University-industry collaboration in translational research

Targeting kinases for cancer therapies

IAX event, Leicester
18th Sep 2019

Li-Ying Lin, PhD

How did we build the collaboration with industry partners?

Key innovation to this project

Some Kinases have essential roles in the DNA damage response and therefore represent exciting and novel potential oncology targets.

There are no inhibitors yet available either as clinical candidates or commercial tools for these kinases.

To use biochemical assays to screen an optimised compound collection provided through the AZ Open Innovation Scheme. (A collaborative agreement has been signed with AZ for this purpose.)

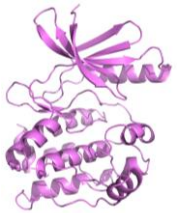
The goal is to get a lead for further cancer drug discovery.

Proximity to Discovery

Confidence in Concept

MRC Medical Research Council

UNIVERSITY OF LEICESTER



Kinase project for cancer therapies

LD3 funding
For translational projects

Compound libraries

Biochemical scientists

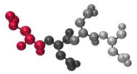
Chemists

AstraZeneca

Staff

Consumables

Industry resource



Access to Leicester Drug Discovery and Diagnostics (LD3) resource

RED

IAX Funding supported secondment at industry

MRC Medical Research Council

Managers
Cell biologist
Structural biologist

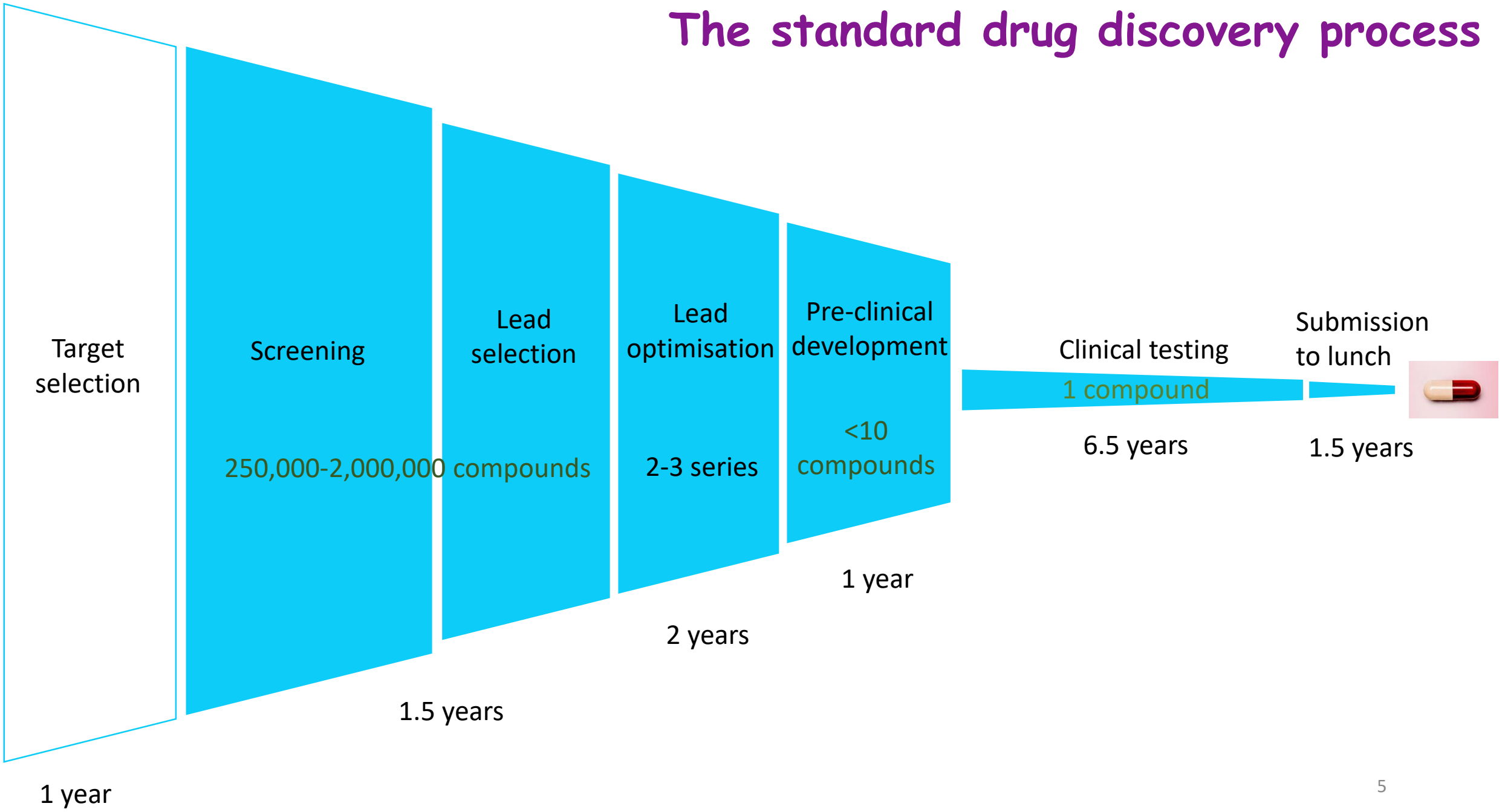
Project outcome

Lead compound
Industry investment
Grants
Publications

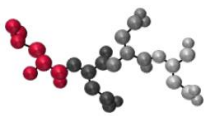
N years

Novel drugs for cancers

The standard drug discovery process



Specific kinase libraries screening



Optimized robust biochemical assays for targets

490 distinct hits and 70 near neighbours from AZ have been validated by IC_{50} determination.

Further screened of 2185 compounds against against targets at AZ HTS center

Tested 33 hits by biochemical assays

co-crystallization experiments of 10 hits

Start

June 2017 | **Sep 2017** | **Apr 2018** | **Aug 2018** | **Sep 2018** | **Nov 2018** | **Jan 2019** | **Apr 2019** | **June 2019** | **July 2019** | **Sep 2019**

Industry investment

Grants

Publications

Further IC_{50} determination and co-crystallization experiments of 4 hits

Confirmed 33 hits and dose response screen by cell-based assay

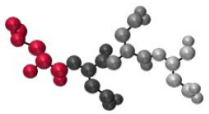
Analyzing SAR by AZ

Further IC_{50} determination of nearest neighbours by ADP-Glo and biochemical assay

Using one of the biochemistry assays, we completed two library screens of 1304 compounds

What we learnt through the work with AZ for early drug discovery

Advantages to work with AZ



Materials

Compounds are provided by AZ

Process

Less time cost for progress

For screening 2000 compounds (based on the capabilities):

Leicester: 4 months

AZ: 1 day to 1 week, dependent on the assays and machinery arrangement

Data analysis

Data are analysed systematically by professional software

Interpret the outcome by experienced scientists

SAR analysis by knowledgeable chemists

In-kind contribution from AZ: £100K

What I learnt when working with industrial partners

Maintaining reliability of the data –
reliable reagents/methods and experience.

Setting up milestones with reasonable time frames for the progress.

Good plan on the cost.

Good communications/regular meetings with collaborators.

Proper expectation on the outcome.

Acknowledgement

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LD3 2019 Autumn Call is now open!