

A woman with blonde hair is looking intently at a molecular model she is holding in her hand. The model consists of black, white, blue, red, and purple spheres connected by white rods. The background is a soft, out-of-focus grey. A dark blue ribbon-like graphic element flows across the top and bottom of the image.

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## **Biotech Concerto #1**

*Brief Introduction to the Pharma/Biotech Business*

**December 2008**

- Drug Research & Development
- Pharma and Biotech
- Biotech and Venture Capital

Drug Research & Development efforts are guided by two principles:

- are the underlying mechanism or cause of a disease understood?
- does this disease represent a significant unmet medical need in patients?

If the answer to both questions is "yes," then a research program is developed aimed at better understanding the disease and finding an effective therapy.

Source: Novartis, adapted

## *Why are new drugs needed?*

... due to unmet medical needs:

- not yet treated diseases
- new diseases
- low efficacy of existing drugs
- side effects of existing drugs
- cost of therapy
- downstream health costs
- etc.

Source: Ian Hughes, University of Leeds, adapted

## *Target Identification and Validation*

This step encompasses a wide range of scientific activities focused on identifying new targets and confirming their role in disease.



Source: Novartis

## Hit Finding

This entails development of robust assays to test small molecule compounds in High-Throughput-Screens. In case of Biologics this stage entails development of antibodies.



Source: Novartis

## *Lead Optimization*

In lead optimization “small molecules” are chemically altered to improved properties. In case of Biologics, antibodies are modified to increase their affinity for their target.



Source: Novartis

## *Preclinical Safety*

To establish an initial safety profile of the drug, extensive toxicological and safety pharmacological profiles are done using in-silico, in-vitro, and appropriate animal models.



Source: Novartis



## *Phase I Clinical Trials*

In Phase I, the drug is tested in small groups of healthy volunteers (~20) to evaluate its safety, determine its safety dosage range and identify side effects.



Source: Novartis

## *Phase II Clinical Trials*

In Phase II the drug is given to a larger group of people (~100-300 patients) to test its effectiveness, determine the effective dose range and to further evaluate its safety.



Source: Novartis

## *Phase III Clinical Trials*

In Phase III the drug is given to a large group of patients (~1000-3000) to confirm its effectiveness, monitor side effects, and compare it to existing treatments.



Source: Novartis

## Registration

For the registration of a new drug, the results of preclinical test and clinical studies, quality data, manufacturing process are reviewed by the regulatory authorities.



Source: Novartis

## Phase IV

Once a drug is on the market, adverse effects need to be monitored/reported. Life-cycle management programs aims at new indications and/or improving formulations of the drug



Source: Novartis

## Example of a Drug Pipeline: Novartis Oncology, Q1/2008

Exploratory	Confirmatory		Registration
	Phase II	Phase III	
HCD122 Hem. tumors	LBQ707 Solid Tumors	EPO906 Ovarian cancer	Tasigna® (JPN) IM <sup>2</sup> res. / intol. CML <sup>2</sup>
TKI258 Hem./solid tumors	PKC412 AML <sup>1</sup>	SOM230 Acromegaly / Cushing's disease	Exjade® (JPN) Chronic iron overload
RAF265 Melanoma	LBH589 Hemat. tumors	Glivec® GIST <sup>2</sup> adjuvant / CML <sup>2</sup>	
LBY135 Solid tumors	ASA404 Solid tumors	RAD001 Neuroend. tum.	
BEZ235 Solid tumors	RAD001 Sol. tumors / breast cancer/ PICT <sup>7</sup>	RAD001 RCC <sup>4</sup>	
AUY922 Solid tumors	SOM230 GEP <sup>11</sup> tumors	Tasigna® GIST <sup>2</sup> / newly diagnosed CML <sup>2</sup> / subop. CML <sup>2</sup>	
BHQ880 Solid tumors	Glivec® Non-oncology indications		
LBH589 Hem. & solid tumors	EPO906 Solid tumors		
Exjade® HH <sup>8</sup>			

■ NME<sup>9</sup>  
■ NME<sup>9</sup> roll-out  
■ LCM<sup>10</sup>

<sup>1</sup> Acute myeloid leukemia <sup>2</sup> Gastrointestinal stromal tumor <sup>3</sup> Chronic myeloid leukemia <sup>4</sup> Renal cell carcinoma <sup>5</sup> Pancreatic islet cell tumor  
<sup>7</sup> Imatinib <sup>8</sup> Hereditary hemochromatosis <sup>9</sup> New molecular entity <sup>10</sup> Life cycle management <sup>11</sup> Gastroenteropancreatic

32 | Lehman Brothers Global Healthcare Conference | P. Costa / R. Boehm | 19 March 2008



Source: Novartis

## Industry—typical Key Data

	Discovery	Preclinical Studies	IND Filing	Clinical Phase 1	Clinical Phase 2	Clinical Phase 3	NDA Filing	FDA/ EMEA	Phase 4
<b>Years</b>	2 - 6	3.5		1	2	3		2.5	
<b>Test Population</b>	Laboratory	Laboratory and animal studies		20 to 80 healthy volunteers	100 to 300 patient volunteers	1'000 to 3'000 patient volunteers		Review and approval	Post-marketing testing
<b>Purpose</b>	Discovery of new chemical/ biological entities	Assess safety and biological activity		Determine safety and dosage	Evaluate effectiveness and side effects	Verify effectiveness and monitor adverse reactions			
<b>Cost (USD mn)</b>				0.1 - 1	10 - 100	10 - 500			
<b>Success Rate</b>	10'000	10 - 20		5 - 10	2 - 5	2		1	

FDA: US Food and Drug Administration  
 EMEA: European Medicine Agency  
 IND: Investigational New Drug Application at FDA/EMEA  
 NDA: New Drug Application at FDA/EMEA

Source: Pharmainfo.net, adapted

In earlier days, there was a specific distinction between old-style pharmaceutical companies and biotechnology companies. Biotechs genetically engineered proteins from the body, like human growth hormone, for use as therapeutics and produced them in mass quantities.

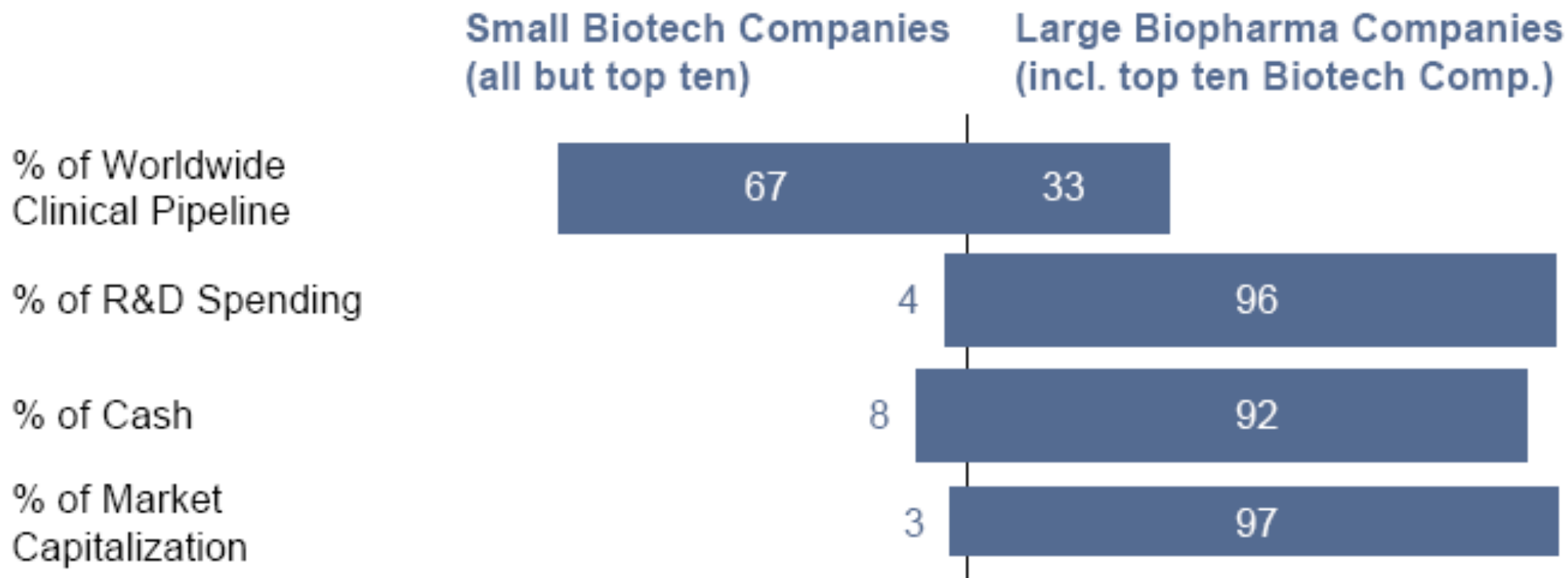
Pharmaceutical companies were medicinal chemistry companies that explored the globe looking for compounds to screen against assays.

Nowadays that distinction is meaningless. When people use the phrase Big Pharma or pharmaceutical companies, they are referring specifically to large, global drug companies that research, develop and sell all kinds of drugs (and sometimes medical devices). Biotech now refers to development-stage companies of many ilks. Biotech encompasses genomics, gene therapy and combinatorial chemistry, as well as traditional protein development companies, and many other permutations.

Source: TheStreet, adapted



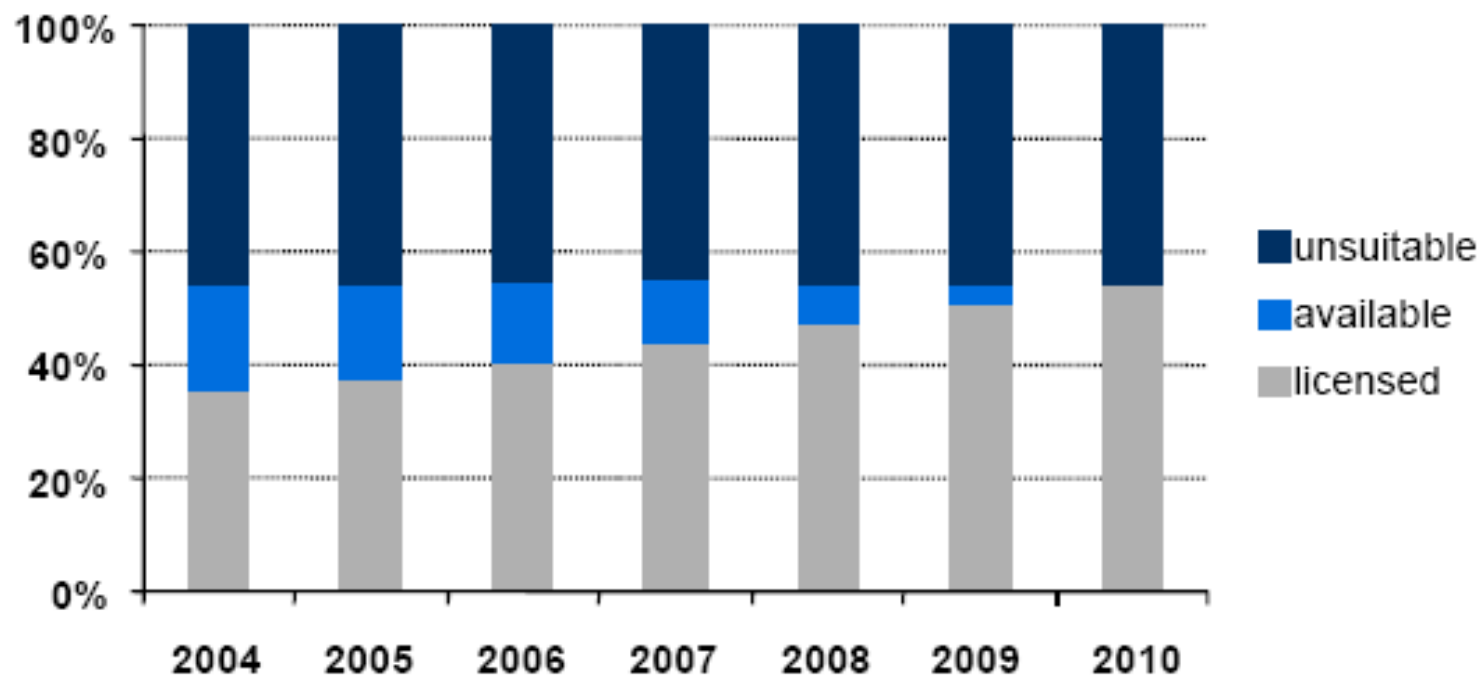
## *Biotech – The Innovation Powerhouse*



Source: Lehman Brothers; Pharmaprojects; Value Lines; BCG

## *The Race for Licensing Deals*

### Clinical Compounds in Phase I – III Trials



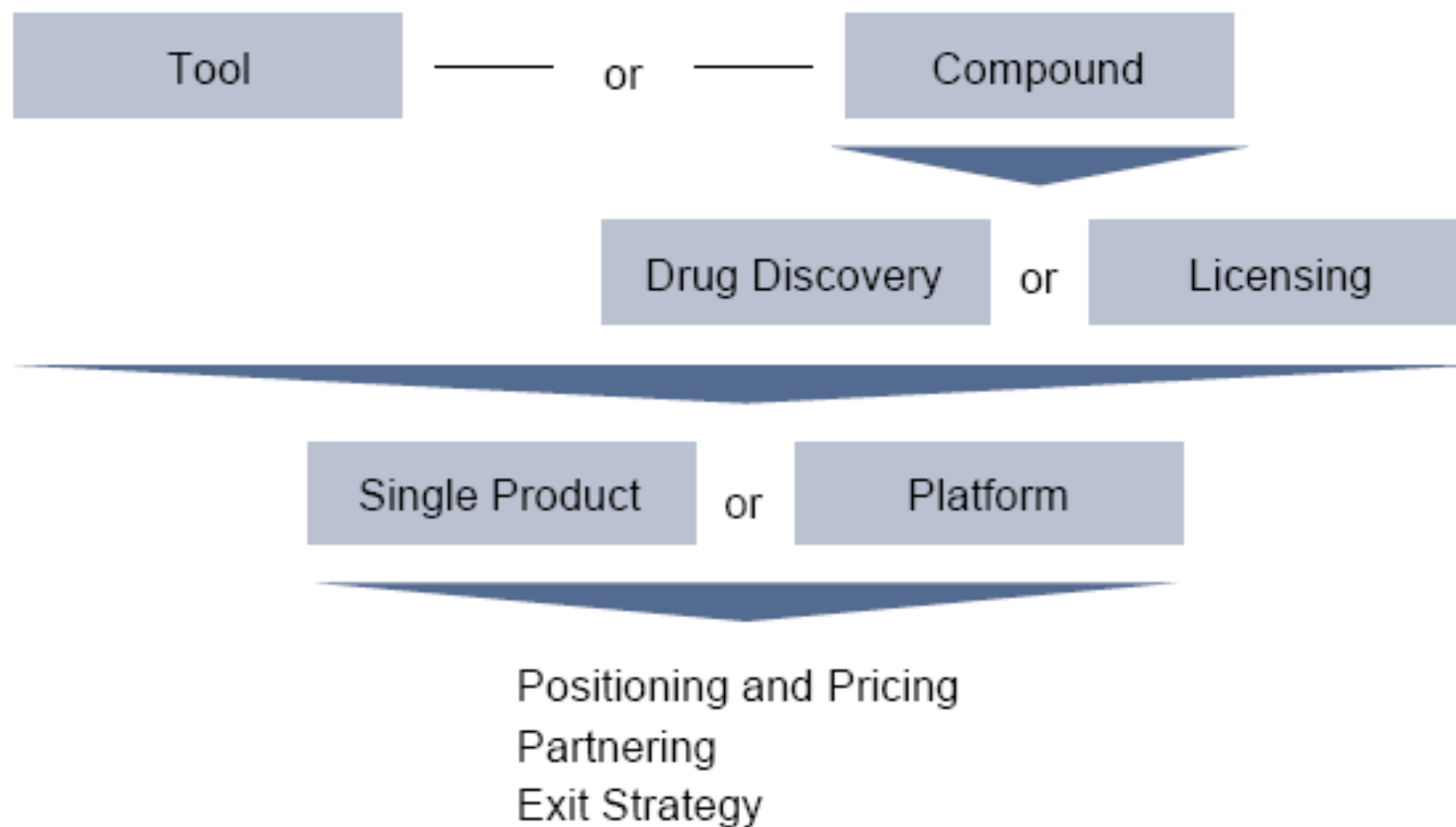
Source: Pharmaprojects; Recombinant Capital; FDA; BCG

## *The Need to Play the “Dating Game”*

Pharma Perspectives	Biotech Perspective
<ul style="list-style-type: none"><li>• Shrinking pipeline</li><li>• Expiring patents</li><li>• Decreasing revenues</li><li>• R&amp;D efficiency</li></ul>	<ul style="list-style-type: none"><li>• Ever existing financing needs</li></ul>

Source: Mayer Brown LLP

## *Biotech's Generic Business Model*

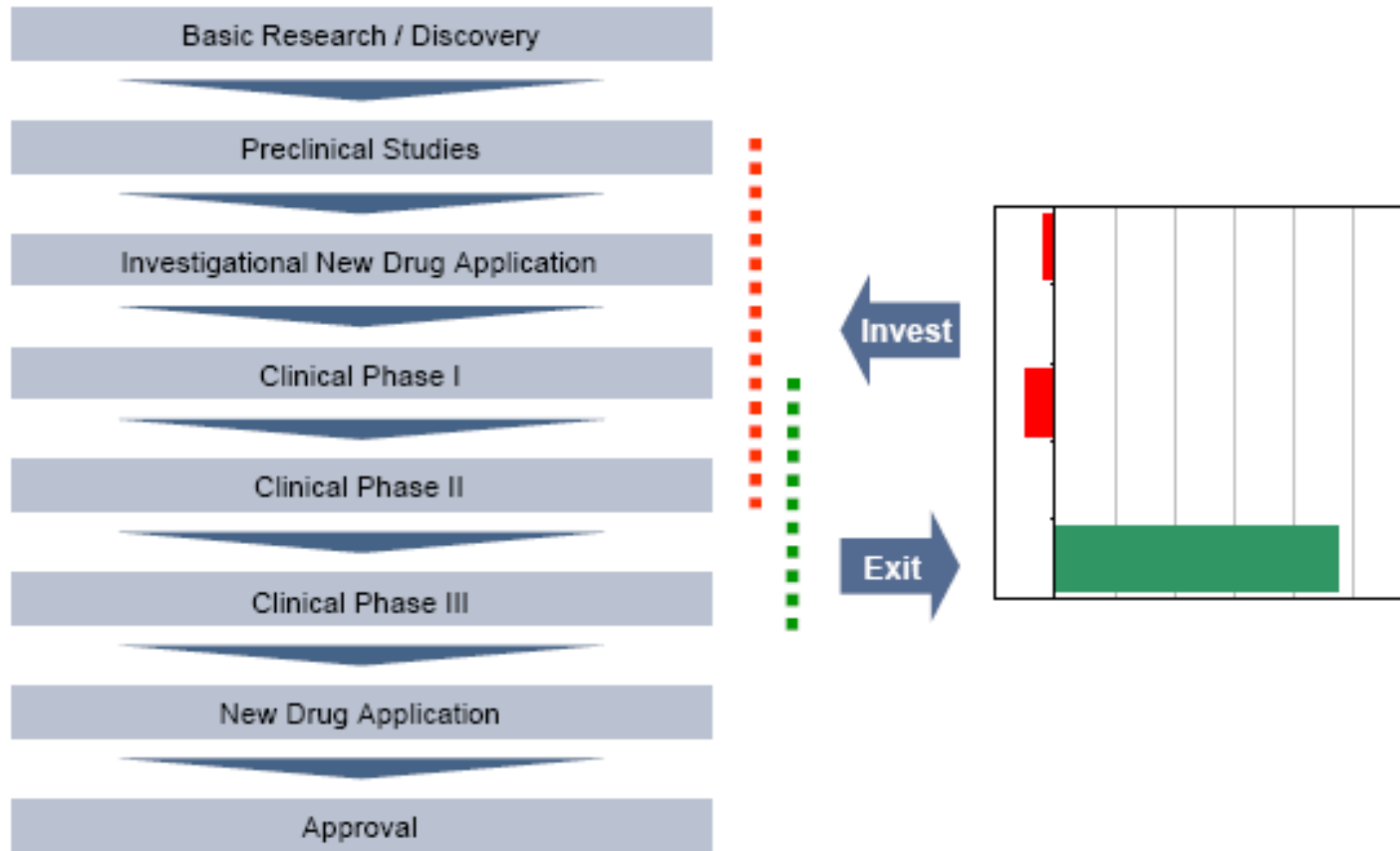


Having a great technology, a promising product pipeline and experienced management is the key to success within the biotech industry, but the proof is in the financing. Venture capital funding within the biotech industry accounts for a significant amount of the total funding, averaging roughly a quarter of all funding, including initial public offerings and additional follow-on funding.

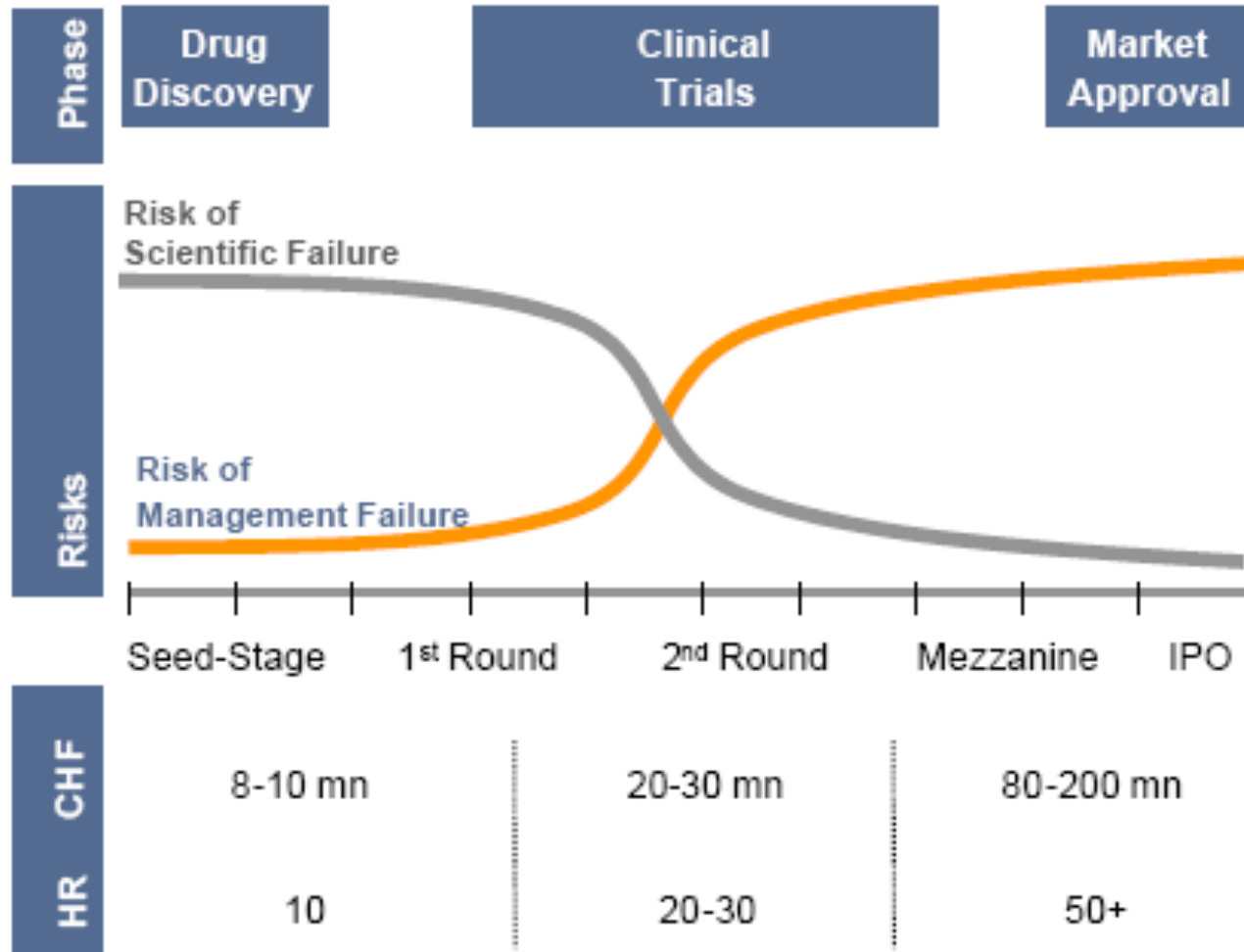
The transition from angel money and early-stage federal grants to venture dollars is a daunting task for many startups and, in this hungry market, a competitive one.

Source: Bioentrepreneur

## Venture Capital Strategy



## Biotech Venture Risk Profile



Source: Aravis Ventures

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