Megafunds: The Concept

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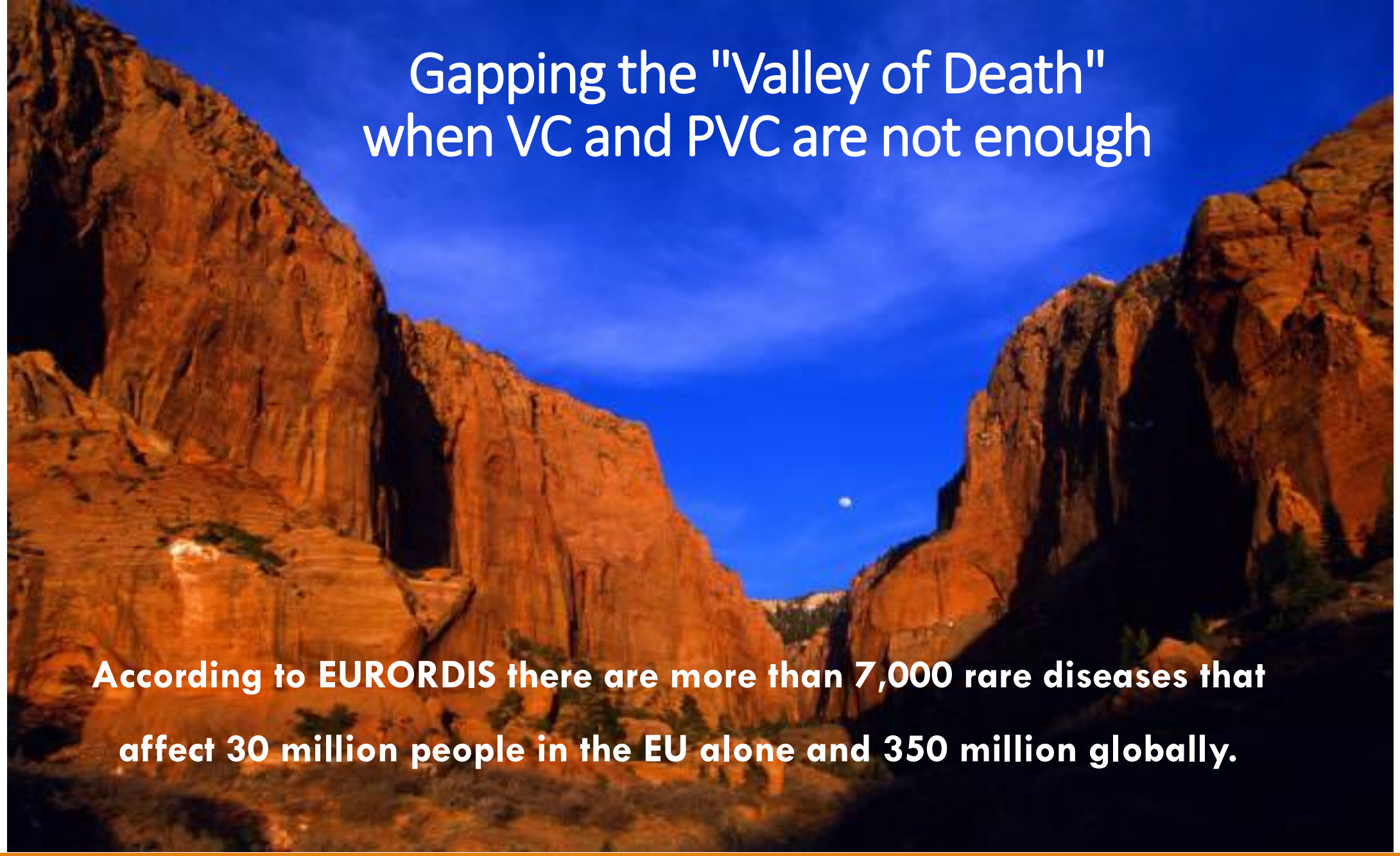
Gapping the "Valley of Death" when VC and PVC are not enough



According to EURORDIS there are more than 7,000 rare diseases that affect 30 million people in the EU alone and 350 million globally.

The Market Size

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- **8%** are living with a rare disease
- **30 million** people in the EU
- **350 million** globally
- Rare diseases affect **more** people than all cancers & HIV combined
- Market value in 2022 at **$209bn**

Extracts from
(a) *Eurordis fact sheet http://www.eurordis.org/sites/default/files/publications/Fact_Sheet_RD.pdf*
(b) *Rare Diseases: Facts and Statistics*, Global Genes (https://globalgenes.org/rare-diseases-facts-statistics/) and
(c) *Rare Diseases: understanding this Public Health Priority* (http://www.eurordis.org/sites/default/files/publications/princeps_document-EN.pdf)
(d) Evaluate Pharma Orphan Drug Report 2017 http://www.evaluategroup.com/public/Reports/EvaluatePharma-Orphan-Drug-Report-2017.aspx

The Market Value

How much Rare Diseases worth?

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- The orphan drug market is expected to almost double between 2016-22, peaking at **$209bn** in 2022 with an **11% growth/year**
- The average cost per patient per year in 2016 for an orphan drug was **$140,443** versus **$27,756** for a non-orphan drug
- Per patient costs for orphan drugs is **5.5 times higher** than non-orphan drugs using median prices

Evaluate Pharma Orphan Drug Report 2017 http://www.evaluategroup.com/public/Reports/EvaluatePharma-Orphan-Drug-Report-2017.aspx
Fortune **Wall Street's next bet: Cures for rare diseases** Andrew W. Lo Jan 21, 2014
Global data Duchenne Muscular Dystrophy - Opportunity and Market Analysis to 2019 April 17, 2015
ACCESSWIRE **/ March 30, 2016 /** The Wealthy Biotech Trader

The DMD Example

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- **DMD Market Size:** The market is expected to grow from $8.2 million for 2014 to nearly $1 billion by 2019, across the six major markets of the US, Germany, France, UK, Italy and Spain.
- This represents a Compound Annual Growth Rate (CAGR) of **160.5%**
- **Budget Impact ?**

Market Research Global Data: Duchenne Muscular Dystrophy-Opportunity Analysis and Forecasts to 2019.
http://www.marketresearch.com/product/sample-9127881.pdf
Global data Duchenne Muscular Dystrophy - Opportunity and Market Analysis to 2019 April 17, 2015 REFERENCE CODE GDHC038POA | PUBLICAT ION DATE APRIL 2015

The Real Impact

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- The economic impact of DMD although is a rare disease, is quite remarkable.
- The total estimated economic burden 2012

Germany	$	278,058,000	Italy	$	154,465,000
UK	$	200,478,000	US	$	1,217,373,000

- Almost **$2 billions for 4** countries in 2012
- The cost to develop and win marketing approval for a new drug is $**2.6 Billion**. (drug failures and exploratory expenses are included)

Landfeldt, Erik, et al. "The burden of Duchenne muscular dystrophy An international, cross-sectional study." Neurology 83.6 (2014): 529-536.
Pammolli, Fabio, Laura Magazzini, and Massimo Riccaboni. "The productivity crisis in pharmaceutical R&D." Nature reviews Drug discovery 10.6 (2011): 428-438.
Tufts University Center for the Study of Drug Development, 2014 (http://csdd.tufts.edu/news/complete_story/pr_tufts_csdd_2014_cost_study)

Current status: a VC overview
the US example

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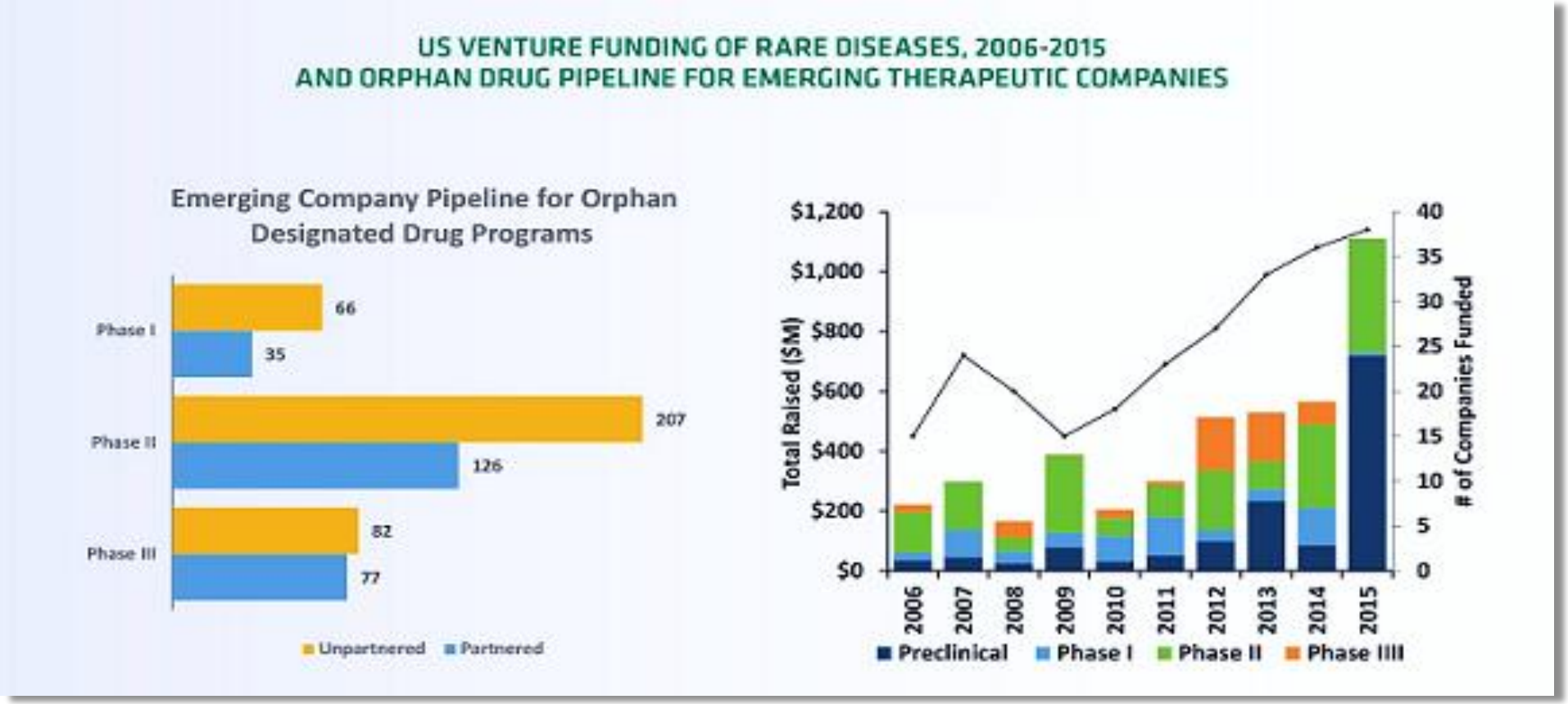

Biotechnology Innovation Organization's 2016 Business Report BIO, Biomedtracker, Amplion 2016 Clinical Development Success Rates 2006-2015
https://www.bio.org/sites/default/files/Clinical%20Development%20Success%20Rates%202006-2015%20-%20BIO,%20Biomedtracker,%20Amplion%202016.pdf

The highlights

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- **Venture Capital:** 2015 was the best year on record for US venture capital, with just under $7 billion raised.
- **Series A Financing:** Series A financing nearly doubled from 2014 to 2015.
- Over **10%** of Series A financings were for rare disease start-ups.
- **IPOs:** The IPO market has continued to be strong, in 2015, 39 US emerging therapeutic companies listed on public exchanges.
- **Licensing:** 2015 saw an all-time high of $7.1 billion for upfront payments in R&D-stage licensing deals.
- **Acquisitions:** Acquisitions of R&D-stage companies in 2015 raised $26.3 billion in upfront payments, a record high.

Most common sources of capital for R&D

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- **Seed**

– Academic funding & Patient organizations

- **Start**

– National research funding (ZONMW etc.) & European research funding (FP7, H2020 etc.)

– Patient organizations

- **Investments**

– Informal investors (Patient organizations and partners)

– Business angels

– Philanthropic Venture Capital (PVC foundations etc)

– Venture Capital

Translational Gap

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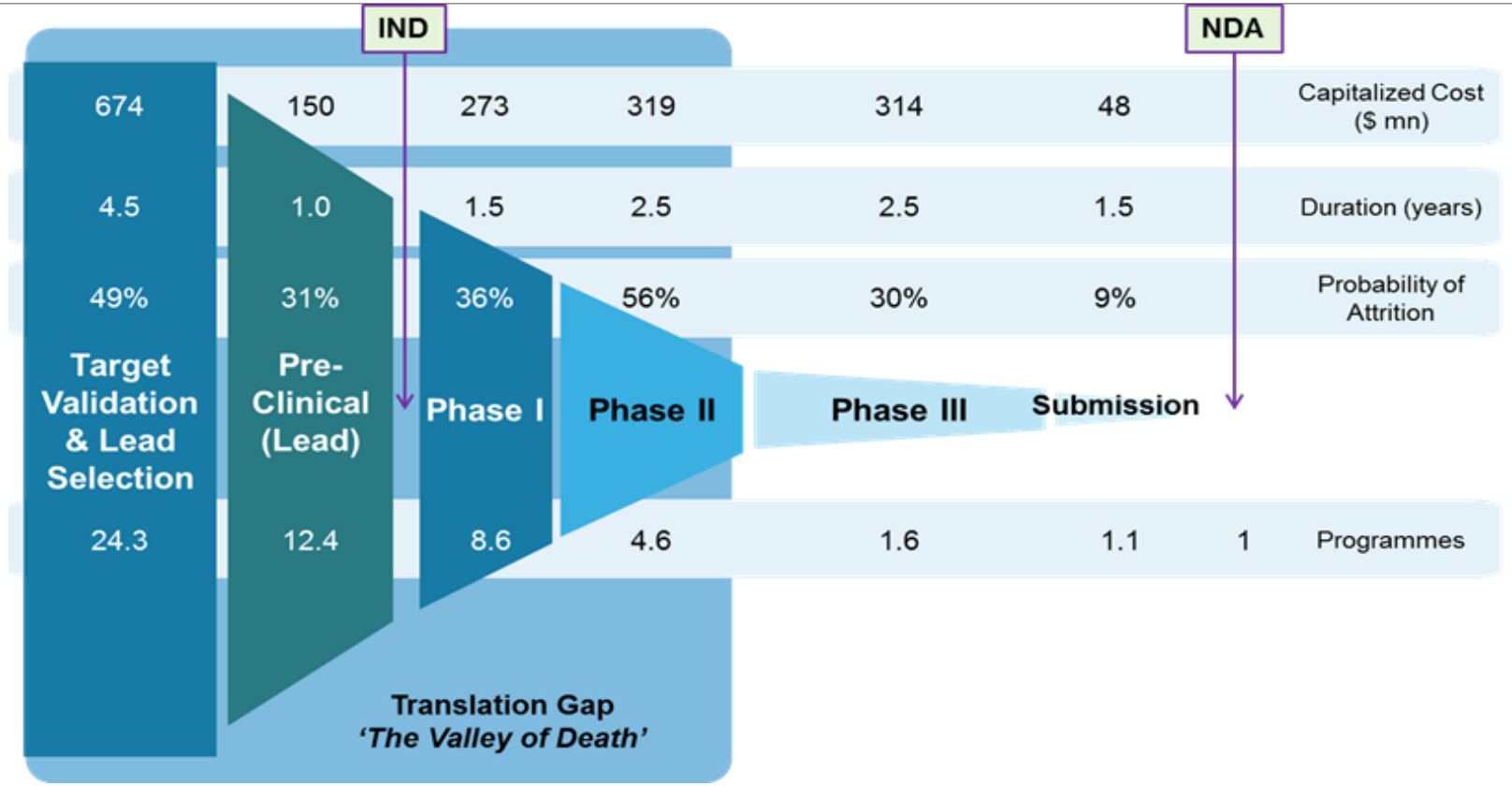

Figure 1. Drug development cycle and the 'valley of death'. Schematics of the drug development lifecycle, duration of each one of the stages, capitalized costs and probability of failure. Adapted from {Paul, 2010 #886} and Michael J. Fox Foundation.

Source : www.lonza.com

The Environment

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- **The current economic conditions**
  - Historically low interest rates
  - Zero growth rates and a stable housing market
  - Government funding has been declining
  - Cost pressures from healthcare reforms

- **The current biomedical RD conditions**
  - Industry shies away from the sponsorship of early clinical research
  - Citing increasing risks and costs
  - Expiration of patents, regulatory hurdles and rising costs of clinical trials
  - Pharma leaders focusing on drug candidates that passed some of the early regulatory hurdles.

Biomedical innovation has become riskier, more expensive and more difficult to finance with traditional sources such as private and public equity.

Source: Getting new drugs through the 'valley of death' New initiative addresses growing gap between academic and clinical research By Quinn Eastman | Emory Medicine | Jan. 27, 2014

When VC and PVC are not enough

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- The VC and PVC and the rest of the financial options available are not enough to help develop drugs for the 7.000 rare diseases.
- New models of orphan drug development are needed to increase efficiency and RD productivity
- New models of financing drug development are needed to attract large scale investment
- New investment options that can offer possible medium and high yield returns with balanced risk exposure
- New path to larger pool of capital

Probabilities

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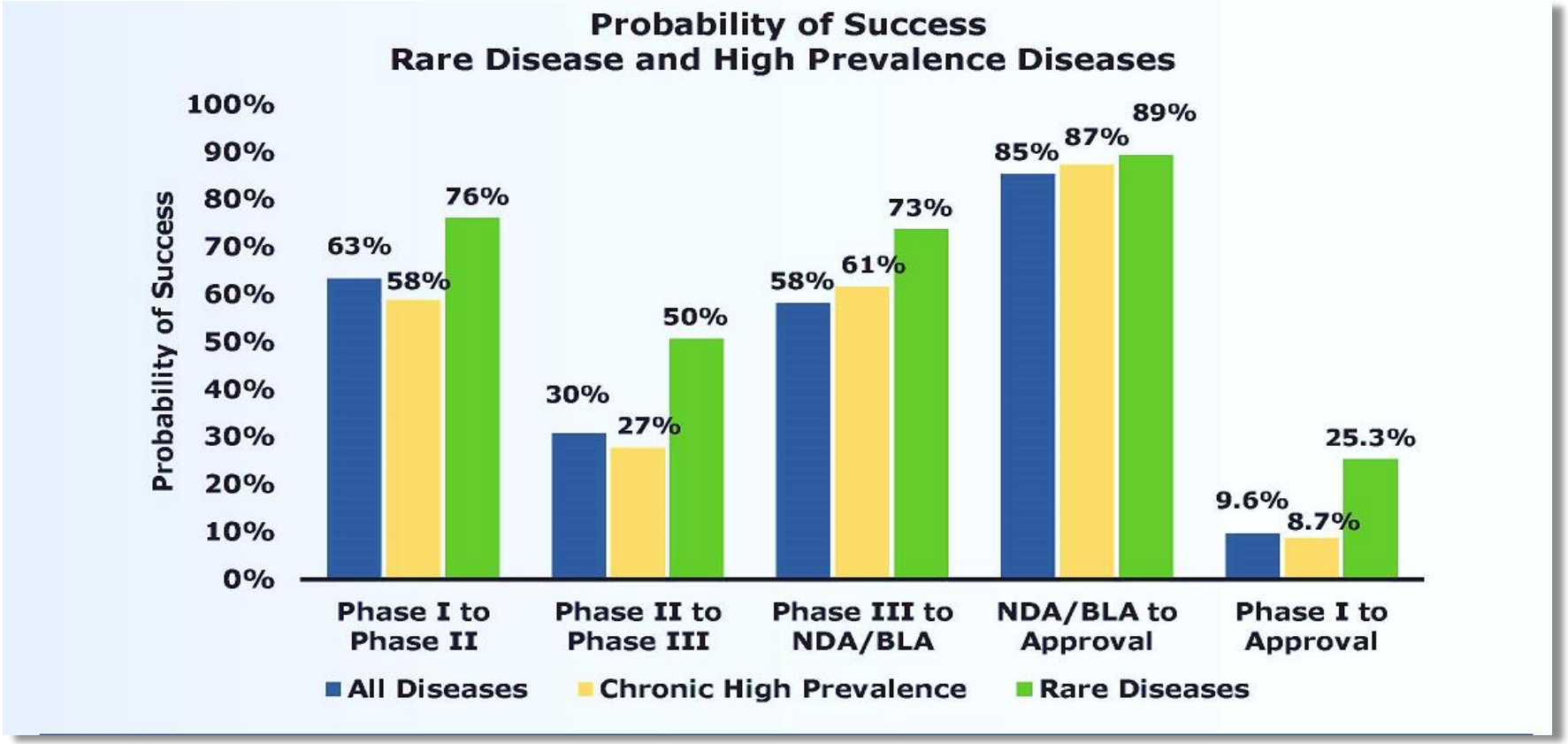

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Does it make economic sense to invest in RD?

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- Commercial benefits of an orphan designation (IP protection, low regulatory cost, adaptive and fast access schemes etc.).
- The orphan drug market is expected to peak at $209bn in 2022 with an **11%** growth/year
- Investing in a drug for rare diseases in the early phases the difference can even be **double** than any other drug development option.
- The accumulative probability from **Phase I to Approval is 300% higher**.

2016 Business Report BIO, Biomedtracker, Amplion 2016 Clinical Development Success Rates 2006-2015
Evaluate Pharma Orphan Drug Report 2017 http://www.evaluategroup.com/public/Reports/EvaluatePharma-Orphan-Drug-Report-2017.aspx

Opening the path to larger pool of capital

A financial structure to :

- **Attract pension funds**, insurance companies and other large institutional and fixed income investors who have traditionally not been able to participate in investments in early-stage drug development
- Attract medium and **long term investors**
- Pool a **number of drug** development programs into a **single** financial entity or “mega-fund”
- Yield a more **attractive risk-adjusted return** on the investment and a higher likelihood of success in finding cures for disease
- **Not very highly associated with the stock market** and that is capable of generating attractive returns

Opening the path to larger pool of capital

A financial structure that can:

- Substantially reduce the portfolio's risk by investing in multiple drug trials simultaneously and in various stages of development
- Issue debt accessing larger pool of capital in **debt versus equity**
- Issue **bonds guaranteed** by the portfolio of possible drugs and their associated intellectual property.
- Use financial engineering, **dynamic leverage** "research-backed obligations" or RBOs that are also starting to appear in the literature.
- Can be directed to the world of pension funds, hedge funds, and other **institutional investors.**

Dream or Reality ?

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- 2012 **NATURE BIOTECHNOLOGY** "Commercializing biomedical research through securitization techniques "**MIT Jose-Maria Fernandez, Roger M Stein & Andrew W Lo**
- 2013 **The Economist / Business Insider / Financial Times**
- 2014 **PubMed, Science Direct** "Financing drug discovery for orphan diseases" **David E. Fagnan, Austin A. Gromatzky,Roger M. Stein,Jose-Maria Fernandez, Andrew W. Lo1 Fortune** "Wall Street's next bet: Cures for rare diseases" **Andrew W. Lo**
- 2015 **WORLD ECONOMIC FORUM** "Can megafunds boost drug research?" **Andrew W Lo london.gov.uk** **"**Mayor considers £10bn megafund as option to boost drug development"
- 2016 **ONCOTARGET** "Cancer megafunds with in silico and in vitro validation: **Xianjin Yang1, Edouard Debonneuil2, Alex Zhavoronkov3, Bud Mishra4**
  New York University "Diminish Risk, Maximize Investment in Cancer 'Megafunds'"

Reality

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- **Royalty Pharma INC.** “business model, which adopted securitization, a new investment method that makes advance payments of future profits”
- **2013**, **$459 million** drug development fund Quintiles, Mitsui&Co. and other investors. Ten drug candidates under development. The fund is already recouping part of its investments.
- **NovaQuest Pharma Opportunities Fund IV $866 million** development fund established by Mitsui & Co., Quintiles and other investors. The new private equity fund will invest mainly in drugs .
- **2015 $100 million** new venture capital fund was announced from U.K. Secretary of State for Health new venture capital fund dedicated exclusively to dementia research, with contributions from the British government, Alzheimer’s Research U.K. and five major pharmaceutical companies.
- **2016 Apollo Therapeutic Fund $57** million joint venture between AstraZeneca, GlaxoSmithKline, Johnson & Johnson and three UK universities.
- **$105 million** development fund **Abingworth international investment group** announced fund to support certain phase III trials.

Source http://www.centerwatch.com/news-online/2016/04/04/megafunds-avenue-boost-drug-development/

Our Reality

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THANK YOU!

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