The future of drug repurposing for rare diseases

Dr Rick Thomson
CEO, Findacure

#DrugRepo  #RareDiseaseDay  @findacure_fdn
An informed patient population with the power and determination to deliver change.

A rare disease is defined by the EU as affecting fewer than 1 in 2,000 people.

In the UK, approximately 3.5 million people live with rare diseases, which can be chronic, life-threatening, and isolating.

75% of rare diseases affect children.

30% of rare disease patients will die before their 5th birthday.

Of the 7,000 recognised rare diseases, only 400 have licensed treatments.

At the current rate of drug development, it would take 500 years to get a treatment for all these conditions.

The average rare disease patient waits 4 years before they receive their final diagnosis, during which time they consult with 5 doctors and receive 3 misdiagnoses.

2 in 3 patients and carers struggle to hold paid employment.

Similarly, 3 in 5 patients felt their rare disease affected their education.

The day-to-day challenges of managing conditions are often made worse by the absence of an effective treatment.

A third of patients do not have access to the medicine that they need and another third only have access after waiting years.
The future of drug repurposing for rare diseases

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The future of drug repurposing for rare diseases*  

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Patient engagement

Personalised medicine

Genomics

Gene editing
Repurposing – Why bother?

I like my medicines new and innovative!
Productivity of the pharma industry

Finding the true cost of a new drug is complex and controversial...

Cost of a new drug in US$ (billions)*

Data: USFDA, PhRMA

* New drug cost and R&D spend could be 30% higher if non-PhRMA members are included
Pricing in rare diseases

Average Cost per Patient per Year 2012-2016

<table>
<thead>
<tr>
<th>Year</th>
<th>Average Cost per Patient ($)</th>
<th>Orphan</th>
<th>Non-Orphan</th>
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<tbody>
<tr>
<td>2016</td>
<td>140,443</td>
<td>27,756</td>
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<tr>
<td>2015</td>
<td>140,352</td>
<td>26,405</td>
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<td>2014</td>
<td>137,545</td>
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<td>2013</td>
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<tr>
<td>2012</td>
<td>116,216</td>
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</tr>
</tbody>
</table>

Source: EvaluatePharma February 2017
What is drug repurposing?

At its most basic level, drug repurposing can be likened to recycling.

It is the act of taking a drug intended to treat one patient population, and demonstrating its efficacy in the treatment of a completely different group of patients.
Working with what you know

- fast, cheap, good for rare diseases
- no de novo discovery
Working with what you know

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- known safety profile and side effects
Working with what you know

- History of human use
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Working with what you know

- Fast, cheap, good for rare diseases
- No de novo discovery
- History of human use
- Known safety profile and side effects
- Reduced requirement for early stage clinical trials
- Safety profile and side effects reduced, requirement for early stage clinical trials
Working with what you know

- fast, cheap, good for rare diseases
- no de novo discovery
- known pathways of action
- reduced requirement for early stage clinical trials
- known safety profile and side effects
- history of human use

Working with what you know
Working with what you know

- Fast, cheap, good for rare diseases
- Known safety profile and side effects
- Reduced requirement for early stage clinical trials
- No de novo discovery
- Known pathways of action
- Ideas or evidence for repurposing candidates
Repurposing of generics should be appealing due to the wealth of data available on their use in humans.

However:

- Hard to secure IP on generics
- Mode of use patents are hard to defend
  - Off-label prescription of alternative generics is hard to detect, and to prevent

Subsequently, it is more difficult for pharmaceutical companies to profit from their development of the drug.
A literature review of published examples of drug repurposing for rare diseases is underway.

167 different cases identified so far

47 are paediatric

70 report off label use in rare conditions

11 are based on case reports

Only 3 are reported through full clinical trials, and 4 are retrospective analyses
Rare Repurposing Open Call

Do you know of a drug repurposing project for a rare disease that is struggling to reach the clinic?

The call, hosted online by CureAccelerator™, was open to ideas from clinicians, researchers, and patient groups worldwide. It aimed to raise the profile of drug repurposing in the rare disease community, find new research projects for Findacure’s innovative Social Impact Bond, and connect projects with funders and professionals with the skills to move them to the clinic.

End of February to end of June 2017
Open Call Results

38 different proposals

Including for some better known conditions such as:
- cystic fibrosis
- sickle cell anaemia
- Duchenne muscular dystrophy

Excitingly, many ultra-rare conditions were also represented, including:
- epidermolysis bullosa
- adult polyglucosan body disease
- PTEN syndrome

Of the proposed open call projects:

- 20 are US based
- 5 are UK based
- 4 are based in Europe
  - 1 Canadian, 1 Australian & 1 South African
- Of those beyond the UK, 21 have a UK collaborator

- 12 conditions have no treatment
- 29 target rare genetic conditions
- 3 target common conditions
- 6 treat rare cancers
- 17 proposals include patient group collaboration
- 1 in 50,000
- 11 proposals target a condition with a prevalence no higher than
- 3 preclinical studies
- 6 phase I studies
- 24 phase II or III studies
Repurposing is an ideal patient group or academic led collaborative model
Drug Repurposing for Rare Diseases

The EspeRare Foundation: a philanthropic venture focused on drug repositioning to accelerate the development of treatments for rare diseases
Caroline Kant  Founder & Executive Director, EspeRare Foundation

Our journey from pre-diagnosis to clinical trial
Tracy Lynch  Co-founder & Chief Executive, Wolfram Syndrome UK

How AI can accelerate drug discovery for rare diseases: The Fragile X example
Michale Bouskila-Chubb  Head of Business Development, Healx

Drug repurposing for Metaphyseal Chondrodysplasia type Schmid
Prof. Michael Briggs  Professor of Skeletal Genetics, Newcastle University

Repurposing for Duchenne Muscular Dystrophy
Emily Crossley  Co-founder & Joint CEO, Duchenne UK

A rare commitment to a rare disease
Dr Feruza Nasirova  Therapeutic Area Medical Head Rare Disease, Novartis
MCDS-THERAPY

MCDS-THERAPY Project has received funding from the European Union’s Horizon 2020 research and innovation programme under grant agreement No 754825.

MCDS = Metaphyseal Chondrodysplasia Type Schmid

MCDS is a rare condition that leads to short stature, disproportionately short limbs, and bowed legs. Patients often suffer from joint pain and can have an unusual gait, both of which limit quality of life.

MCDS is caused by a mutation in collagen X.

A generic drug, Carbamazepine, has been shown to restore bone growth and form in MCDS mice. The collaboration will trial this drug in humans for the first time.
MCDS partners

MCDS-Therapy Project has received funding from the European Union’s Horizon 2020 research and innovation programme under grant agreement No 754825.
Findacure’s role in MCDS-Therapy

To disseminate information about the project, its aims, and its progress to the patients, rare disease community, and general public.

To help to build the MCDS patient community so that they are able to support the trial and provide their insights to enable us to deliver the best possible project for the patients.

Findacure’s aim

Help to build an open and collaborative project, that puts patient need, and patient input at the heart of the research and delivery.

To make MCDS-Therapy a gold standard example of academic collaboration delivering repurposed drugs for rare diseases, and to share its progress, successes, and challenges with the rare disease world.
MCDS-Therapy aims

The MCDS-Therapy project aims to develop a low cost treatment for a rare skeletal condition, alleviating the pain and bone malformations that patients live with on a daily basis. We will do this by forming a strong collaboration of scientists around the world, working closely with patients to deliver the treatment they need outside of the usual drug development pathway.

We are trying to pioneer an academic drug repurposing pathway, delivering a transformative treatment for a rare patient population from bench to bedside, independent of the pharmaceutical industry.

Ultimately we hope to develop a new paradigm in orphan drug development, and inspire more research into rare skeletal conditions.

Get involved - @mcds-therapy      Website and Facebook coming soon!

Contact Findacure to join our new MCDS newsletter
Summary – repurposing IS the future

- Traditional drug discovery routes cannot deliver for all rare diseases on their own.

- Repurposing offers a quicker, cheaper, and collaborative route to the development of effective treatments.

- Academic and patient led collaborations are proving successful, and more approaches are being developed right now.

- The MCDS-Therapy project aims to deliver a new low-cost treatment from bench to bedside in an ultra-rare skeletal condition.

- Findacure will continue to promote drug repurposing for rare diseases, and to gain traction with the NHS for it SIB idea.
Thank you