New Directions, New Hope

James R. Baker, Jr., MD

Chief Executive Officer
and Chief Medical Officer
Food Allergy Research & Education

January 21, 2015
Today’s Presenter

James R. Baker, Jr., MD
FARE : Our Mission

Life

The ability to live a safe, productive life with the respect of others on food issues

Health

Enhance access to healthcare that provides state of the art diagnosis and treatment

Hope

Research that promises new therapies that improve the condition
Where we are now.....

- The epidemic continues and expands
- Research has not provided a quick cure
- Patient frustration with healthcare and lack of treatments increases
- We need to work harder to get new drugs for food allergy.....
Challenges to Pharmaceutical Development

- Long timelines and high risk in development (especially compared to IT)
  - Difficulty in obtaining early stage and venture funding
  - Regulatory hurdles in clinical development
- Expertise and funding required for development beyond the capabilities of small companies and academia
- Cost of development prohibitive without market!
Types of New Drugs

- Generic Drugs
- Novel Delivery Systems
- “Me-too” Drugs
- Devices (e.g., heart valves, etc.)
- New Chemical Entities
- Biologics
- Vaccines
- Therapeutic Natural Substances
Problem: Moving a Drug from Concept to Finished Product Takes More Than a Decade

Preclinical development
Discovery, Synthesis, Purification, Animal testing, Institutional Review Board
3-11 years (6.5 average)

Clinical trials
Phase I
1-2 years
Phase II
1-2 years
Phase III
2-3 years

FDA Review
1-2 years
Phase IV clinical trials
Ongoing

Investigational New Drug Application submitted to FDA
New Drug Application submitted to FDA
Drug approval

SOURCE: Food & Drug Administration
PHASE 1 CLINICAL TRIALS
“FIRST IN HUMAN” STUDIES

- To investigate safety and tolerance of single and multiple-dose administration of a drug

- Dose escalation
  - gathering experience at lower doses before proceeding to higher doses
  - may be conducted in healthy volunteers

- Initial characterization of pharmacokinetic and pharmacodynamic responses to the drug
PHASE 2 CLINICAL TRIALS

- Assessment of safety and efficacy in a relevant population
  - Subgroup analysis of different populations
- Dose-ranging
- Use of validated surrogate endpoints that provide “proof of concept”
- Controls
  - Double-blinded, randomized, placebo-controlled
- Drug interactions and metabolism
PHASE 3 CLINICAL TRIALS
“Pivotal” STUDIES for Drug Approval

- Goals:
  - Confirm efficacy
    - endpoint must reflect true clinical benefit
  - Characterize magnitude of clinical benefit / treatment effect
  - Demonstrate acceptable safety profile in large number of subjects
Number of subjects necessary for each stage of drug development

- **Phase 1**
  - First-in-human, safety studies (~20-80 patients or healthy volunteers)

- **Phase 2**
  - First efficacy trials (~100-300 patients)
  - Expanded safety assessments

- **Phase 3**
  - “Approval” studies (~500-3000 patients)
  - Optional: Compare to current standards

- **Phase 4**
  - Post-marketing studies — Long-term safety, economics, label expansion
When Might Large Pharmaceutical Companies Get Involved?

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Discovery, Synthesis, Purification, Animal testing, Institutional Review Board

3-11 years (6.5 average)

**Clinical trials**

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- **Phase II**
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**FDA Review**
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**Phase IV clinical trials**
Ongoing

**Investigational New Drug Application submitted to FDA**

**New Drug Application submitted to FDA**

**Drug approval**
## Roadblock: Pre-Clinical Cost

<table>
<thead>
<tr>
<th>Milestone</th>
<th>Cost ($ thousands)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Revise Synthesis of the Material</td>
<td>$100k</td>
</tr>
<tr>
<td>2. Chemical Synthesis Process</td>
<td>$100K</td>
</tr>
<tr>
<td>3. Preliminary Scale-up (100-200 g batch)</td>
<td>$300k</td>
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<tr>
<td>4. Scale-up to 2-5 kg GMP for Clinical Trial</td>
<td>$600-1,500k</td>
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<tr>
<td>5. Stability Studies</td>
<td>$250k</td>
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<tr>
<td>6. Pre-formulation Studies</td>
<td>$80k</td>
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<tr>
<td>7. Formulation into Sterile Injectable</td>
<td>$250-400k</td>
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<tr>
<td>8. Pre-clinical Toxicity Testing (FDA)</td>
<td>$500-750k</td>
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*Minimal Total Funding Before Phase I Trial*: $2.5 - $4.0M
## Deciphering Tough Diseases

Ten drug companies and the National Institutes of Health are collaborating in the Accelerating Medicines Partnership, a project to try to unlock the biology behind Type 2 diabetes, rheumatoid arthritis, Alzheimer’s disease and lupus, and to discover targets for novel drugs.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Prevalence in the U.S.</th>
<th>Leading drugs</th>
<th>World-wide drug sales, in billions</th>
<th>Pharmaceutical companies participating in NIH project</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>31.3 million Type 1, 31.3 million Type 2</td>
<td>Lantus, Januvia</td>
<td>$36.3</td>
<td>$60.7</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>1.8 million</td>
<td>Humira, Enbrel</td>
<td>$41.1</td>
<td>$52.1</td>
</tr>
<tr>
<td>Alzheimer’s disease</td>
<td>4.8 million</td>
<td>Exelon, Aricept</td>
<td>$5.3</td>
<td>$4.6</td>
</tr>
<tr>
<td>Lupus</td>
<td>340,000</td>
<td>Benlysta, CellCept</td>
<td>$0.4</td>
<td>$1.2</td>
</tr>
</tbody>
</table>

*Alzheimer’s disease drug sales projected to decline between 2012 and 2018 because some drugs will begin facing generic competition*

Sources: EvaluatePharma; IMS Health; Kantar Health; National Institutes of Health

The Wall Street Journal
How will FARE speed up drug development for food allergy?
Why are new drugs for food allergy gaining interest?

- Mylan and Sanofi: Epinephrine shows a market
- DBV and ARC: Show investor interest
- DBV and ARC: Show a path toward drug approval
- Barrier that remains is a way to accomplish large scale, Phase III trials.....
FARE’s Approach to Meeting its Mission

Life

Education and Advocacy

Health

FARE Clinical Network and New investigators

Hope

Short term: encourage pharma to test drugs for food allergy
Establish FARE Clinical Network

**What and why**
- Network of clinical care and clinical research centers
- Furthers quality care for patients and fosters best practices
- Gives FARE access to patients for registry and bio-repository
- Builds FARE capabilities for late stage clinical research

**How**
- Issued open RFA, with invitation letter to desired sites
- Criteria include qualifications of staff, procedure capabilities, etc.
- Sites will get formal acknowledgement plus financial support

**Next steps**
- Announced 3 months ago
- Over 20 positive responses nationwide
- Total cost $5M over 5 years
Expanding the Scientific/Medical Community

- Build careers and participation of investigators in the field
  - Re-energize Gittis Award (fellowship award).
  - Five and two year career development awards (mid and early career award)
    - 5 Awards at $750K ($150/year X 5 years) and 2 at $150K ($75/year X 2 years) respectively
    - 20 applicants for mid-career awards, 5 for early career awards
  - Include junior investigators on review and advisory boards
Example: Viaskin® Peanut Patch

- Placed on skin and releases peanut antigen
- Delivered via dendritic cells to the immune system
- 100 subjects (70 with a non-severe and 30 with a severe allergy), were treated for two weeks with 20 µg to 500 µg
- The dose of 500 µg in adults and adolescents, and the dose of 250 µg of Viaskin® Peanut in children, were shown to be well-tolerated
- Suggests satisfactory safety of Viaskin® Peanut in patients allergic to peanuts.
Example: Dupilumab

- New England Journal Article
- Sanofi-Regeneron biologic finished phase II/III
  - Highly effective for asthma and atopic dermatitis
- Approval within 1-2 years for atopic dermatitis
- Blocks “atopic march”
- Dan Rotrosen (head of allergy at NIAID) related company’s interest in food allergy treatment but inability to conduct trials
Effect of Dupilumab on Atopic Dermatitis
Remarkable Efficacy

C. EASI-50, Study M12

- Skin Healing

D. Change in Average Weekly Pruritus Numerical-Rating Scale Score, Study M12

- Reduction in Itching
Our findings provide evidence that allergic asthma and atopic dermatitis might have related drivers — in particular, interleukin-4 and interleukin-13 — and that these diseases may benefit from the same therapeutic approach. Furthermore, this commonality suggests that other atopic diseases may share these drivers, providing a rationale for studying dupilumab in such conditions.

Other Anti-Allergic Biologicals in Late Stage Development

- **Amgen: Anti-TSLP**
  - Prevents inflammation in human asthma after antigen challenge

- **Novartis: More effective anti-IgE**
  - Depletes IgE very effectively-short term cure

- **KaloBios Pharma: Antibody to eosinophils EMR1**
  - Kills eosinophils, can treat esophagitis
FARE: Our Mission

Life
Health
Hope
Questions?
Our Next Webinar

Cathy Owens, RN, M.Ed
Coordinator of Health Services and Lead Credentialed School Nurse
Murrieta Valley Unified School District

Wednesday, February 18
1:00 – 2:00 PM ET

Register at:
http://www.foodallergy.org/tools-and-resources/webinars