# Public funding of clinical research with societal return

Lydie Meheus, PhD
Managing Director @ *the Anticancer Fund, Brussels, Belgium*
November 15th 2019
Morningside CIAM, Emory, Atlanta

# Public funding

Definition?

- **Comes from:**
  - Governmental money
  - Foundations (private & public)
  - Crowdfunding
  - Health Insurers
  - Companies (CSR)
- **Outcome:**
  - No (monetary) ROI
  - Serves the public (health)

# Societal return

For patients and governments

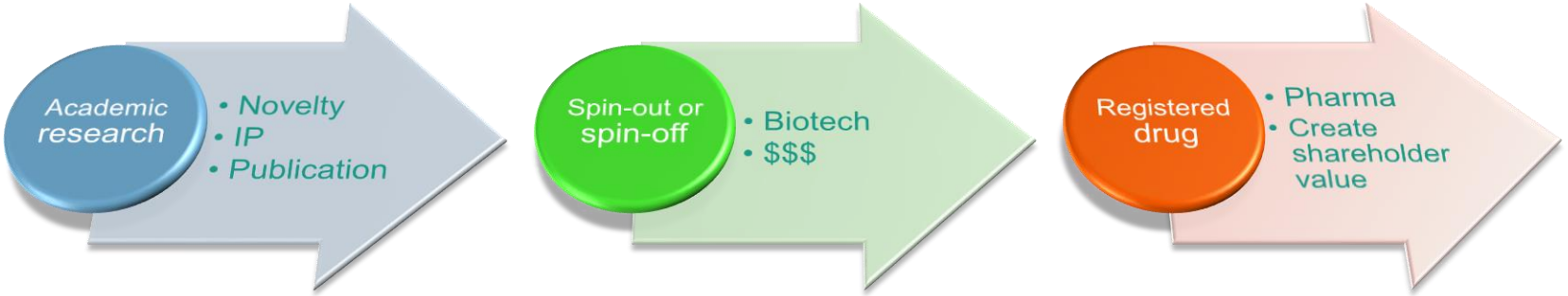
- added therapeutic value
  - the incremental "therapeutic value" brought by a new drug or intervention compared with the best available treatment options already on the market (IP/A/ENVI/2014-17 June 2015 PE 542.219).
  - Overall survival of at least 4-6 months ("*Pricing of cancer medicines and its impacts*" Geneva: World Health Organization; 2018)
  - Quality of Life
- unmet needs: rare cancers
- Affordability/accessibility

# Why is public funding a necessity?

Current “private”system focuses on ROI first
Need for a complementary “public” development pathway

Anticancer Fund

# Cancer treatment development drivers



Anticancer Fund

OPEN ACCESS

# Availability of evidence of benefits on overall survival and quality of life of cancer drugs approved by European Medicines Agency: retrospective cohort study of drug approvals 2009-13

Courtney Davis,[1] Huseyin Naci,[2] Evrim Gurpinar,[2] Elita Poplavska,[3] Ashlyn Pinto,[2] Ajay Aggarwal[4,5]

[1]Department of Global Health and Social Medicine, King's College London, London WC2R 2LS, UK
[2]LSE Health, Department of Health Policy, London School of Economics and Political Science, London, UK
[3]Faculty of Pharmacy, Riga Stradins University, Riga, Latvia
[4]Department of Health Services Research and Policy, London School of Hygiene and Tropical Medicine, London, UK
[5]Institute of Cancer Policy, King's College London, London, UK
**Correspondence to:** C Davis
courtney.davis@kcl.ac.uk

Additional material is published online only. To view please visit the journal online.
**Cite this as:** *BMJ* 2017;359:j4530
http://dx.doi.org/10.1136/bmj.j4530
**Accepted:** 28 September 2017

- 68 indications with EMA approval
- 51% showed sign of improvement in survival and quality of life
- 5 year follow-up
- Magnitude of benefit of overall survival = 2.7 months

Table 1. Food and Drug Administration (FDA) Drug Approvals in Solid Tumors 2002 Through 2014[a,b]

| Agent | Approval Date | Enrolled, No. | Cancer Indication | Gain, mo | | Would Have Met ASCO Committee Criteria[d] |
|---|---|---|---|---|---|---|
| | | | | PFS[c] | OS | |
| Imatinib[10] | 2/1/2002 | 147 | First-line GIST | NA | NA | Yes |
| Fulvestrant[11,12] | 4/25/2002 | 400/451 | Second-line breast cancer | 0.4/2 | NA | No |
| Oxaliplatin[13] | 8/9/2002 | NA | Second-line mCRC | 2.8 | 1.5 | No |
| Oxaliplatin[13] | 1/9/2004 | 531 | First-line mCRC | 2.8 | 5.6 | Yes |
| Pemetrexed[14] | 2/4/2004 | 456 | First-line mesothelioma | 1.8 | 2.8 | Yes |
| Bevacizumab[15] | 2/26/2004 | 813 | First-line mCRC | 4.4 | 4.7 | Yes |
| Cetuximab[16] | 2/12/2004 | 1198 | Refractory CRC | 1.5 | 3.5 | Yes |
| Docetaxel[17] | 5/19/2004 | 1006 | Hormone-refractory prostate cancer | NA | 0.9-2.4 | No |
| Gemcitabine[18] | 5/19/2004 | 266 | First-line breast cancer | 2.8 | 2.16 | No |
| Erlotinib[19] | 11/18/2004 | 731 | Second/third-line NSCLC | 0.46 | 2 | No |
| Abraxane[20] | 1/7/2005 | 460 | Refractory breast cancer | 1.4 | 2.1-2.2 | No |
| Erlotinib[21] | 11/2/2005 | 569 | First-line pancreatic cancer | 0.2 | 0.33 | No |
| Sorafenib[22,23] | 12/20/2005 | 903 | Second-line renal cell carcinoma | 2.7 | 2.6 | Yes |
| Sunitinib[24] | 1/26/2006 | 312 | Second-line GIST | 4.2 | NR | Uncertain |
| Sunitinib[25,26] | 1/26/2006 | 750 | Metastatic renal cell carcinoma | 6 | 4.6 | Yes |
| Cetuximab[27] | 3/1/2006 | 424 | With RT in SCCHN | 4.7 | 19.7 | Yes |
| Docetaxel[28] | 3/22/2006 | 445 | First-line gastroesophageal cancer | 1.9 | 0.6 | No |
| Topotecan[29] | 6/14/2006 | 364 | First-line cervical cancer | 1.7 | 2.9 | No |
| Bevacizumab[30] | 6/20/2006 | 829 | Second-line mCRC | 2.6 | 2.1 | No |
| Gemcitabine[31] | 7/14/2006 | 356 | With carboplatin in ovarian cancer | 2.8 | 0.7 | No |
| Panitumumab[32] | 9/27/2006 | 463 | Refractory mCRC | 0.16 | 0 | No |
| Bevacizumab[33] | 10/11/2006 | 878 | First-line NSCLC | 1.7 | 2 | No |
| Docetaxel[34] | 10/17/2006 | 358 | Unresectable SCCHN | 2.8 | 4.3 | Yes |
| Lapatinib[35,36] | 3/17/2007 | 324 | Refractory breast cancer | 1.9 | 0.3 | No |
| Temsirolimus[37] | 5/30/2007 | 626 | Advanced renal cell carcinoma | 2.4 | 2.6 | Yes |
| Ixabepilone[38,39] | 10/16/2007 | 752 | Second-line breast cancer | 1.6 | 1.8 | No |
| Sorafenib[40] | 11/16/2007 | 602 | First-line hepatocellular carcinoma | 2.7 | 2.8 | Yes |
| Pemetrexed[41] | 9/26/2008 | 1725 | First-line NSCLC | 0 | −0.3 | No |
| Bevacizumab[42,43] | 5/5/2009 | 215 | Second-line glioblastoma | NA | NA | No |
| Everolimus[44,45] | 3/30/2009 | 410 | Advanced renal cell carcinoma | 3 | 0.4 | No |
| Pemetrexed[46] | 7/2/2009 | 663 | Maintenance NSCLC | 1.7 | 2.8 | Yes |
| Bevacizumab[47,48] | 7/31/2009 | 649 | First-line renal cell carcinoma | 4.8 | 2 | No |
| Pazopanib[49] | 10/19/2009 | 435 | Advanced renal cell carcinoma | 5 | −0.6 | Uncertain |
| Lapatinib[50,51] | 1/29/2010 | 1286 | With letrozole in breast cancer | 5.2 | 1 | No |
| Erlotinib[52] | 4/16/2010 | 1949 | Maintenance NSCLC | 0.28 | 1 | No |
| Sipuleucel-T[53] | 4/29/2010 | 127 | Hormone-refractory prostate cancer | 0.39 | 4.5 | Yes |
| Cabazitaxel[54] | 6/17/2010 | 755 | Second-line prostate cancer | 1.4 | 2.4 | No |
| Trastuzumab[55] | 10/20/2010 | 594 | Advanced gastroesophageal cancer | 1.2 | 2.7 | Yes |
| Eribulin[56] | 11/15/2010 | 762 | Third-line breast cancer | 1.5 | 2.5 | Yes |
| Ipilimumab[57] | 3/25/2011 | 502 | First-line melanoma | 0 | 2.1 | Uncertain |
| Vandetanib[58] | 4/6/2011 | 331 | Advanced medullary thyroid carcinoma | 11.1[e] | NA | Yes |
| Abiraterone[59] | 4/28/2011 | 1195 | Second-line CRPC | 2 | 3.9 | Yes |
| Everolimus[60] | 5/5/2011 | 429 | Advanced PNET | 5.1 | NR | Uncertain |
| Sunitinib[61] | 5/20/2011 | 171 | Advanced PNET | 5.9 | NR | Uncertain |
| Vemurafenib[62] | 8/17/2011 | 675 | First-line BRAF-mutated melanoma | 3.7 | NA | Yes |
| Cetuximab[63] | 11/7/2011 | 220 | First-line SCCHN | 2.3 | 2.7 | No |
| Axitinib[64] | 1/27/2012 | 723 | Second-line renal cell carcinoma | 2 | NA | No |
| Pazopanib[65] | 4/26/2012 | 369 | Soft-tissue sarcoma | 3 | NA | Uncertain |
| Pertuzumab[66] | 6/8/2012 | 808 | HER2-positive breast cancer | 6.1 | NA | Yes |
| Cetuximab[67] | 7/6/2012 | 1217 | First-line K-ras wild-type, EGFR-expressing CRC | 1.4 | 4 | Yes |

(continued)

Table 1. Food and Drug Administration (FDA) Drug Approvals in Solid Tumors 2002 Through 2014[a,b] (continued)

| Agent | Approval Date | Enrolled, No. | Cancer Indication | Gain, mo | | Would Have Met ASCO Committee Criteria[d] |
|---|---|---|---|---|---|---|
| | | | | PFS[c] | OS | |
| Ziv-Aflibercept[68] | 8/3/2012 | 1226 | Second-line mCRC; with FOLFIRI | 2.2 | 1.44 | No |
| Everolimus[69] | 8/30/2012 | 724 | HER2-positive breast cancer | 4.6 | NA | No |
| Enzalutamide[70] | 8/31/2012 | 1199 | Second-line CRPC | NA | 4.8 | Yes |
| Regorafenib[71] | 9/27/2012 | 760 | mCRC | 0.3 | 1.4 | No |
| Nab-paclitaxel[72] | 10/11/2012 | 1052 | First-line NSCLC; with carboplatin | NA | NA | Uncertain |
| Cabozantinib[73] | 11/29/2012 | 330 | Advanced medullary thyroid carcinoma | 7.2 | NA | Yes |
| Abiraterone[74] | 12/10/2012 | 1088 | First-line CRPC | NA | 5.2 | Yes |
| Bevacizumab[75] | 1/23/2013 | 820 | Second-line CRC | NA | 1.4 | No |
| TDM-1[76] | 2/22/2013 | 991 | HER2-positive metastatic breast cancer | NA | 4.2 | Yes |
| Regorafenib[77] | 2/25/2013 | 199 | Imatinib- and sunitinib-resistant GIST | 3.9 | NA | No |
| Erlotinib[78] | 5/14/2013 | 174 | First-line NSCLC with EGFR exon 19 deletion or exon 21 L858R substitution | 5.2 | NA | Yes |
| Radium-223[79] | 5/15/2013 | 809 | CRPC with bone metastases but no visceral metastases | NA | 2.8 | Yes |
| Dabrafenib[80] | 5/29/2013 | 250 | Unresectable and/or metastatic melanoma | 2.4 | NA | Yes |
| Trametinib[81] | 5/29/2013 | 322 | Unresectable and/or metastatic melanoma | 3.3 | NA | Yes |
| Afatinib[82] | 8/12/2013 | 345 | NSCLC with EGFR exon 19 deletion or exon 21 L858R substitution | 6.7 | NS | Uncertain |
| Nab-paclitaxel[83] | 9/6/2013 | 861 | Metastatic pancreatic cancer; with gemcitabine | 1.8 | 1.8 | No |
| Crizotinib[84,85,86] | 11/20/2013 | 347 | NSCLC expressing *ALK* gene | 4.7 | NA | Yes |
| Sorafenib[87] | 11/22/2013 | 417 | Metastatic and/or differentiated thyroid cancer | 5 | NA | Yes |
| Trametinib + Dabrafenib[88] | 1/10/2014 | 162 | Unresectable and/or metastatic melanoma | NA | NA | No |
| Ramucirumab[89] | 4/21/2014 | 355 | Stomach and/or esophageal junction cancer | 0.8 | 1.4 | No |
| Ceritinib[90] | 4/29/2014 | 163 | Second-line ALK-positive NSCLC | NA | NA | Uncertain |
| **Total** | | **44 218** | | | | |
| **Mean** | | **632** | | | | |
| **Median** | | **582** | | **2.5** | **2.1** | |

Special Communication

## Unintended Consequences of Expensive Cancer Therapeutics—The Pursuit of Marginal Indications and a Me-Too Mentality That Stifles Innovation and Creativity

### The John Conley Lecture

Tito Fojo, MD, PhD; Sham Mailankody, MD; Andrew Lo, PhD

JAMA Otolaryngology–Head & Neck Surgery December 2014 Volume 140, Number 12

# Let's be honest – our research centres on drugs not patients


Denis Lacombe is Director General

Precision oncology is about understanding what is driving an individual's cancer growth, resistance and metastasis, and then targeting those pathways accordingly. Our current research models are good at developing drugs to hit targets. They are bad at learning about which targets need hitting in which patients and how best to do that.

A truly patient-centred approach would not involve just adding the expression of a target of interest as an inclusion criterion to a given trial protocol. That is an inefficient and wasteful way of finding the right therapy for each patient, as it would have to be repeated time and again until the drug–target match is found – if it is eventually found. In addition, scarce biological materials are usually lost in commercially siloed biobanks, and no one addresses treatment questions for those patients who do not express the target.

These are outdated research models, which

Putting the patient at the centre would require replacing the process by which trial protocols seek access to the patients they need, by a process that helps patients get access to the latest science that could help them. Such a process would start with systematic screening of every newly diagnosed patient and the biology of their disease. It would follow the patient through the course of the disease, providing longitudinal clinically annotated bio-collection, addressing tumour heterogeneity and the challenges of recurrence. This process would give patients the best chance to be matched with the best treatment for them, including via access to regulatory trials. Questions about treatment duration, combinations and sequences could be addressed by independent research.

Clinical research and healthcare models are long overdue for transformation. Systems need to be re-engineered to place patients at the centre.

# Where is public clinical research required?

## DEVELOPMENT

- (generic) drug repurposing
- Autologous cell therapy

## ACCESS

- Registration trials, pivotal trials
- De-escalation trials, therapy optimisation trials
- Cancer registries, real-world data

Anticancer Fund

# A good example: The Netherlands

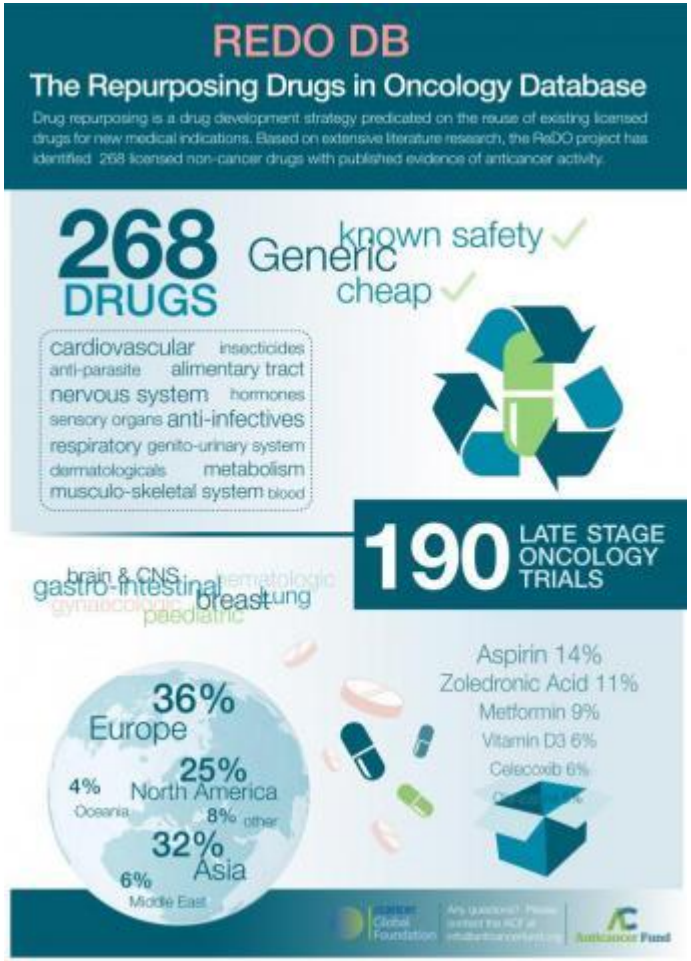
## Identify where non-commercial drug development is desirable

Drug rediscovery, cell and gene therapy


Commissioned by Minister Schippers to RVS, 2016

**Hard repurposing:** build on of the increasing knowledge of the tumor biology ⇨ Microenvironment: immunological, metabolic, inflammatory pathways


**Soft repurposing:** unmet needs in rare cancers, especially paediatric oncology



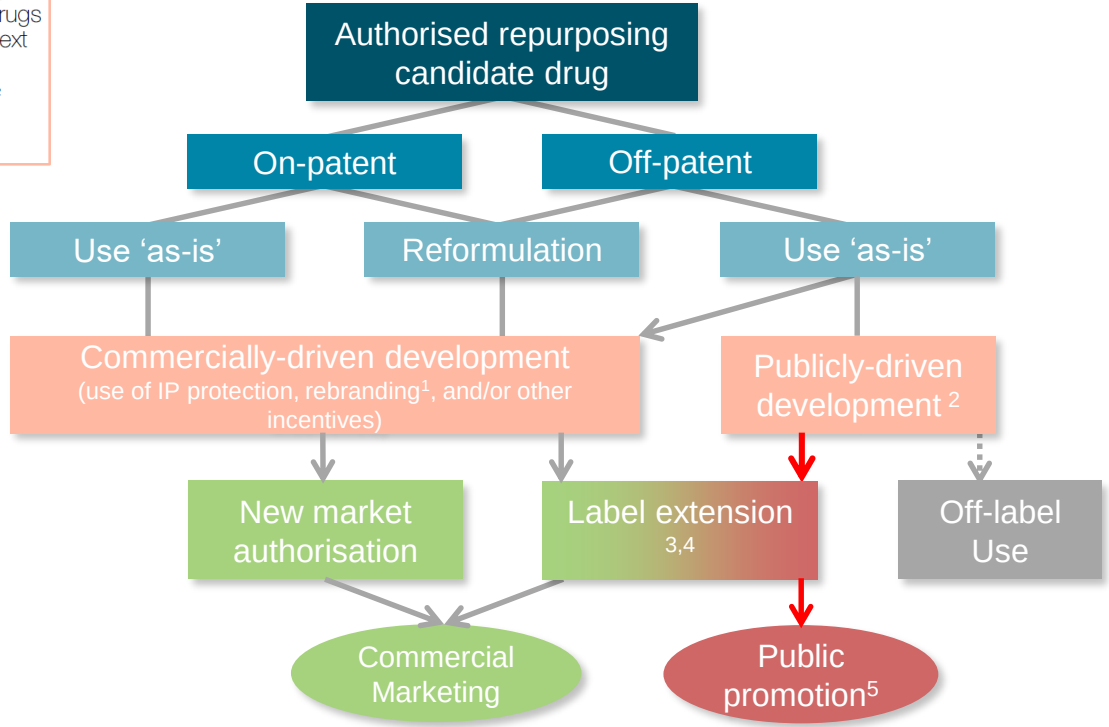

Pantziarka et al. 2018, *ecancer* 2018,12:886

Trends in Cancer

Science & Society

# Repurposing Drugs in Oncology: Next Steps

Ciska Verbaanderd,[1,2] Lydie Meheus,[1] Isabelle Huys,[2] and Pan Pantziarka[1,3,*]




[1] Rebranding cannot be combined with label extension; [2] Both philanthropic and governmentally-funded development; [3] One additional year of market exclusivity if new indication is registered in first 8 years and brings significant clinical benefit over existing therapies; [4] Currently, label extension can only be obtained by the market authorisation holder, label extension by third parties is not yet an option in the EU legal framework; [5] Public promotion: adoption in clinical guidelines, communication with HTA and national reimbursement bodies

The Scientist » January 2017 Issue » Features

# Repurposing Existing Drugs for New Indications

**An entire industry has sprung up around resurrecting failed drugs and recycling existing compounds for novel indications.**

By Anna Azvolinsky | January 1, 2017

Due to this **lack of monetary incentive**, *"generic drugs found to work for a new disease are in a state of purgatory,"* says Wegner. Indeed, no generic drug has ever been approved for a new indication by a manufacturer without modification of the drug's delivery or its dose, which would provide renewed patent protection. **Someone needs to step up to help move preliminary findings about these cheap and available drugs into the clinic where they can help patients**, Wegner adds. *"This is where foundations, advocacy groups, and the NIH can play a huge role."*

**Craig Wegner, Astra Zeneca**

# What should change?

Collaboration between government and philanthropy: “public”

Adapt the regulatory/legal system (EU, US )

Anticancer Fund

FRIENDS of CANCER RESEARCH

SEARCH

ABOUT

SCIENCE & POLICY

NEWS

EVENTS

PATIENTS

EDUCATION

PUBLICATIONS

DONATE

On June 19, 2019, Senate health committee Chairman Lamar Alexander (R-Tenn.) and Ranking Member Patty Murray (D-Wash.) introduced S.1895, the Lower Health Care Costs Act of 2019, including Section 213 titled "Modernizing the labeling of certain generic drugs." Section 213 of S. 1895 addresses the public health issue of outdated labels identified by *Friends* work as well as the previously introduced MODERN Labeling Act.

| LABELING | From Concept to Whitepaper | From Peer Reviewed Publication to Briefing | From Legislation to Passage |
|---|---|---|---|
| **Building toward a solution for patients by modernizing prescribing information and protecting public health.** | November 2017: At the *Friends* Annual Meeting, a panel of experts explores the issue of outdated product labels with the panel commenting on a potential regulatory framework for label updates. The panel also releases a whitepaper detailing this framework for updating product labels, including input from the FDA. | March 2018: *Friends* releases a peer reviewed publication detailing statistics and prevelance of outdated product labels. In conjuction, *Friends* hosts a Congressional briefing, bringing together experts from industry, academia, physicians, and the FDA to discuss the problems stemming from outdated product labels for patient safety and medical accuracy. | September 2018: Senators Michael Bennet (D-CO) and Orrin Hatch (R-UT) release their bill, the MODERN Labeling Act. The bill provides a solution to outdated product labels building on the *Friends* framework and study.<br><br>*Friends* urges immediate passage by the Senate. |
| **Timeframe** | July 2017 - November 2017 | December 2017 - March 2018 | April 2018 - Present |

Therapeutic Innovation & Regulatory Science
1-7

DOI: 10.1177/2168479018759652
dirs.sagepub.com

# Outdated Prescription Drug Labeling: How FDA-Approved Prescribing Information Lags Behind Real-World Clinical Practice

Michael B. Shea, BA[1], Mark Stewart, PhD[1], Hugo Van Dyke, MS[2], Linda Ostermann, BA[1], Jeff Allen, PhD[1], and Ellen Sigal, PhD[1]

**Abstract**

*Background:* Prescription drug labeling is an authoritative source of information that guides the safe and effective use of approved medications. In many instances, however, labeling may fail to be updated as new information about drug efficacy emerges in the postmarket setting. When labeling becomes outdated, it loses its value for prescribers and undermines a core part of the FDA's mission to communicate accurate and reliable information to patients and physicians. *Methods:* We compared the number of drug uses indicated on product labels to the number of uses contained in a leading drug compendium for 43 cancer drugs approved between 1999 and 2011. We defined a "well-accepted off-label use" of a drug as one that was not approved by the FDA and received a category 1 or 2A evidence grade. *Results:* Of the 43 drugs reviewed in this study, 34 (79%) had at least one well-accepted off-label use. In total, 253 off-label uses were identified; 91% were well accepted, and 65% were in cancer types not previously represented on labeling. Off-patent drugs had more well-accepted off-label uses than brand-name drugs, on average (mean 13.7 vs 3.8, $P = .018$). *Conclusions:* The labeling for many cancer drugs, particularly for older drugs, is outdated. Although FDA-approved labeling can never be fully aligned with real-world clinical practice, steps should be taken to better align the two when high-quality data exist. Such steps, if taken, will assist patients and prescribers in discerning which uses of drugs are supported by the highest quality evidence.

**Keywords**

FDA, labeling, off-label use, compendia, postmarket evidence

## Introduction

Each time a new drug is approved for marketing in the United States, an accompanying collection of drug-related information, called "labeling," is made available to health care practitioners to inform safe and effective prescribing. Federal regulations state that labeling must contain a summary of the essential scientific information about a drug, and that the information contained therein must be informative and accurate.[1] The content of labeling is written by drug manufacturers, but must be approved by the Food and Drug Administration (FDA) to ensure that it meets standards laid out in regulations.[2]

Labeling is a crucial source of trusted information about prescription drugs, but it can easily become outdated if new evidence of drug effectiveness is not submitted to the FDA in a timely manner. Most often, labeling becomes outdated when high-quality scientific evidence is generated that supports a new use of a drug, but the drug's manufacturer does not file a supplemental application requesting the new use be added to the drug's labeling. This may occur because the manufacturer did not sponsor the research investigating the new use, or because the manufacturer lacked sufficient incentives to pursue a labeling expansion. Drug manufacturers are not required by law to update their products' labeling with new uses, though they may choose to do so voluntarily when they wish to market their products in new settings.[3]

Uses of drugs in patient populations or for indications that differ from those prescribed on labeling are referred to as "off-label" uses. Off-label use in oncology is common: it has been estimated that more than half of all uses of cancer drugs are beyond the scope of approved labeling.[4,5] The fact that a particular use is off-label does not preclude it from being incorporated into routine practice and covered by insurers. A policy dating back to 1993 requires Medicare to cover off-label cancer drug uses that have been deemed medically accepted by at least

[1] Friends of Cancer Research, Washington, DC, USA
[2] American University, Washington, DC, USA

Submitted 19-Sep-2017; accepted 12-Jan-2018

**Corresponding Author:**
Michael B. Shea, BA, Regulatory Policy Analyst, Friends of Cancer Research, 1800 M St NW Ste. 1050 S Washington, DC 20036, USA.
Email: mshea@focr.org

Supplemental NDA
21CFR314.70
((b)(2)(v)(A))

# Bennet, Hatch Introduce Bill to Update Prescription Drug Labels

**September 28, 2018**

**Washington, D.C.** — U.S. Senators Michael Bennet (D-CO) and Orrin Hatch (R-UT) this week introduced the *Making Objective Drug Evidence Revisions for New (MODERN) Labeling Act*. The bipartisan legislation would authorize the U.S. Food and Drug Administration (FDA) to modify outdated drug labels to reflect new evidence relevant to the drug and its use.

"Medical providers need the most up-to-date information to make the right health care decisions for their patients," **said Bennet.** "We must ensure the FDA has the authority to update prescription drug information for older treatments using the latest clinical evidence. Passing this bipartisan legislation is an important step we can take to modernize prescribing in our health care system."

"In an ideal world, a drug's label would contain all available information healthcare professionals need to prescribe it effectively. Due to a variety of reasons, that is not always the case and physicians are sometimes left to consult outside sources for up-to-date prescribing information," **said Hatch.** "I am pleased today that Senator Bennet joins me in providing the tools the FDA needs to better protect public health. I look forward to continuing to work with my colleagues, stakeholders, and the FDA to advance this policy into law."

*"(c) SELECTION OF DRUGS FOR UPDATING.—If the Secretary determines, with respect to a covered drug, that the available evidence is sufficient to meet the standards under section 505 for adding information to the labeling or modifying information in the labeling regarding the use of the covered drug, the Secretary may initiate the process under subsection (d)*

EUROPEAN COMMISSION
DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY

Health systems and products
**Medicinal products – authorisations, European Medicines Agency**
Head of Unit

Brussels,
SANTE/D5/FS/iv(2015)ddg1.d5. 6563827

Dear Mrs Meheus,

**Subject:** **Cancer research - Your email dated 30 November 2015**

I refer to your above mentioned email to Commissioner Thyssen, which has been forwarded to Commissioner Andriukaitis. He asked me to provide you with an answer.

Despite some progress in recent years in the fight against cancer, this disease remains a key public health concern. The European Commission has been supporting the fight against cancer for over 30 years with a wide range of actions. This includes collaborative research, public-private partnerships and coordination of national cancer research efforts.

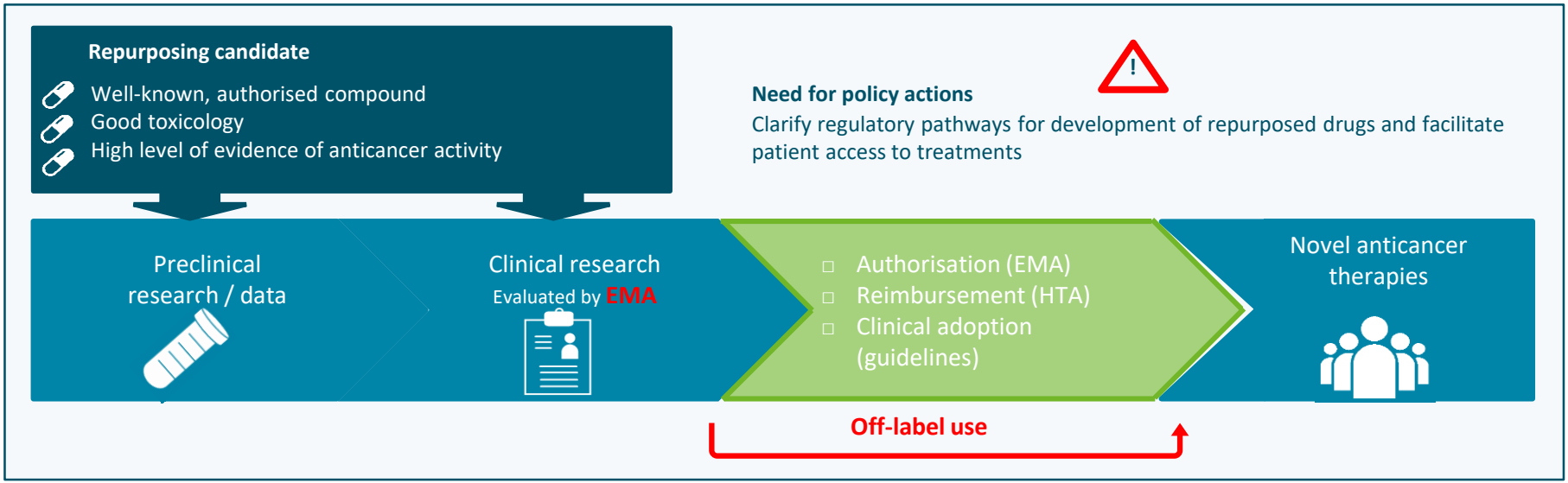
Many different stakeholders are active in this field, including organisations such as yours that support independent research. Their contribution is highly valued.

I agree with you that it is necessary that advances in the laboratory and new scientific findings are translated in actual treatment options that are available to concerned patients. In case of medicinal products this will require a marketing authorisation in accordance with the currently applicable standards. Those standards are necessary to ensure the quality, safety and efficacy of products that are used by patients in the European Union.

The submission of marketing authorisations or of applications for new indications is however, company driven. The competent authorities cannot extend the scope of a marketing authorisation on their own initiative. This being said, the EU legal framework contains provisions that incentivise line extensions of well-known substances. Moreover, new combination products, even if based on well-known substances, may benefit from market protection periods, which are intended to allow companies to recuperate their investment.

**Type 2 variation (C.I.6) Annex II Reg. (EC) No 1234/2008**

# Regulatory Changes needed




**STAMP**
(**S**afe and **T**imely **A**ccess to **M**edicinal **P**roducts expert group within DG Santé B5): Approved proposal for a framework to support not-for-profit organisations in drug repurposing within the current legislation through Scientific Advice (SA)

TAGS: Research and Development Strategies | Regulation | Europe

ASK THE ANALYST | EMAIL

TAGS: Drug Review | Generic Drugs | Market Access

ASK THE ANALYST

# ‘Champions’ To Lead European Drug Repurposing Project

30 Oct 2018 | NEWS

by Ian Schofield

@ScriplanS | ian.schofield@info

## Executive Summary

Work is under way on a new European procedure
uses. It would mainly be used for active substance
authorization holder and the relevant data were g

# EU ‘Repurposing’ Project Plans Pilot Phase

05 Mar 2019 | NEWS

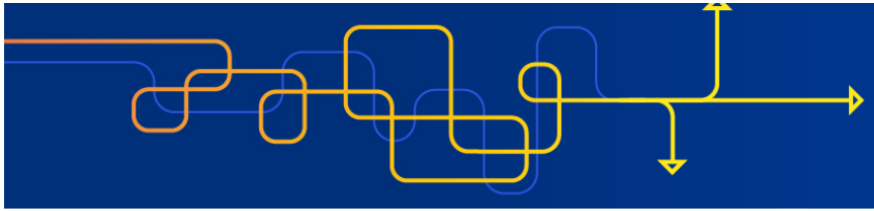
The Economist

rma.com

g repurposing proposal originally devised by
ing the procedures to be used and running a

Cross purposes

## “Repurposing” off-patent drugs offers big hopes of new treatments



# Repurposing Off-Patent Drugs:

## RESEARCH & REGULATORY CHALLENGES

December 5 – 6, 2019 | FDA, NCATS & the Reagan-Udall Foundation for the FDA

Register

## Repurposing Off-Patent Drugs: Research & Regulatory Challenges

Finding a new therapeutic use for an existing drug seems like a simple way to get more treatments to more patients more quickly. However, finding new uses for drugs that are off-patent is like navigating through a sea of icebergs without an icebreaker. No single entity owns the territory the icebergs are in. It is difficult to see the full scope of individual challenges, to prioritize which challenges are addressable, and to choose the most effective vehicle to navigate the challenges.

Join us for a free workshop on December 5-6, 2019. First, we will map out the challenges to repurposing drugs that are already on the market but lack commercial and regulatory incentives for research and development. Then, we will host interactive work sessions focused on capturing possible solutions to core questions:

- Which problems impede progress the most?
- What are the possible solutions?
- Are there unanticipated problems with the proposed solutions?
- Which solutions can be implemented in the short term?
- Who owns the individual challenges?
- What challenges are shared space, and how do we establish a collaboration to address challenges faster?

**Potential discussion topics**

- Accessing existing data
- Identifying appropriate comparators
- Regulatory approval
- Drug labeling
- Health economics
- Payor perspectives
- Real world evidence & real world data challenges
- Historical attempts to fix similar problems

**Who should attend**

- Patients
- Philanthropists
- Non-governmental organizations
- Academics
- Pharmaceutical developers & manufacturers
- Healthcare economists
- Patent/intellectual property lawyers
- Regulatory policy experts
- Computational scientists
- Payors & funders

Hilton Rockville Hotel & Executive Meeting Center
1750 Rockville Pike
Rockville, MD 20852

View on map

Deadline to reserve hotel rooms: October 25, 2019

Reserve a hotel room

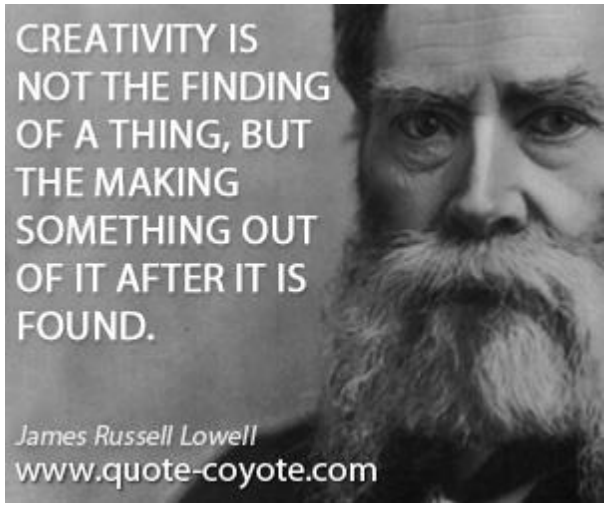
Download preliminary agenda

NIH National Center for Advancing Translational Sciences

FDA

REAGAN-UDALL FOUNDATION

*“As a society we need to ensure that we do not leave any reasonable opportunity for anticancer treatment untapped”*



# NUTRACEUTICALS: "*Winnowing the Chaff of Charlatanism from the Wheat of Science*"

## US: Dietary supplements: not regulated for safety and efficacy under the DSHEA of 1994

JAMA, May 15, 2013: clinical trial for age-related macular degeneration

- more than 3000 patients randomized
- antioxidant vitamins C and E, lutein, zeaxanthin , and zinc and cupper (specific dosing)
  - Investigation of 11 products from 5 top-selling brands making claims on vision and eye health
  - Claims are made for primary prevention: unproven
  - 4 products: lower doses
  - 4 products: additional compounds

## Europe (EFSA) Food Supplements directive

Directive 2002/46/EC:

Article 6

1. For the purposes of Article 5(1) of Directive 2000/13/EC,the name under which products covered by this Directive are sold shall be 'food supplement'.

2. The labelling, presentation and advertising must not attribute to food supplements the property of preventing, treating or curing a human disease, or refer to such properties

Anticancer Fund

# Conclusion

- Public funding is essential in a health system that centres on patient benefit.
- Valuable treatment options are not developed if there is no monetary incentive for the private sector to invest in the trials.
- Public funding is required not only for development of innovative treatments neglected by pharma but also to make these therapies accessible (on-label drugs) and affordable for all patients.

Anticancer Fund

# Thanks to the ACF team.
# Thank you for your attention.
# Any questions?

“Never doubt that a small group of thoughtful, committed, citizens can change the world.
Indeed, it is the only thing that ever has.”

— **Margaret Mead**

Antikankerfonds

# Back-up slides

Antikankerfonds

NCI Press Release

# Study quantifies impact of NCI-sponsored trials on clinical cancer care

**Posted:** September 18, 2019

**Contact:** NCI Press Office
240-760-6600

A new study shows that nearly half of phase 3 cancer clinical trials carried out by the National Cancer Institute (NCI)-sponsored SWOG Cancer Research Network, one of five groups in NCI's National Clinical Trials Network (NCTN), were associated with clinical care guidelines or new drug approvals. NCI is part of the National Institutes of Health.

The analysis was published in JAMA Network Open and conducted by researchers affiliated with SWOG from several institutions around the country. The study suggests that NCTN trials add value regardless of whether findings were positive or negative. In addition, the authors calculated the cost of running NCTN trials, and they also found that the cost of a U.S. Food and Drug Administration (FDA) approval from an NCTN trial was much less than the cost of an FDA approval from a trial run by pharmaceutical companies.

"We found that the NCTN program contributes clinically meaningful, cost-effective evidence to guide care of cancer patients," said Joseph Unger, Ph.D., a health services researcher and biostatistician for SWOG at the Fred


A study shows that 82 of 182 phase 3 clinical trials led by SWOG or by other NCTN groups with SWOG participation were "practice influential."
Credit: National Cancer Institute

JAMA Network Open

Original Investigation | Oncology

## Association of National Cancer Institute–Sponsored Clinical Trial Network Group Studies With Guideline Care and New Drug Indications

Joseph M. Unger, PhD, MS; Van T. Nghiem, PhD; Dawn L. Hershman, MD, MS; Riha Vaidya, PhD; Michael LeBlanc, PhD; Charles D. Blanke, MD

While reaffirming the important contribution that industry makes in funding RCTs for developing new drugs to treat advanced disease, these findings also reveal the critical role that academic groups and public funding plays in identifying interventions that yield the biggest public health benefits, highlighting the value of continued public funding and support of academic trials.

# Lung Cancer Survival Gains:
## Contributions of Academia and Industry

Health Policy Portal

*Bishal Gyawali, Gauthier Bouche, Pan Pantziarka, Aaron S. Kesselheim, and Ameet Sarpatwari*

Non-small cell lung cancer (NSCLC) is the leading cause of cancer death worldwide.[1] Although overall survival rates among patients with the disease remain low,[2] modest improvements have been reported in recent decades.[3] These improvements have been achieved in large part due to practice-changing randomized controlled trials (RCTs), some related to drug products and others to interventions such as surgery and radiotherapy. Understanding which interventions have yielded overall survival gains and which institutions have contributed to the RCTs revealing these benefits can help identify the greatest drivers of public health benefit and inform the allocation of scarce health care resources. Accordingly, we reviewed the sponsorship and funding of RCTs demonstrating life-extending outcomes in non-small cell lung cancer.

We used the National Comprehensive Cancer Network (NCCN) guidelines for NSCLC (v.5.2017) to identify the cohort of interventions for this study. We chose the NCCN guidelines because they are the most widely used multi-disciplinary guidelines in cancer and include drug and non-drug interventions. For each intervention, we assessed its supporting evidence, selecting only interventions that were tested in at least one RCT. We collected the report of the RCT from PubMed and evaluated whether it found overall survival gains related to the intervention. Interventions for which RCTs did find overall survival gains were categorized as taking place in the curative (non-metastatic) or non-curative (advanced or metastatic) setting. For each RCT, we recorded the overall survival gains (5-year overall survival rates were available in the curative setting, and median overall survival was available in the non-curative setting; hazard ratios were obtained for each setting), the sponsor (defined as the person or entity that takes responsibility for a clinical investigation), and the funder (defined as the organization providing financial support for a study). We categorized sponsors into industry, academia, or both; and funders into industry, public, or mixed. When this information was not available from the published literature, we searched Clinicaltrials.gov; if unavailable there, we contacted the corresponding author. Results were analyzed descriptively.

Among 57 NCCN-recommended interventions, 39 (68%) were based on at least one RCT, of which 19 (49%) showed an improvement in overall survival in 26 RCTs published between 1990 and 2017 (**Table**). These 19 interventions included the same drug in different settings (e.g., pembrolizumab as first-line and second-line treatment). Combining these, there were 17 distinct interven-

**About This Column**

Aaron Kesselheim serves as the editor for Health Policy Portal. Dr. Kesselheim is the *JLME* editor-in-chief and director of the Program On Regulation, Therapeutics, And Law at Brigham and Women's Hospital/Harvard Medical School. This column features timely analyses and perspectives on issues at the intersection of medicine, law, and health policy that are directly relevant to patient care. If you would like to submit to this section of *JLME*, please contact Dr. Kesselheim at akesselheim@bwh.harvard.edu.

**Bishal Gyawali, M.D., Ph.D.**, *is with the Program On Regulation, Therapeutics, And Law (PORTAL), Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA, the Anticancer Fund, Belgium, and the Department of Oncology and Division of Cancer Care and Epidemiology, Queen's University, Kingston, Canada.* **Gauthier Bouche, M.D., M.P.H.**, *is with the Anticancer Fund, Belgium.* **Pan Pantziarka, Ph.D.**, *is with the Anticancer Fund, Belgium.* **Aaron S. Kesselheim, M.D., J.D., M.P.H.**, *is with the Program On Regulation, Therapeutics, And Law (PORTAL), Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA.* **Ameet Sarpatwari, Ph.D., J.D.**, *is with the Program On Regulation, Therapeutics, And Law (PORTAL), Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA.*



*The Journal of Law, Medicine & Ethics*, 47 (2019): 465–467. © 2019 The Author(s)
DOI: 10.1177/1073110519876182