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Public and philanthropic financial contributions to the development of new active substances: a bibliographic analysis

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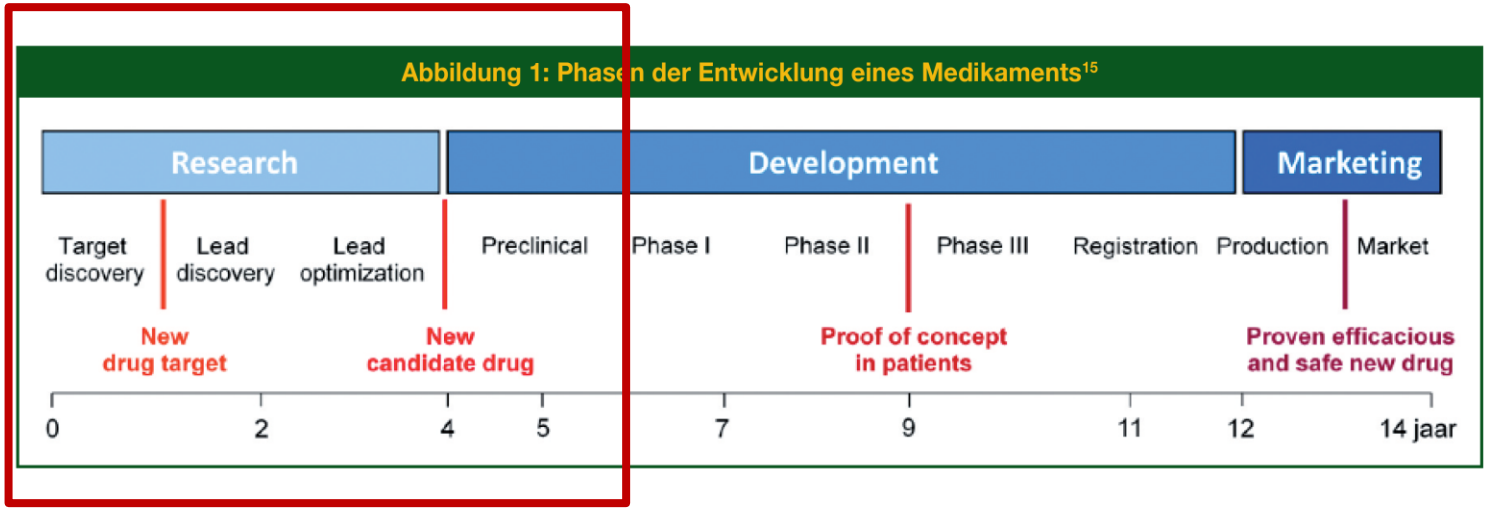
Context

Mariana Mazzucato
„public return of public investment in R&D“



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Objective

- to collect information on public & philanthropic contributions to research funding
- to contribute to the discussion on return on investment of public investment

Report: http://eprints.hta.lbg.ac.at/1214/

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Methods: main steps

Step 1: identification of all generic and molecular names and terms,

Step 2: systematic search for pre-marketing pathway information and related research funding

Step 3: systematic search for corresponding research funding amounts.

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Pilot drugs

Three Paediatric Orphan Drugs with EMA approval in 2017:

- Spinraza® (nusinersen) for treating children with spinal muscular atrophy
- Brineura® (cerliponase alpha) for treating children with neuronal ceroid lipofuscinosis
- Crysvita® (burosumab) for treating children with X-Linked hypophosphatemia

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Inclusion- / exclusion criteria

- **Inclusion**: academic papers, grey literature, online information relating to drug development; no restriction on type of publication/information
- **Date range**: time of identification of gene or mechanism of action to date of market authorisation
- **Exclusion**: publications or information relating to funding by the pharmaceutical company

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Data Extraction

We attempted to extract the following data:

- study title; date of funding; amount of funding; stage of development/content of project; lead institution; principal investigator; co-operating institutions

using websites of the appropriate funding organization e.g.

- NIH-RePORTER, CORDIS, MRC in the U.K., BMBF in Germany, Batten Disease Support and Research Organisation..

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Databases used for searching

Drug histories	Orphanet (https://www.orpha.net) Google search for review and timeline papers FDA (https://www.fda.gov/home), EMA (https://www.ema.europa.eu/en) submissions Pubmed https://www.ncbi.nlm.nih.gov/pubmed/ US Securities and Exchange Commission Filings https://www.sec.gov/edgar/searchedgar/companysearch.html
Trial Databases	WHO international trials registry: http://apps.who.int/trialsearch/ US-Clinical Trials.Gov: https://www.clinicaltrials.gov/ and EU clinical trials registry/EudraCT: https://www.clinicaltrialsregister.eu/ctr-search/search.
Patent Databases	USA: FDA orange book/ US PTO: https://www.accessdata.fda.gov/Scripts/cder/ob/index.cfm; https://www.uspto.gov/, Worldwide: Espacenet patent database: https://worldwide.espacenet.com/, Health Canada Patent Database: https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/patent-register.html, Medicines Patent Pool Patent Search: https://www.medspal.org/, Pat-informed (**Pat**ent **In**formation Initiative **for Med**icines) database: https://www.wipo.int/pat-informed/en/

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Public funding results: Spinraza® (nusinersen)

- 6 projects funded by Canadian Institute of Health Research: Can $ 3,269,130.
- 10 NIH (USA) projects: US $ 22,253,949
- E-Rare EU calls 1 project funded (amount not reported).
- 1 BMBF (German national funding programme): € 387,854
- 1 project co-funded by the Deutsche Forschungsgesellschaft (no information on funding amount)
- Other national European funding bodies (Italian and French) identified but no funding amounts could be identified on the websites of these organisations

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Charity funding results: Spinraza® (nusinersen)

- 15 Muscular Dystrophy Association (MDA) funded projects: $ 3,768,516
- Families of SMA/Cure SMA (USA) involved in supporting 4 projects and Kids' Cures in 1 project (exact funding amount unavailable although 1 project amounted to $ 381,138)
- Cure SMA annual report states funding for research projects in 2018 totaled 5 million US $.
- SMA Europe lists a number of projects funded in this area before the date of market authorization; these total just over € 3 Million.
- According to its website, the Spinal Muscular Atrophy Foundation (SMA Foundation) has spent around $150 Million on basic, translational and clinical research since its inception in 2003.

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Final figure: Spinraza® (nusinersen)

- Total funding estimate of ~ € 165 Million for research into therapies for SMA.
- Conservative approach (only projects named in patents/development documents or conducted by the same researchers): ~ € 20 Million can be directly attributable to Spinraza®.

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Public funding results: Brineura® (cerliponase alpha)

- 13 National Institute for Health (NIH) research projects: US $ 28,775,650.
- US National Science Foundation: $ 94,931.
- European funding: Academy of Finland (€ 740,120), German Ministry for Education and Research (BMBF) (€ 390,457) & another 2 BMBF-funded projects (no information available).
- The European Union Seventh Framework Programme (FP7/2007-2013) DEM-Child project: budget of € 3,971,420.

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Charity funding results: Brineura® (cerliponase alpha)

- The Batten Disease Support and Research Association lists *some* information on projects and project fundings. Only US $ 297,391 could be specifically identified.
- For the Neuronale Ceroid-Lipofuszinose (NCL) Stiftung, BDFA UK, Beyond Batten Disease Foundation, Charlotte & Gwenyth Gray Foundation: no specific projects or funding amounts could be identified for CNL2 although funding is likely

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Final figure: Brineura® (cerliponase alpha)

- Lack of information from charitable/philanthropic organisations so no total funding estimate possible.
- Conservative estimate (only including projects named in patents/development documents or conducted by same researchers): ~ € 31 Million public funding

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Public funding results: Crysvita® (burosumab)

- 13 NIH projects: US $ 25,828,081
- Austrian Science Fund € 423,832.50
- Genome Canada, Ontario Genomic Institute Canadian Institutes of Health Research, Centre for Modeling Human Disease all named but no funding details.
- Canadian Institutes of Health Research: Can $ 709,152
- Swedish Research Council: no funding details
- Ministry of Education, Culture, Sports, Science and Technology of Japan, Ministry of Health, Labor and Welfare of Japan & Japan Society for the Promotion of Science: named but no details.

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Charity funding results: Crysvita® (burosumab)

- Japan Foundation for Pediatric Research
- Ralph W & Grace M Showalter Research Trust Fund
- Indiana Genomics Initiative and the Indiana University School of Medicine
- American Heart Association Postdoctoral Fellowship European Society for Pediatric Endocrinology Research Fellowship
- National Kidney Foundation
- Swedish Society of Medicine

…named but no funding amounts reported.

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Final figure: Crysvita® (burosumab)

- Funding estimate of ~ € 26.8 Million
- Bulk of known, specified funding was from the NIH
- Financial contribution of Japanese sources could not be quantified.

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Conclusion/ discussion

- Consistency in conservative estimates: on product related R&D € ~ 20 to 30 Million
- Nature and extent of publicly-available information varies; no systematic, standard reporting esp. from charities
- Difficulty in ascribing research funding to specific products as basic research about the disease and mechanisms of action benefit several products/classes

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Limitations & next steps

- Tax concessions (e.g. for orphan products) not considered
- No estimate of total R&D funding so cannot calculate *proportion* from public and philanthropic sources
- Next steps: refinement of search strategy and further piloting

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- “Médecins Sans Frontières (MSF)”
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- “Knowledge Ecology International (KEI)”
- “Universities Allied for Essential Medicines (UAEM)”
- “Brazilian Ministry of Health (Intellectual Property Coordination)”
- “Treatment Action Group (TAG)”
- “University College London (UCL) Institute for Innovation and Public Purpose “