 FDA “Framework for Regenerative Medicine Products” to provide clarity
- ISSCR “A Closer Look at Stem Cells” information and “red flags” for patients
- National Academy of Sciences & WHO convening gap analysis and policy discussions on regulating the stem cell industry

Build on Existing CA Policy Framework

- Senate Bill 512 Dr. Hernandez (2017)
  - Human cells, tissues or cellular or tissue-based products “HCT/Ps” as defined by FDA
  - If HCT/Ps are not FDA-approved, then patient must be informed of the following:
    
    "THIS NOTICE MUST BE PROVIDED TO YOU UNDER CALIFORNIA LAW. This health care practitioner performs one or more stem cell therapies that have not yet been approved by the United States Food and Drug Administration. You are encouraged to consult with your primary care physician prior to undergoing a stem cell therapy."

- Apply consent and professional certification requirements to products and caregivers covered under SB 512
Professional Standards for Patient Disclosure

- Informed Consent Process
  - Rationale for providing the treatment and perceived benefits
  - Potential risks or adverse events
  - Oversight and monitoring
  - Cost to patient
  - Qualifications of organization / treatment team
  - Alternatives treatments for this condition

- Certified Caregivers Providing Consent

For Consideration:

- Publicly available registries of stem cell treatment options
  - Consider a designated section for patient self-reports from unregulated treatments that is clearly labeled as unregulated

- Requirement of clear visibility to treatment team’s credentials at clinics offering regenerative medicine treatments

- A mechanism for investigating those holding healthcare licenses suspected of violating professional standards when providing unproven stem cell interventions, particularly those outside their scope of training

- Registration of treatments that involve HCT/P’s regulated under the PHS Act and clearly distinguish between FDA-authorized treatments and practice of medicine
Regulated Reputable Reliable
Can We Leverage Existing Capacity?

- Licensing
- Enforcement
- Outreach

• Alpha Clinics Network and Clinical Sites- Model & Standards creation
• Fellowships in specialty-based regenerative medicine research
• Alignment with FDA
• Patient navigation & education resources
• Potential involvement in registry

CIRM: Partnerships & Stakeholders

- Patient Advocates
- Consortia & Partners
- CIRM Researchers

Alpha Stem Cell Clinics Network

Hub for Interactions with and between grantees, non profit Organizations, the Public & Industry
Multi-Stakeholder Effort

The Washington Post

New Google policy bars ads for unproven stem cell therapies

“Untested, deceptive treatments” can endanger consumers, Internet giant says.

Its new policy will prohibit ads for treatments that have “no established biomedical or scientific basis.”

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Thank You!

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