Seuls les médiocres sont toujours à leur meilleur

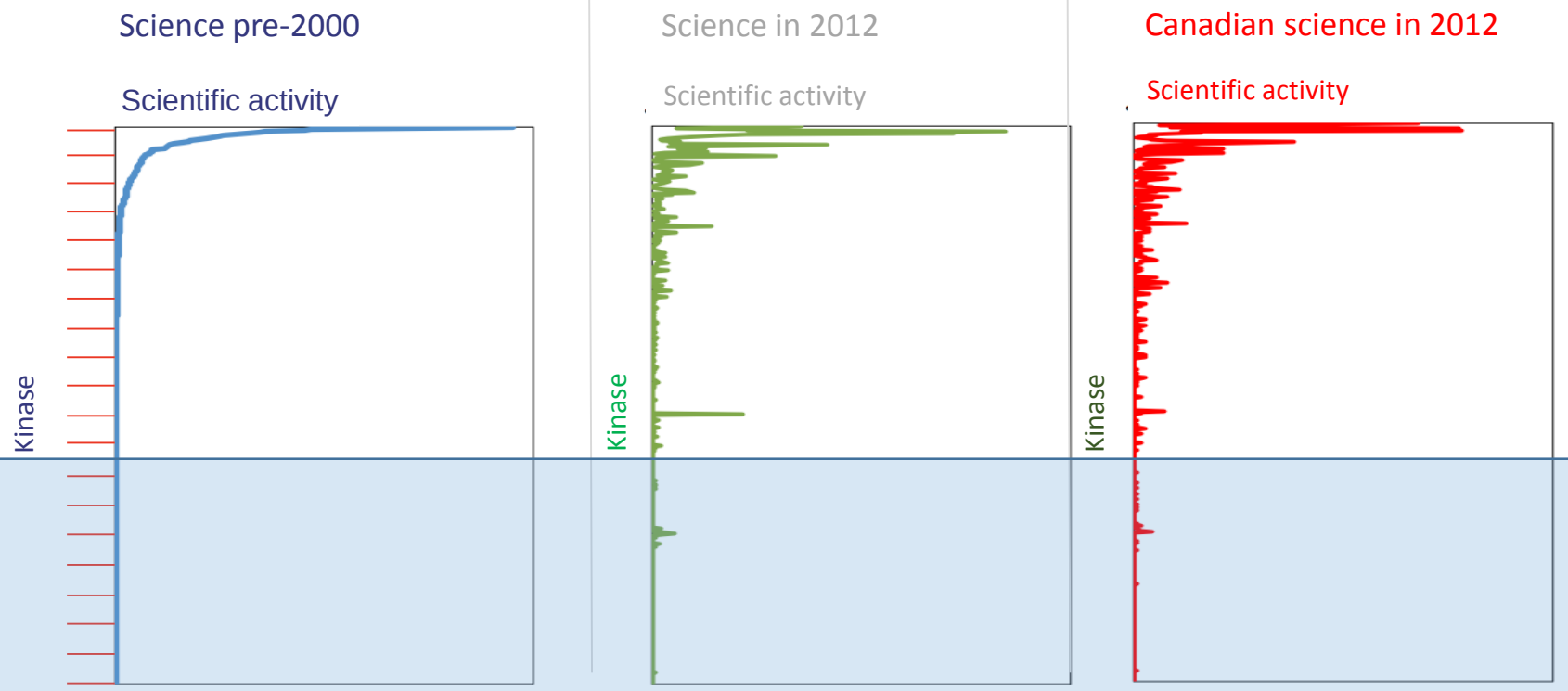
Only the mediocre are always at their best

Jean Giraudoux

How are we doing?

- >$250B a year invested in biomedical research
- For many diseases, we still don’t even understand molecular mechanisms, let alone how to design a therapeutic strategy
- Medicines are not affordable for most people in the world

Science resists change and is parochial and redundant



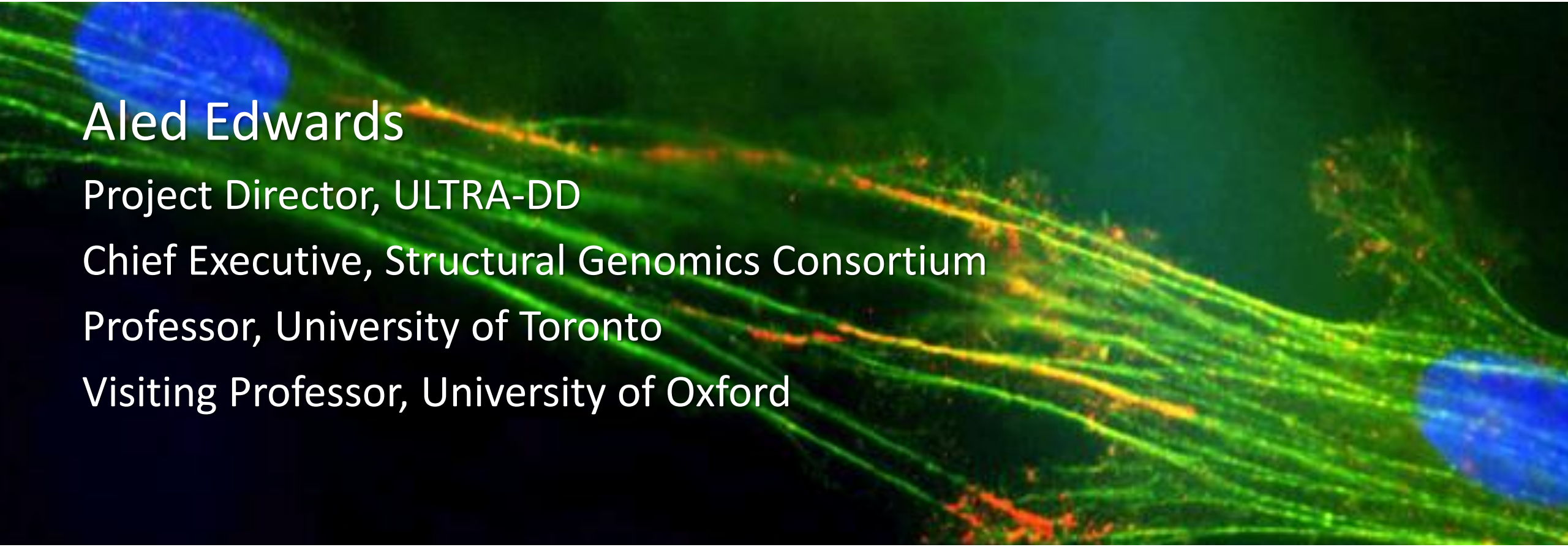
This is where innovation lies

Open science is the most efficient way to innovate, reduce redundancy and carry out frontier fundamental and translational science

What do I mean by “open science”?

- Open data and open publishing, of course *(but remember - this was at cutting edge last century)*
- Materials, knowledge made available without restriction to anyone - academia and industry
- No “deals”, no preferred access to knowledge
- Share data prior to publication whenever possible
- No patents on <u>any</u> output

Unrestricted Leveraging of Targets for Research Advancement and Drug Discovery



Aled Edwards

Project Director, ULTRA-DD

Chief Executive, Structural Genomics Consortium

Professor, University of Toronto

Visiting Professor, University of Oxford

SGC Founding Open Science Partnership Concept

CREATIVE COMMONS | **PROPRIETARY**

Public–Private Partnership	Public Domain	Commercial
Tools & Basic Knowledge **NOVEL Proteins only!** • Structure • Chemistry • Antibodies • Screening • Cell Assays	**Discovery and Exploration** • No patent • No restriction on use • Open access to tools and data. • Target identification & validation	**Drug Discovery and Development** Facilitated by access to increased amount of information in the public domain – (re)Screening – Lead Optimisation – Pharmacology – Metabolism – Pharmacokinetics – Toxicology – Chemical development – Clinical development

Weigelt J. EMBO Reports **10**:941-5 (2009)

Evolution of Open Science PPPs 2003 -

- Open structural biology (SGC) 2003 –
- Open chemical probes (SGC) 2009 -
- ***Open hospital network (IMI)*** ***2015 -***
- ***Open lab notebooks (SGC-IMI-CHDI)*** ***2016 -***
- Open academic institutions (MNI @McGill) 2016 -
- Open annotated chemogenomic libraries (SGC) 2017 -
- ***Open drug discovery (SGC, IMI, Patient foundations)*** ***2018 -***

Open science outcomes 2003 -

• Open structural biology	13% of world's human protein structures
• Open chemical probes (drug-like compounds)	>10,000 samples sent, referenced in 3,000 papers
• *Open hospital network (IMI)*	*New indication for drug and new commitments of $2M USD*
• *Open lab notebooks (SGC, IMI, CHDI)*	*>7,500 visitors; 15 new collaborations (academic & industry)*
• Open academic institutions (MNI @McGill)	Two new investment by pharma in basic science ($3M USD)
• Open annotated chemogenomic libraries	9 companies have donated >1,000 advanced compounds
• Open drug discovery (SGC/IMI/Foundations)	Company formed – CEO identified – seed funding raised

More project outcomes since 2003

- 2.5 papers published every week
- >25% of papers in journals with impact >10
- 10 new companies formed

Reputation for reproducibility

COMMENT

MUSEUMS To whom do collected objects belong, why and what for? p.302

ENTOMOLOGY A hymn to Vladimir Nabokov's powers of observation p.304

SUSTAINABILITY Cuts to environment and climate jobs are short-sighted p.305

FOOD IPBES must account for contribution of biodiversity to agriculture p.305

Team up with industry

Combining commercial and academic incentives and resources can improve science, argues **Aled Edwards**.

Case study:
Clinical Impacts from High Quality Chemical Tools

The Inception of Open-Source Chemistry

SGC

COMMENTARY

Nature Chemical Biology 5:436 (2009)

- Small molecules to explore biology
- PPP = sharing expertise
- Open tools = exploration by all

Open access chemical and clinical probes to support drug discovery

Aled M Edwards, Chas Bountra, David J Kerr & Timothy M Willson

Drug discovery resources in academia and industry are not used efficiently, to the detriment of industry and society. Duplication could be reduced, and productivity could be increased, by performing basic biology and clinical proofs of concept within open access industry-academia partnerships. Chemical biologists could play a central role in this effort.

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BET domain chemical probe

nature International weekly journal of science

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Archive > Volume 468 > Issue 7327 > Articles > Abstract

NATURE | ARTICLE previous abstract next abstract

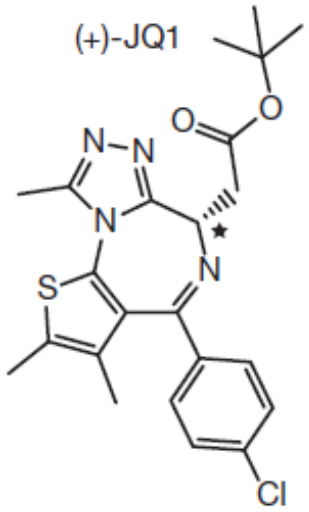
Selective inhibition of BET bromodomains

Panagis Filippakopoulos, Jun Qi, Sarah Picaud, Yao Shen, William B. Smith, Oleg Fedorov, Elizabeth M. Morse, Tracey Keates, Tyler T. Hickman, Ildiko Felletar, Martin Philpott, Shonagh Munro, Michael R. McKeown, Yuchuan Wang, Amanda L. Christie, Nathan West, Michael J. Cameron, Brian Schwartz, Tom D. Heightman, Nicholas La Thangue, Christopher A. French, Olaf Wiest, Andrew L. Kung, Stefan Knapp & James E. Bradner

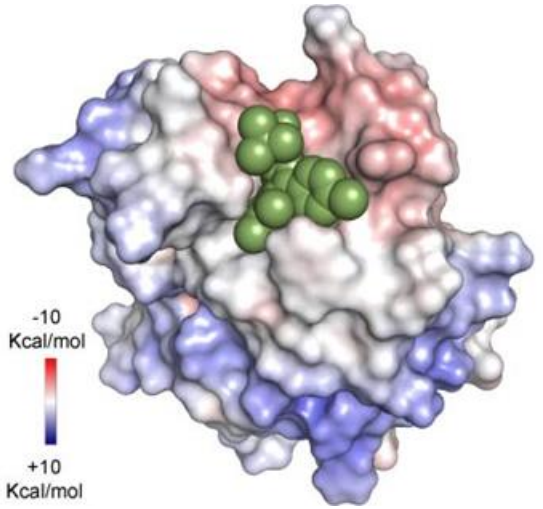
Affiliations | Contributions | Corresponding authors

Nature **468**, 1067–1073 (23 December 2010) | doi:10.1038/nature09504

Received 05 May 2010 | Accepted 17 September 2010 | Published online 24 September 2010



Co-crystal (JQ1 + BRD4)



BET – an open science story

2 Years and 2 months

6 Months | 11 Months | 1 Month | 6 Months | 3 Months

July 2009

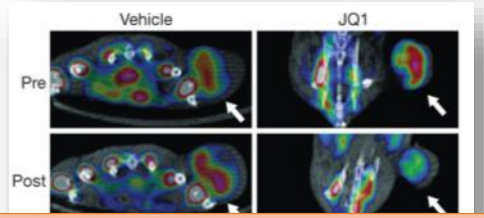
GSK informs SGC about Mitsubishi compound

Jan 2010

Oxford and Harvard start collaboration

Dec 2010

Jan 2011



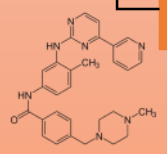
Co -publications
JQ1 probe (SGC; cancer)
I-BET probe (GSK; inflammation)

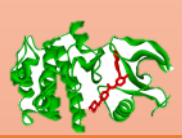
July 2011

Mar 2012

GSK carries out first in man (for open access - discovered indication!)

Glivec (Tk_{inh}) discovered



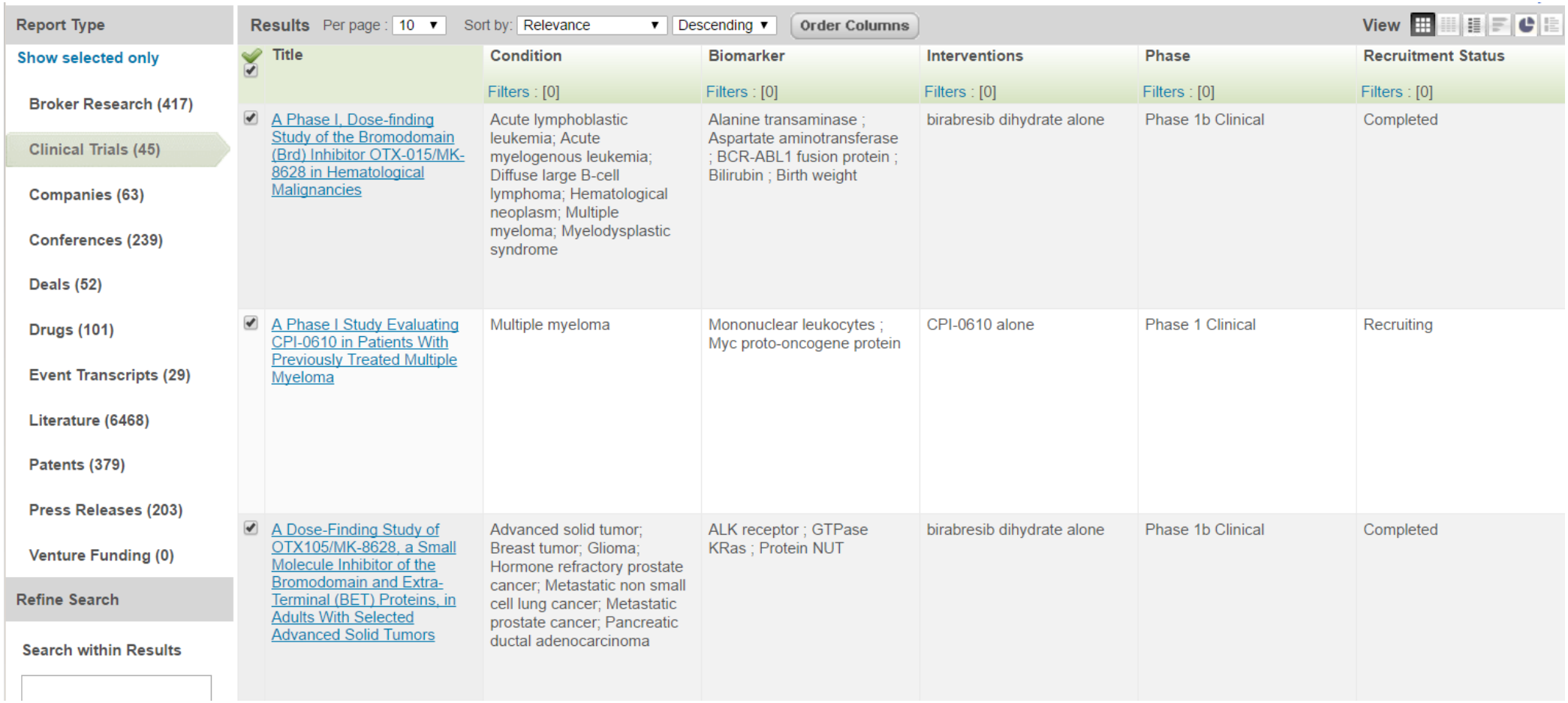


First-in-man study

1992 ⟷ 1998

6yrs

Bromodomain Inhibitors in the Clinic - 2017



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Refine Search

Search within Results

Results Per page : 10 Sort by: Relevance Descending Order Columns View

Title	Condition	Biomarker	Interventions	Phase	Recruitment Status
	Filters : [0]	Filters : [0]	Filters : [0]	Filters : [0]	Filters : [0]
A Phase I, Dose-finding Study of the Bromodomain (Brd) Inhibitor OTX-015/MK-8628 in Hematological Malignancies	Acute lymphoblastic leukemia; Acute myelogenous leukemia; Diffuse large B-cell lymphoma; Hematological neoplasm; Multiple myeloma; Myelodysplastic syndrome	Alanine transaminase ; Aspartate aminotransferase ; BCR-ABL1 fusion protein ; Bilirubin ; Birth weight	birabresib dihydrate alone	Phase 1b Clinical	Completed
A Phase I Study Evaluating CPI-0610 in Patients With Previously Treated Multiple Myeloma	Multiple myeloma	Mononuclear leukocytes ; Myc proto-oncogene protein	CPI-0610 alone	Phase 1 Clinical	Recruiting
A Dose-Finding Study of OTX105/MK-8628, a Small Molecule Inhibitor of the Bromodomain and Extra-Terminal (BET) Proteins, in Adults With Selected Advanced Solid Tumors	Advanced solid tumor; Breast tumor; Glioma; Hormone refractory prostate cancer; Metastatic non small cell lung cancer; Metastatic prostate cancer; Pancreatic ductal adenocarcinoma	ALK receptor ; GTPase KRas ; Protein NUT	birabresib dihydrate alone	Phase 1b Clinical	Completed

Around 40 ongoing Phase I and II trials, from Abbvie, Bayer, GSK, MSD, Roche *et al*

The future:

Open science, drug discovery and affordable medicines

M4K Pharma
Using open science to discover new medicines

M4K Pharma is a virtual company formed to aggregate, align and coordinate existing public and philanthropic investments to discover and develop *affordable* medicines for rare childhood cancers

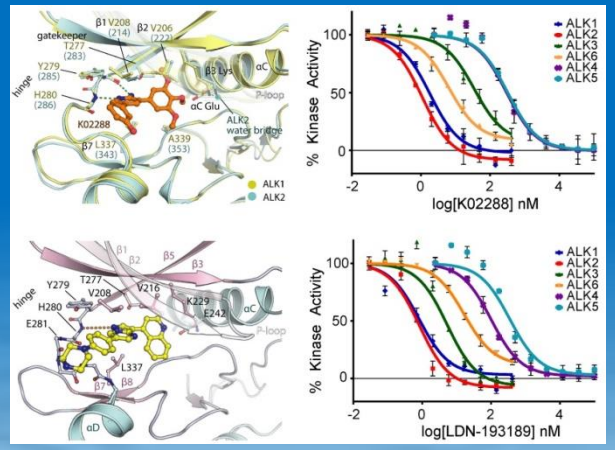
M4K Pharma will share all the scientific results with the community, but will restrict the use of the pre-clinical and clinical data for regulatory filings, *thus preserving exclusive marketing rights*

M4K Pharma is being led by Owen Roberts, a seasoned biotech executive

owen@m4kpharma.com

M4K Pharma
Targeting DIPG: an Incurable Pediatric Cancer

- Focused on the discovery and development of new and affordable medicines for pediatric brain tumours, focusing first on *Diffuse Intrinsic Pontine Glioma (DIPG)*
- Targeting the ALK2 kinase, a validated disease driver of DIPG
- Progress: Highly potent, selective and brain penetrant chemistry programs, requiring 18 - 24 months optimization to IND stage
- 2 lead series in development
- Currently optimizing series to improve drug properties
- Chemistry programs available for back-up epigenetic targets



Conclusions

- Open science leads to competitive scientific outcomes
- Open science leads to more reproducible science
- Open science builds trust with public and patients
- Open science reduce redundant research
- Open collaborations with industry enable academics to learn the market, spot commercial opportunities and launch companies
- Pharma will fund open science
- Open drug discovery may be the key to fixing the “broken pharmaceutical model”


ULTRADD


imi
innovative
medicines
initiative

M4K Pharma
Protecting marketing rights

- M4K will own the marketing rights derived from regulatory exclusivity:
  - *United States:*
    - *Orphan Drug Exclusivity – 7 years + 6 months for pediatric*
    - *New Chemical Entity – 5 years*
  - *European Union:*
    - *Orphan Drug Exclusivity – 10 years + 2 years for pediatric*
  - *Japan:*
    - *New Chemical Entity – 8 years*
  - *Canada:*
    - *Orphan Drug Exclusivity – 6 years + 2 years data exclusivity*

- Compares favourably to average post approval patent life of 11.7 years
- Regulatory exclusivity provisions *do not require* a drug to be patented

Meds 4 Kids Pharma

Protecting Marketing Rights

- Regulatory exclusivities are awarded upon marketing approval → Could a competitor use previously disclosed open data to get to market first?

  - United States → No: a competitor may not submit a new drug application containing third party data unless it has obtained a "right of reference" from the owner, meaning the specific "authority to rely upon an investigation for the purpose of obtaining approval of an application" (21 CFR § 314.3(b))