Healthcare Business Summit,
P-Bio, Braga

Clinical Validation

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Isabel Fonseca Santos

Medical Director Bayer Portugal

Clinical Validation

// What we know

// Trends

// Key success factors – our own experience @Bayer

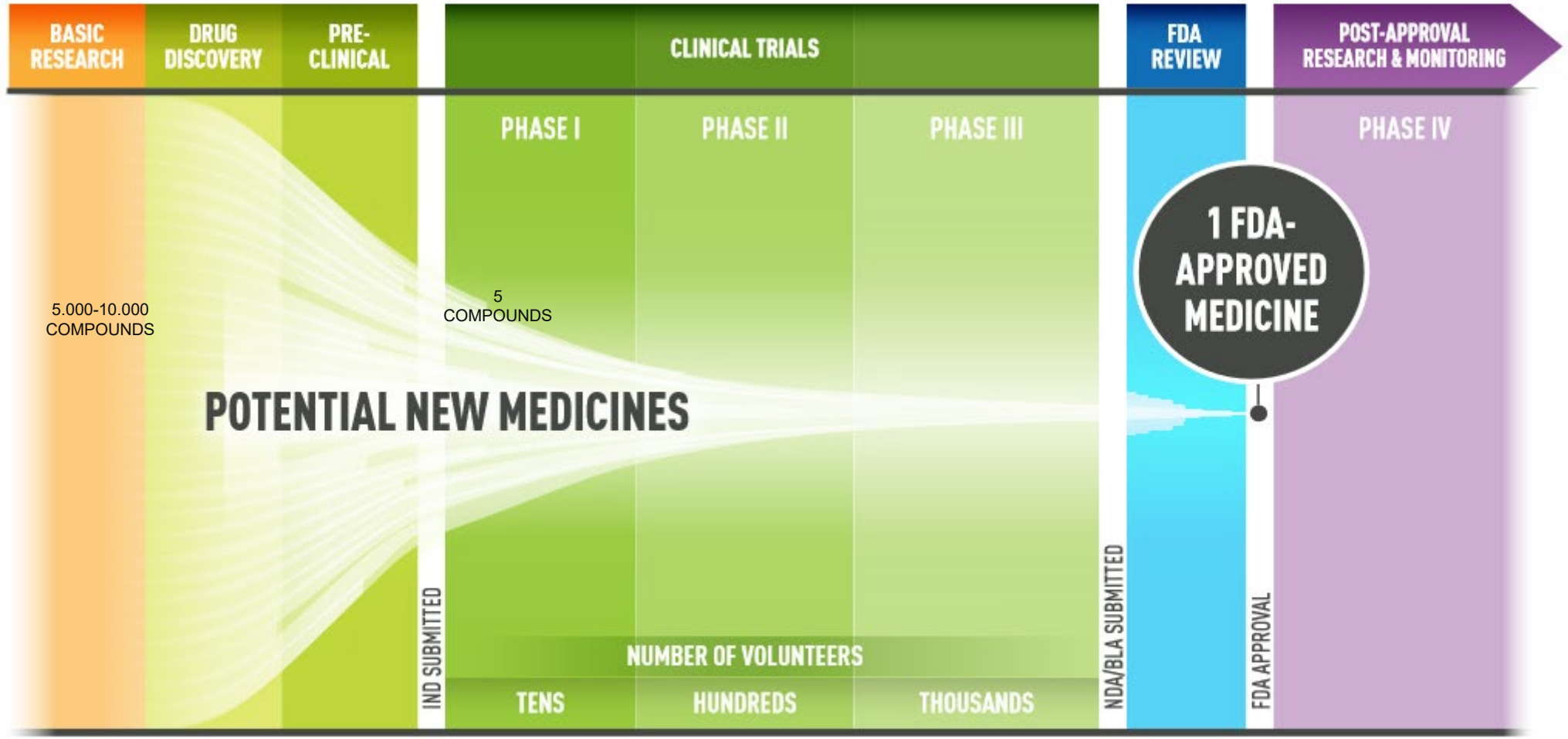
What we know

What we know

- Clinical development (CD) takes around 7,5 -12 years
- From 5 IND entering into CD only 1 will be approved
- Development costs rising, currently between USD 161M – USD 2B
- Inefficient patient recruitment (80% of trials fail to meet recruitment timelines)
- Patient retention problems (~30% drop-out)
- New approaches (gene therapy, cell therapy, personalised medicine) create new challenges

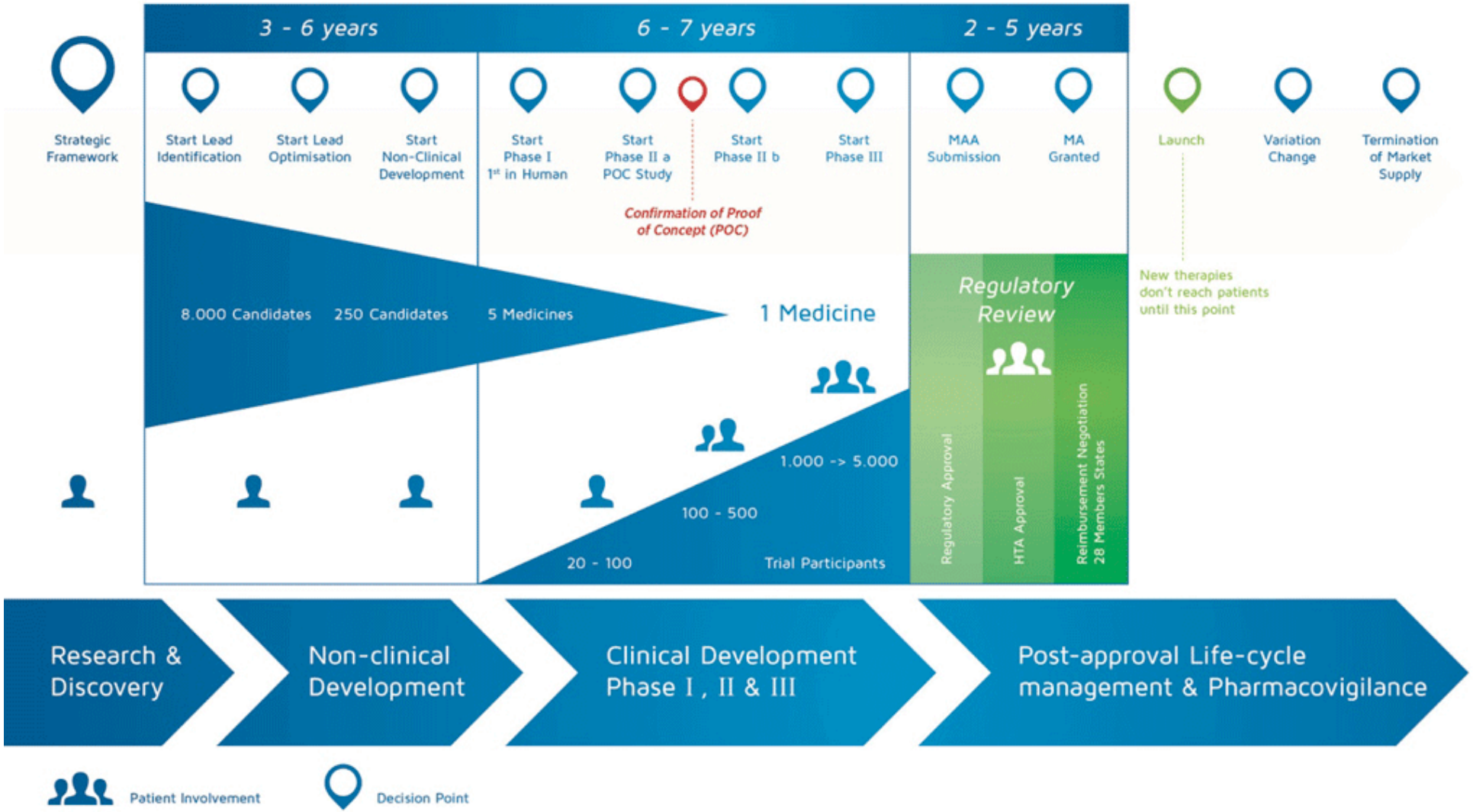
https://www.asco.org/research-progress/clinical-trials/clinical-trial-resources/basic-requirements-starting-research-site

The Lengthy, Costly, and Uncertain Biopharmaceutical Research and Development Process



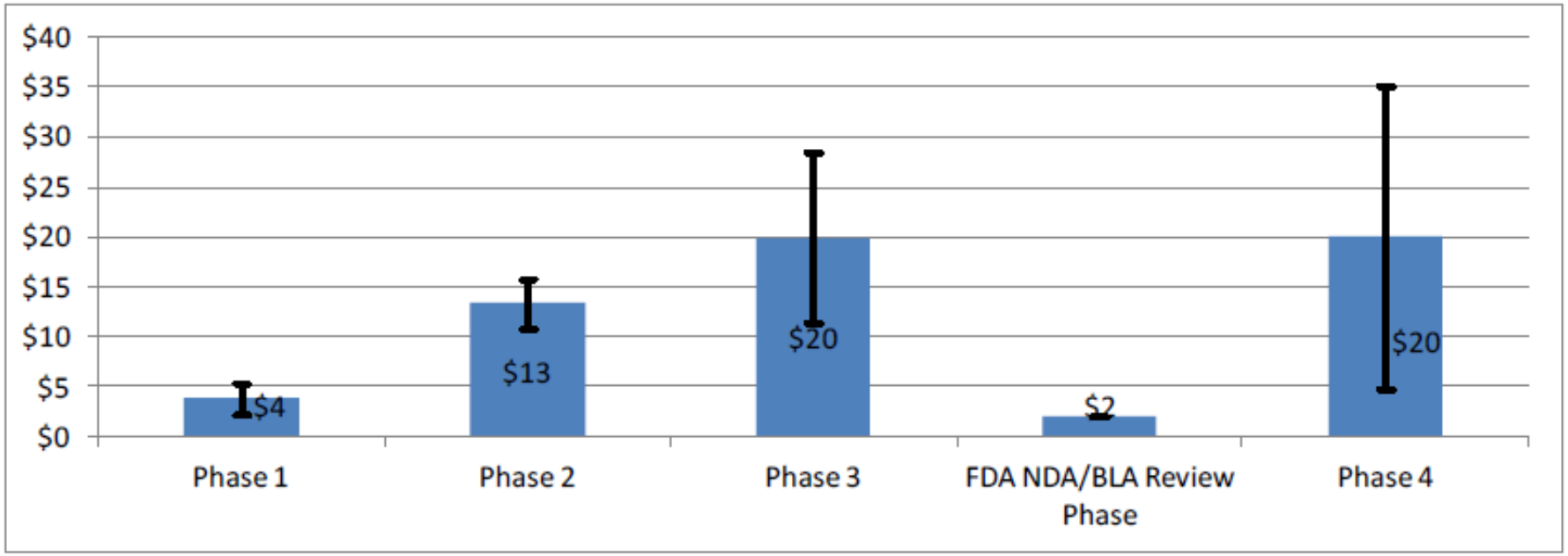
Sources: PhRMA adaptation based on DiMasi JA, Grabowski HG, Hansen RW. Innovation in the pharmaceutical industry: new estimates of R&D costs. J Health Economics . 2016;47:20-33; DiMasi, JA, Grabowski HG, Hansen RW; Tufts Center for the Study of Drug Development. Innovation in the pharmaceutical industry: new estimates of R&D costs. In: Briefing: Cost of Developing a New Drug. http://csdd.tufts.edu/files/uploads/Tufts_CSDD_briefing_on_RD_cost_study_-_Nov_18,_2014..pdf. Published November 18, 2014. Accessed April 2016; US Food and Drug Administration. US Food and Drug Administration drug approval process. http://www.fda.gov/downloads/Drugs/ResourcesForYou/Consumers/UCM284393.pdf. Accessed April 2016

Overview of Decision Points and Development Steps in Medicines R&D



Trial costs by Phase

Figure 4: Average Per-Study Costs by Phase (in $ Millions) Across Therapeutic Areas



Note: The error bars represent one standard deviation below and above the mean.

[11] The number of contracts by therapeutic area and trial phase cannot be publicly reported because they are confidential and proprietary.

Barriers to Clinical Trials

- High finantial cost
- Lengthy timelines
- Difficulties in recruiting and retaining patients
- Increasing competition for qualified investigators and sites
- Regulatory and administrative barriers
- Drug sponsor imposed barriers
- Disconect between clinical research and medical care
- Barriers at academic institutions
- Barriers related to the globalization of CTs

Barrier mitigation strategies

- Use of electronic health records (EHR)
- Looser trial enrollment restrictions
- Simplified clinical trial protocols and reduced amendments
- Reduced source data verification (SDV)
- Wider use of mobile technologies, including electronic data capture (EDC)
- Use of lower-cost facilities or at-home testing
- Priority Review vouchers
- Improvements in FDA review process efficiency and more frequent and timely interactions with FDA

Trends in Clinical Validation

Trends in Clinical Validation

Patient centricity

- Early involvement of patients/patient associations
- Get patient's input regarding CT endpoints and its relevance for patients
- Get patient's input into Informed Consent and other trial documents
- Involve Patient's Associations in the dissemination of available CTs for that therapeutic area
- Publication of Lay Summary with CT results
- Improve patient's experience during CT (telemonitoring, securing transportation, home visits by nurses, telemedicine, etc)

Fusing biosensors with AI for daily monitoring

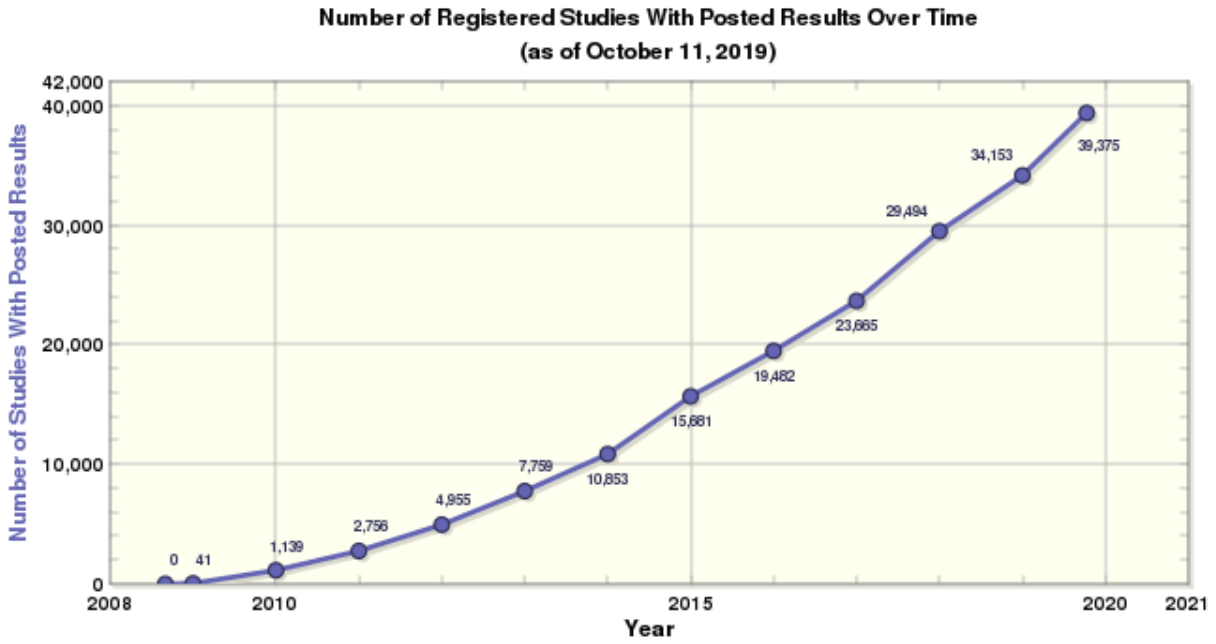
AI-IoT in clinical trials holds the potential for continuous, real-time monitoring of physiological and behavioral changes in patients, potentially reducing the cost, frequency, and difficulty of on-site check-ups.

Trends in Clinical Validation

Transparency – results posting and **CT Lay Summary publication**

Number of Registered Studies With Posted Results Over Time

The graph and table below show the number of registered studies with results posted on ClinicalTrials.gov, based on the Results First Posted date. ClinicalTrials.gov launched its results database in September 2008, at which time sponsors or investigators could begin submitting results for their registered studies. The results database was first developed to accommodate the results submission requirements outlined in FDAAA. See About the Results Database for more information.



Source: https://ClinicalTrials.gov

https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-10/2017_01_26_summaries_of_ct_results_for_laypersons.pdf

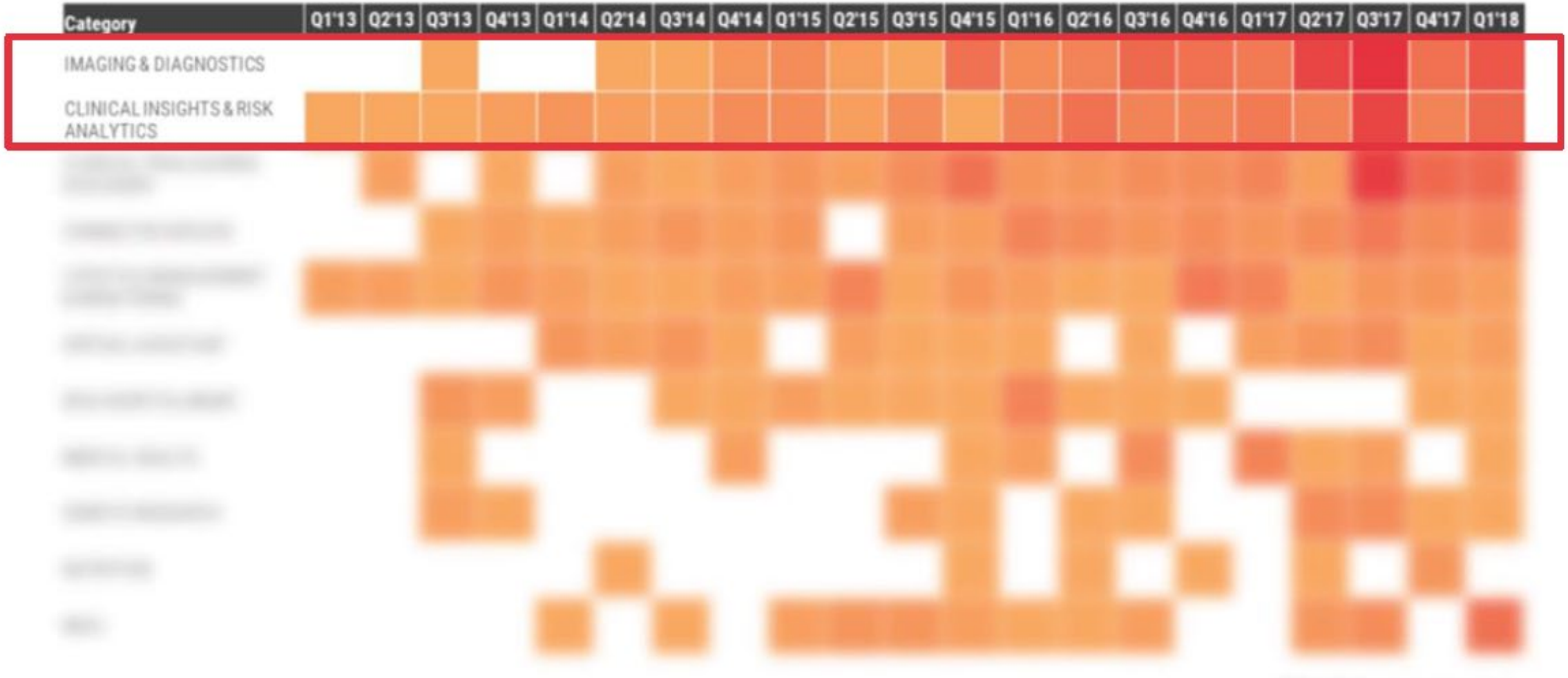
Trends in Clinical Validation

Artificial inteligence

// “Testing new drugs is a slow, expensive, and manual process. Artificial intelligence has the potential to disrupt every stage of the clinical trials process — from matching eligible patients to studies to monitoring adherence and data collection.”

In The Future Of Clinical Trials: How AI & Big Tech Could Make Drug Development Cheaper, Faster, & More Effective
https://www.cbinsights.com/research/clinical-trials-ai-tech-disruption/#pharma

Extracting data from medical records is the most sought-after application of AI



CBINSIGHTS

DEEP 6

Funding

$150K

AI startups are using deep learning and NLP to automate clinical trial matching by directly partnering with health institutions. Deep 6 AI works with clients like Cedars-Sinai Medical Center and TD2, an oncology CRO.

Select Investors

Healthbox, Techstars

antidote

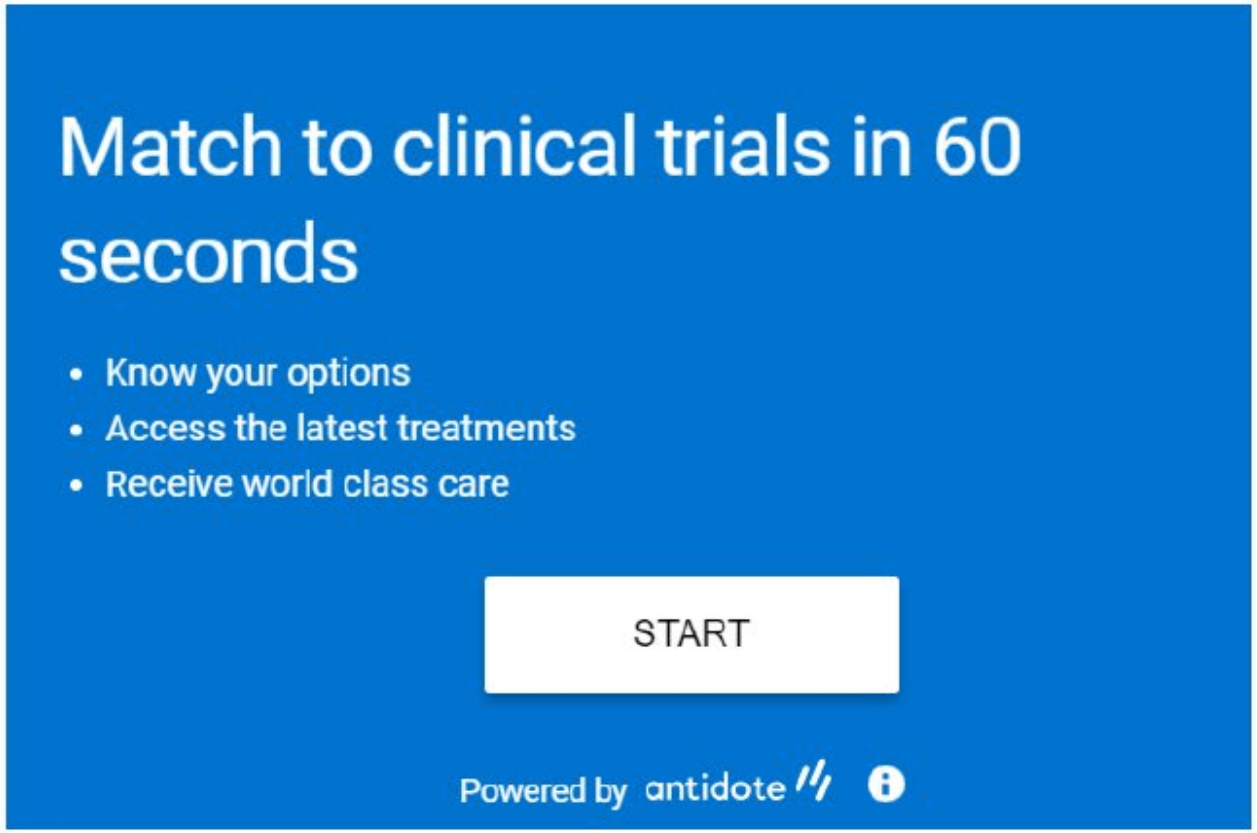
Funding

$34M

Antidote uses natural language processing to simplify the complexity of the inclusion/exclusion criteria in clinical trials. Patients answer a few simple questions on its search platform to receive a list of suggested studies they may be eligible for.

Select Investors

Merck Global Health Innovation Fund, Octopus Ventures, Amadeus Capital Partners, Smedvig Capital



Trends in Clinical Validation

New kids on the block – Apple and Google

https://mobisoftinfotech.com/resources/blog/apple-research-kit-revolutionizing-medical-research-clinical-trials/

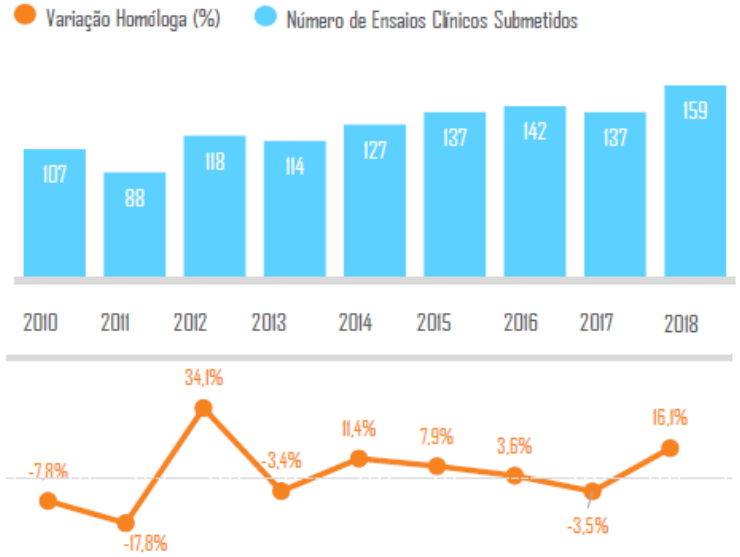
CAN PATIENT-GENERATED DATA ELIMINATE THE NEED FOR CONTROL GROUPS?

Patient-generated data — like data gathered by Apple and Google's Project Baseline— may **eliminate the need for a control group**, providing the data required from the control and ultimately reducing recruitment bottlenecks.

Key success factors
Our own experience@Bayer …

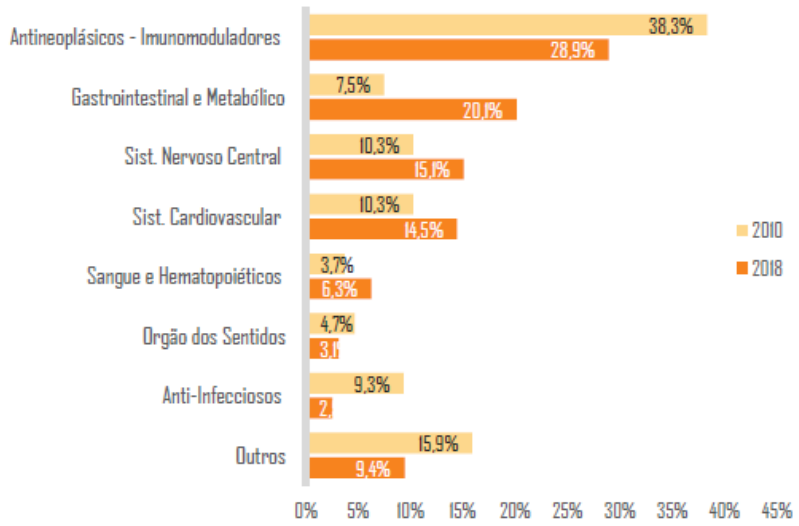
Indústria Farmacêutica em Portugal

Número de Ensaios Clínicos Submetidos



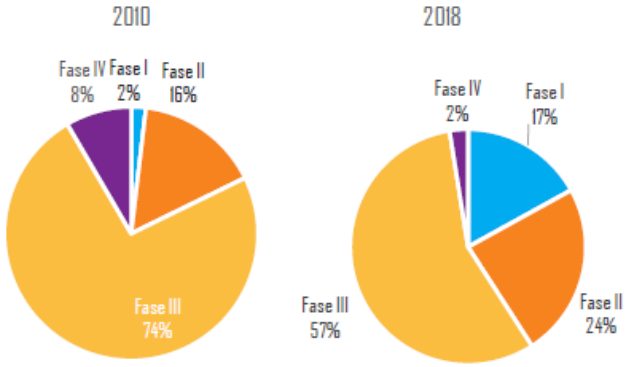
Fonte: INFARMED I.P.

Distribuição por área terapêutica

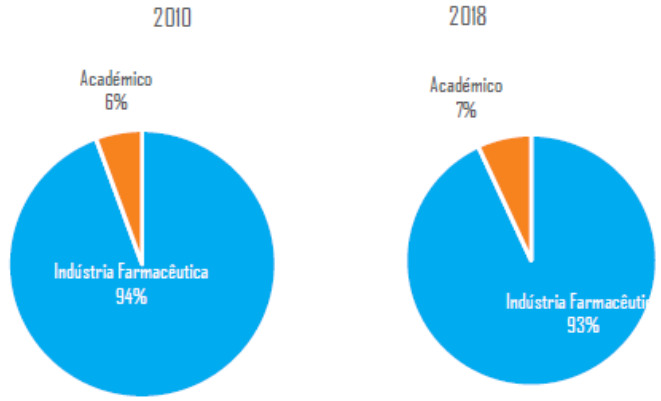


Fonte: INFARMED I.P.

Fases de Desenvolvimento Clínico



Tipo de Promotor

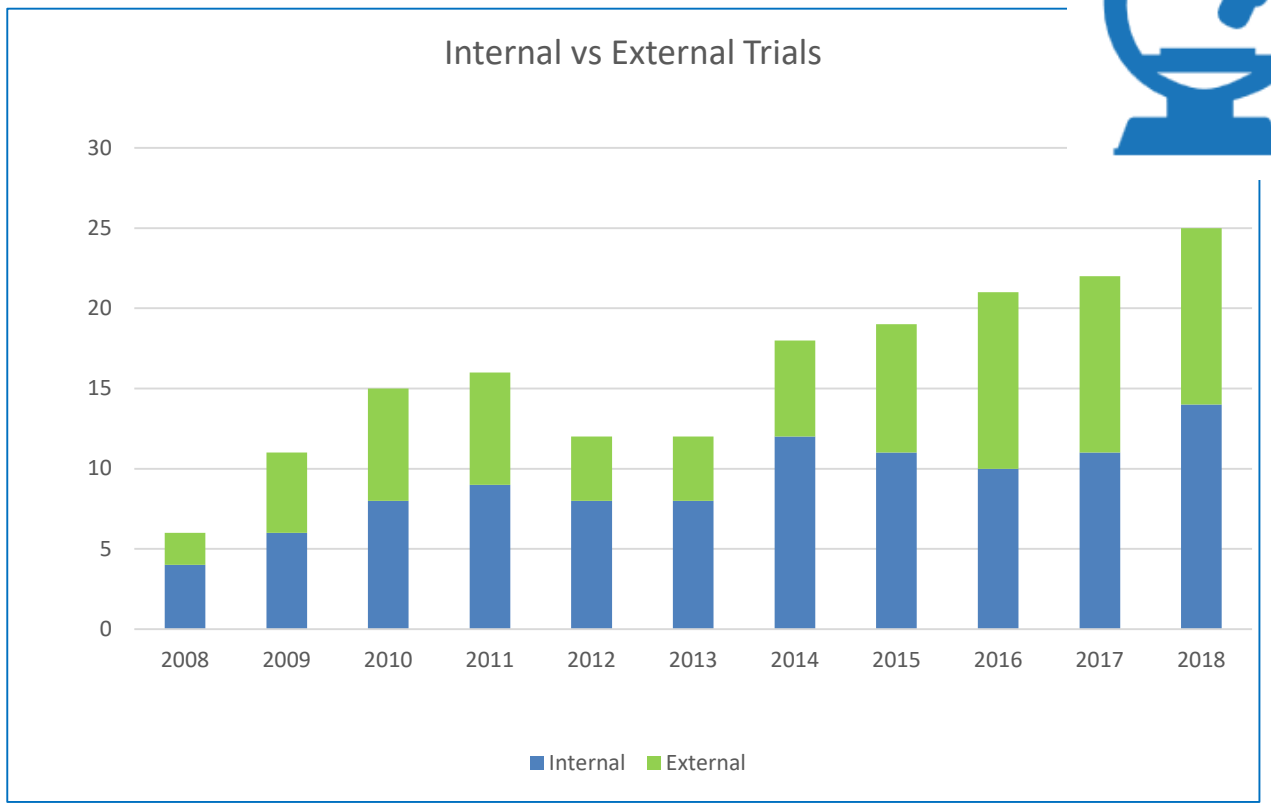


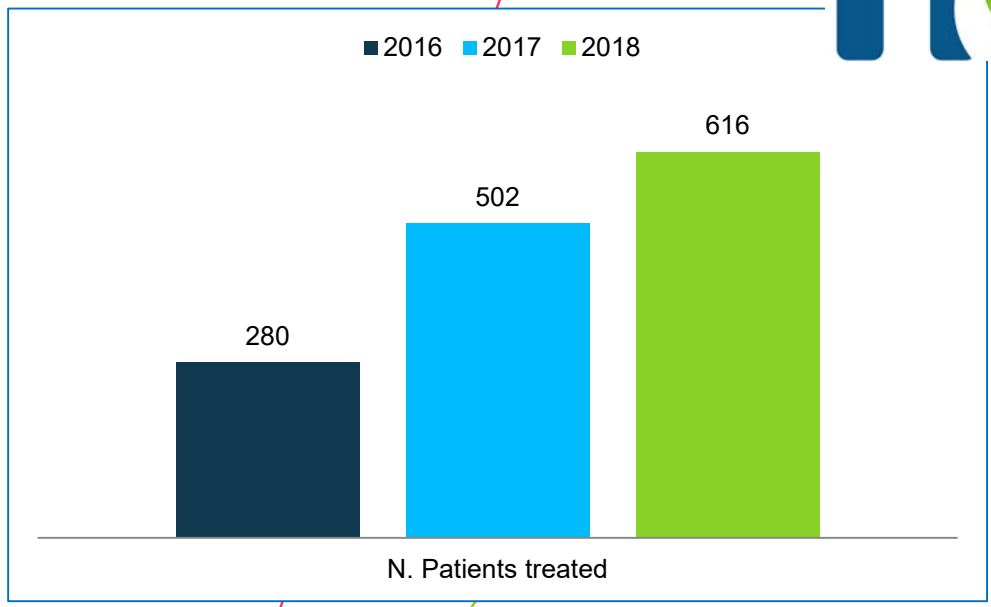
Fonte: INFARMED I.P.

NEA - Núcleo de Estudos e Análise da APIFARMA

Clinical Trials @ Bayer PT

25
CLINICAL TRIALS





Key success factors
Excellent Protocol and Site feasibility

- Protocol feasibility
- Site feasibility
- Combined feasibilities

A robust and thorough feasibility is a key element to implement a CT!

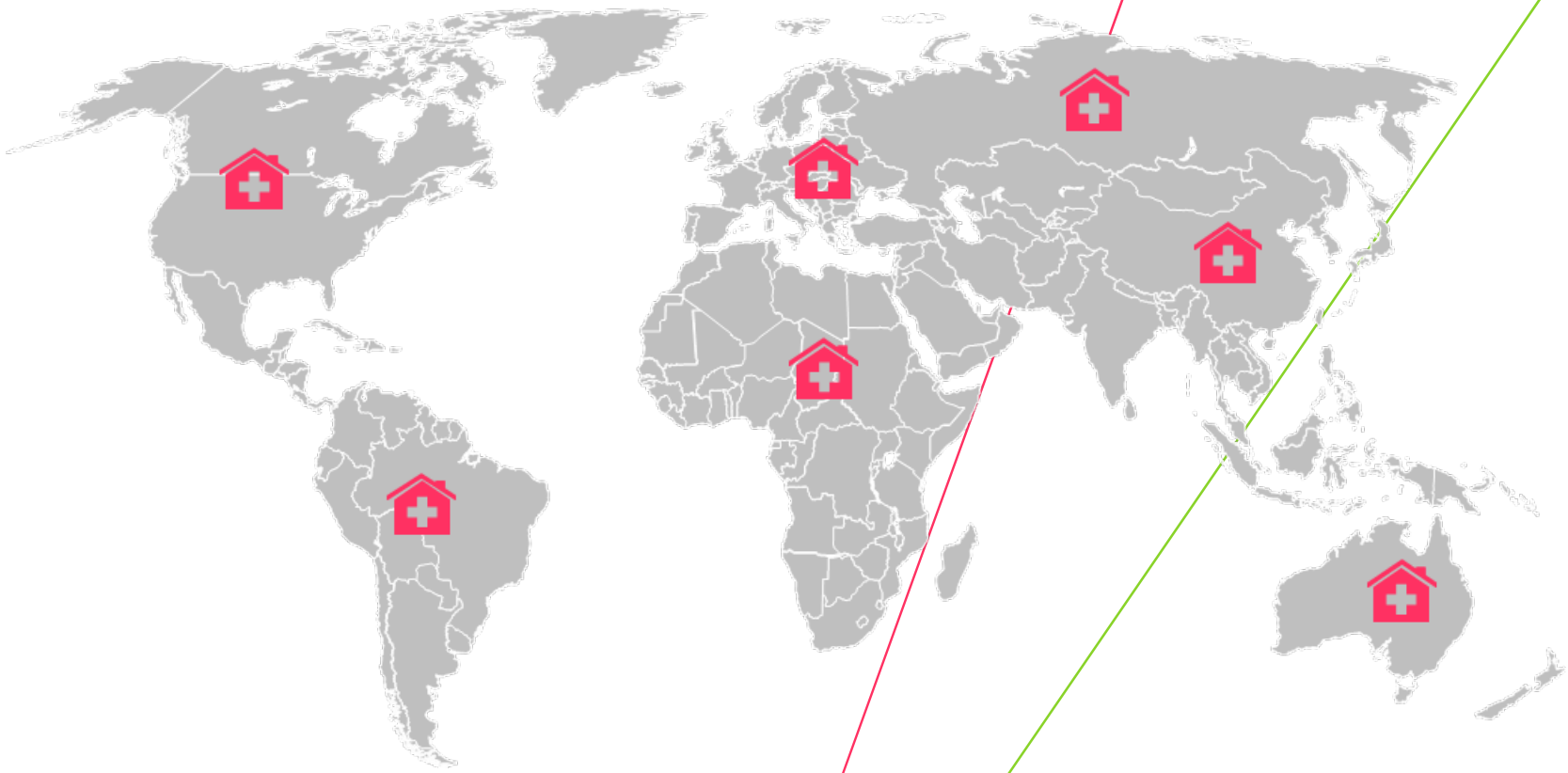
- Based on:
  - Intelligent site analytics
  - Country knowledge about investigators and sites
  - Input from Clinical Operations Country Unit/Medical Affairs
  - Professional and data driven feedback from Centers

Clinical Feasibility

Identifying the Best Hospitals for Our Clinical Studies

Database Knowledge

On-Site Experiences



INTERNAL

Key success factors

- Well designed CD program that meets the Target Product Profile – get Scientific Advice and protocol assistance from Authorities, input from Patients
- Statistically robust
- Consider adaptative, basket or umbrella trials and need for a Pediatric Investigation Plan

  - Adaptive designs can make clinical trials more flexible by utilising results accumulating in the trial to modify the trial's course in accordance with pre-specified rules.

  - Umbrella Trial: Umbrella trials (or studies) have many different treatment arms within one trial. People are assigned to a particular treatment arm of the trial based on their type of cancer and the specific molecular makeup of their cancer.

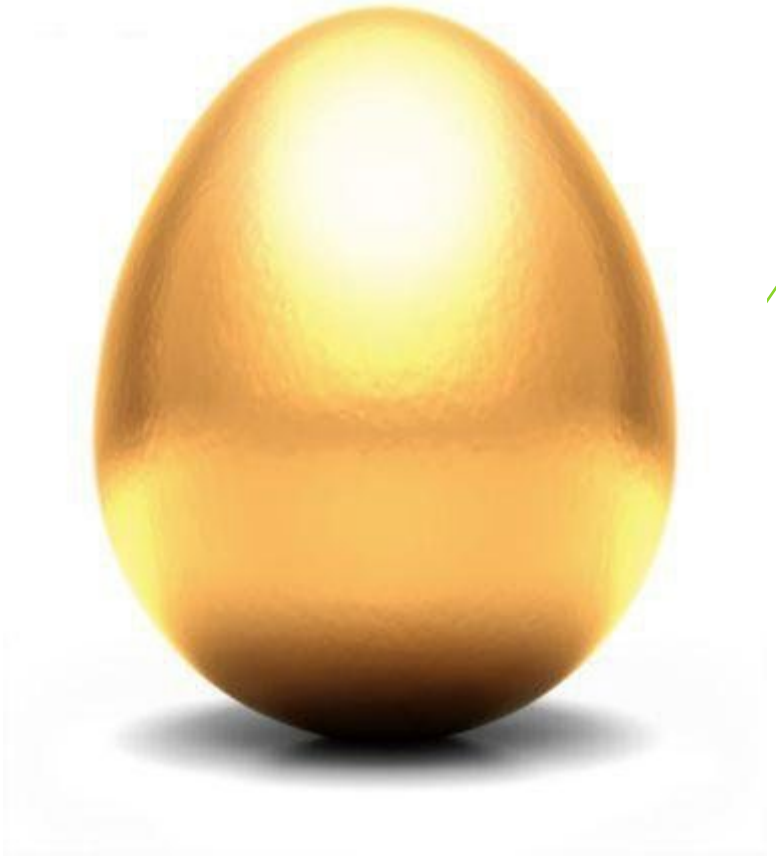
  - Basket Trial: Basket trials (or studies) test the effect of one drug on a single mutation in a variety of tumor types, at the same time. These studies also have the potential to greatly increase the number of patients who are eligible to receive certain drugs relative to other trials designs.

Key success factors

- Access to apropriate population and investigators/sites with **professional and dedicated CT teams at the sites**
- Quality control
  - Harmonization of trial procedures
  - Central labs
  - Avoid audit or inspection issues
- Putting patient's safety first (Independent Data Monitoring Committee)
- Making expedite decisions
  - Interruption of a trial due to superiority, inferiority, futility or safety
- Prioritize the patient experience (patient's input, securing transportation, telemonitoring, PROs, etc)
- Correct budgeting considering all possible costs

Main achievements @ Bayer Portugal

- World top recruiter center in a diabetic nephropathy CT
- 1st Pediatric trial in 2018
- 1st Phase 1 trial in 2019
- Infarmed award to the partnership between Bayer and IBET in drug research (Jan 2019)



At the end … it's all about people!

Robust, dedicated and proficient clinical operations team or CRO

Dedicated, professional, site team

Regulatory and CEC support

Site Management Team @ Bayer

Thank you!

Any questions?

References

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