Die Herausforderungen einer Ausgründung aus der Universität

October 2022

A surfer riding the standing wave of the synthetic stream Eisbach in Munich, Germany. 48° 8’ 36.9” N 11° 35’ 16.1” E

Eisbach

Taming the forces within

Presenter:

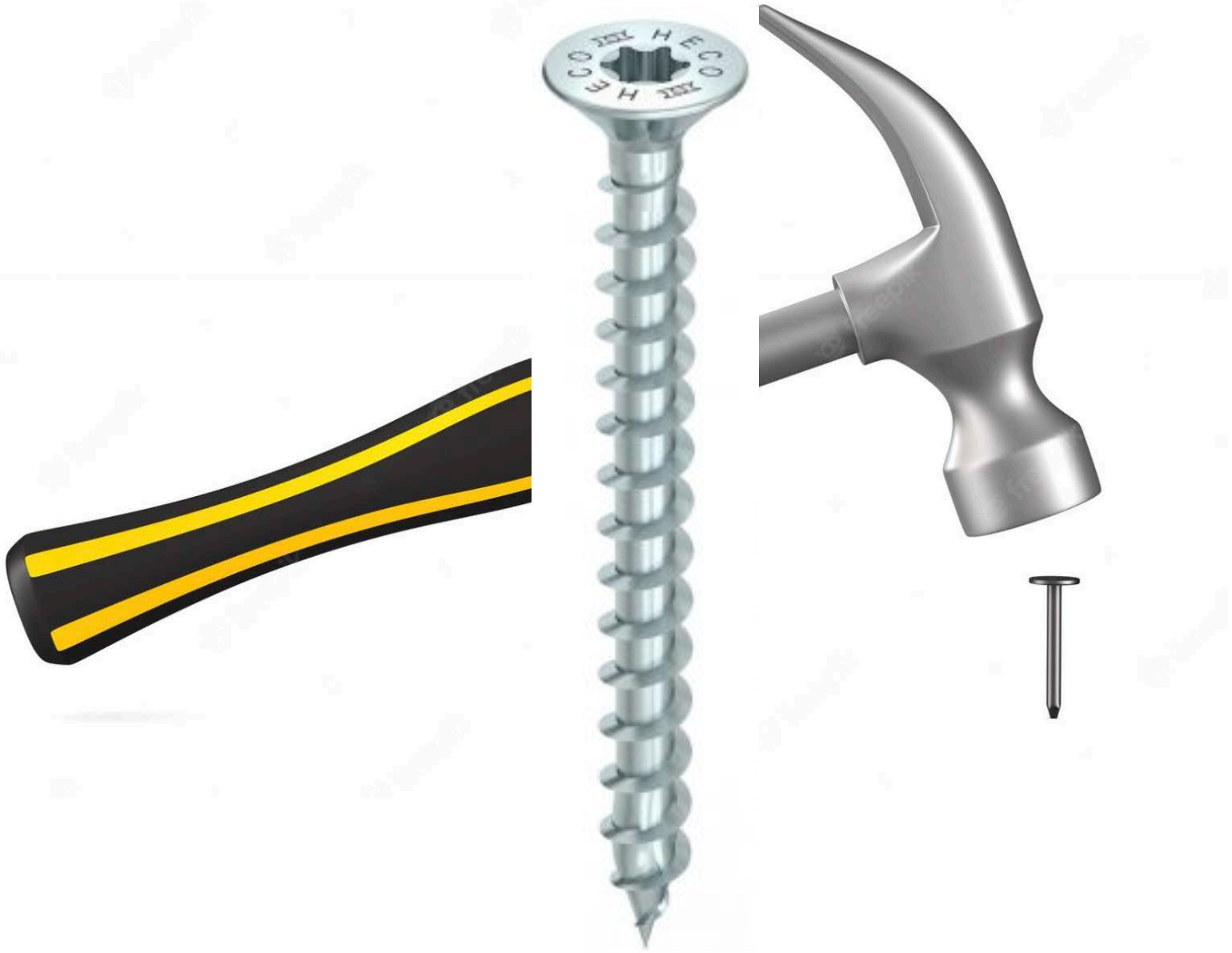
Dr. Adrian Schomburg, CPEA

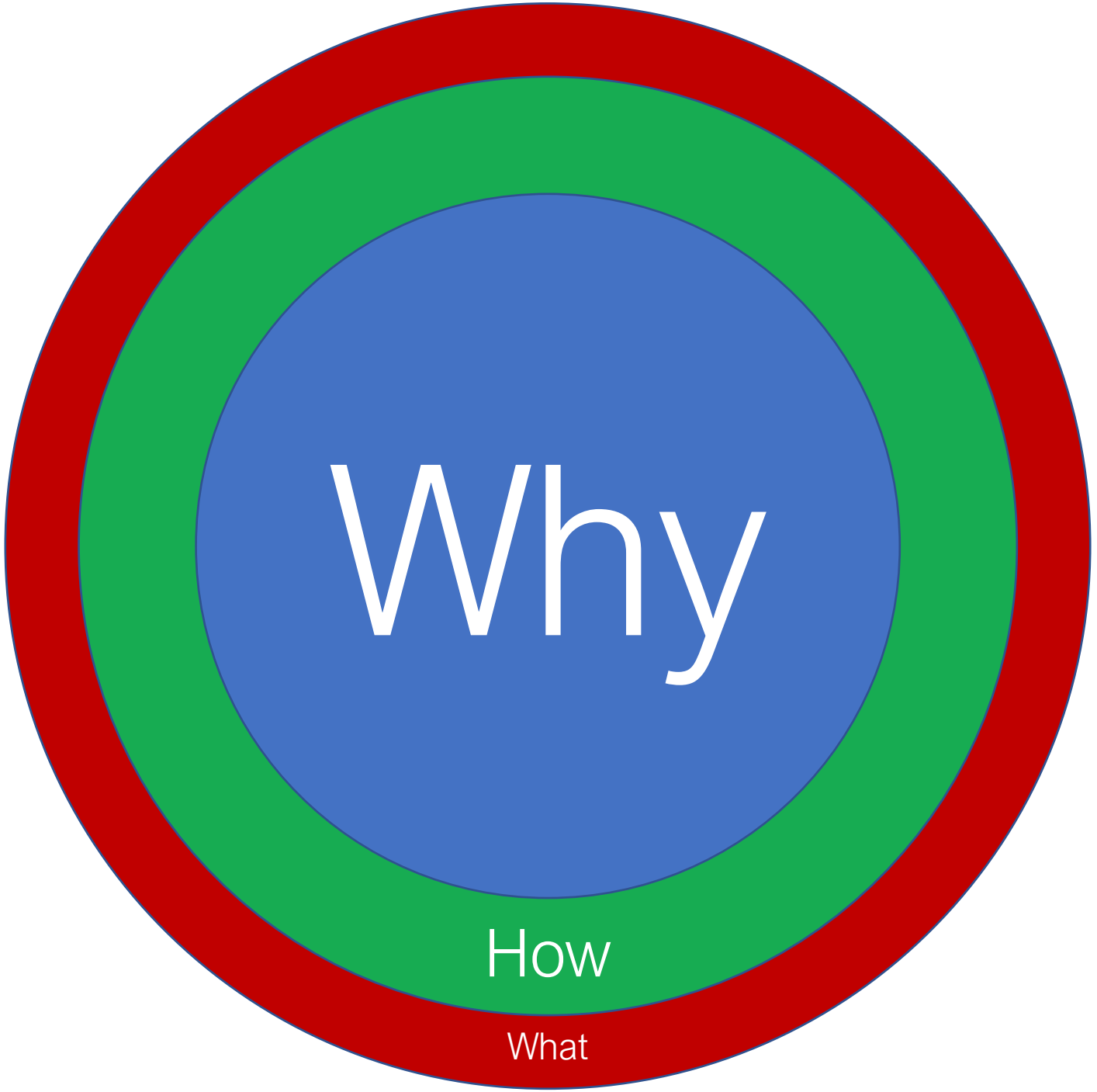
→ CEO, founder, shareholder of Eisbach Bio GmbH
→ CEO, founder, Genwerk UG
→ Investment manager, Tellco AG, Schwyz
→ CEO, shareholder of Volition Germany (NSE:VNRX)
→ Employee (5%) of Ludwig Maximilians University, Munich (teaching medical students)

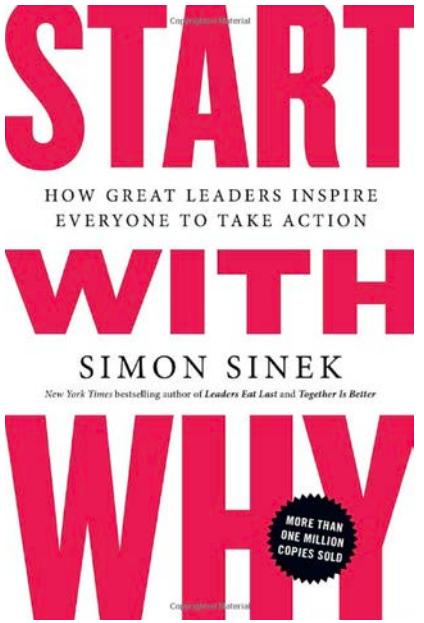
→ Student TUM (MBA)

→ BioM Bootcamp Alumnus

adrian@eisbach.bio, adrian.schomburg@lmu.de, adrian.schomburg@tum.de




Why
How
What


START
HOW GREAT LEADERS INSPIRE
EVERYONE TO TAKE ACTION
WITH
SIMON SINEK
New York Times bestselling author of Leaders Eat Last and Together Is Better
WHY
MORE THAN
ONE MILLION
COPIES SOLD

DNA damage repair defects (BRCA, ATM et al.) promote genome rearrangements

Tumors mutate further and become resistant

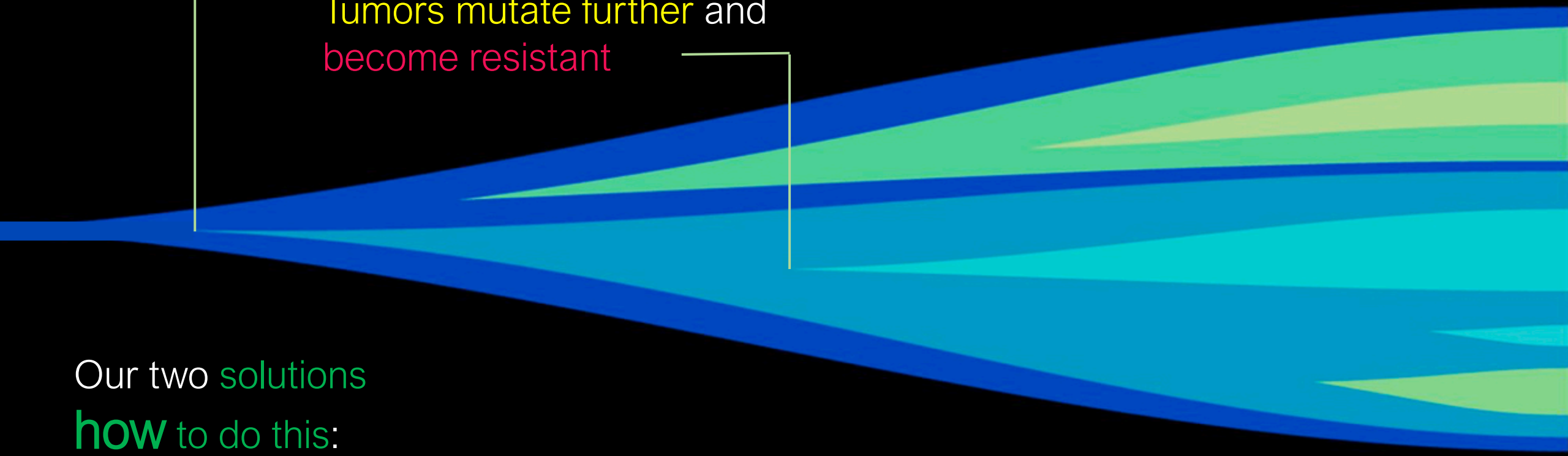
Why to target tumors differently

Two big problems:

- *These tumors have no obvious therapeutic target*
- *The underlying DNA sequence keeps evolving*

DNA damage repair defects (BRCA, ATM et al.)
promote genome rearrangements

Tumors mutate further and
become resistant



Our two solutions

how to do this:

- *These tumors are addicted to druggable ddr chromatin remodelers*
- *Our selective, allosteric inhibitors induce synthetic lethality*

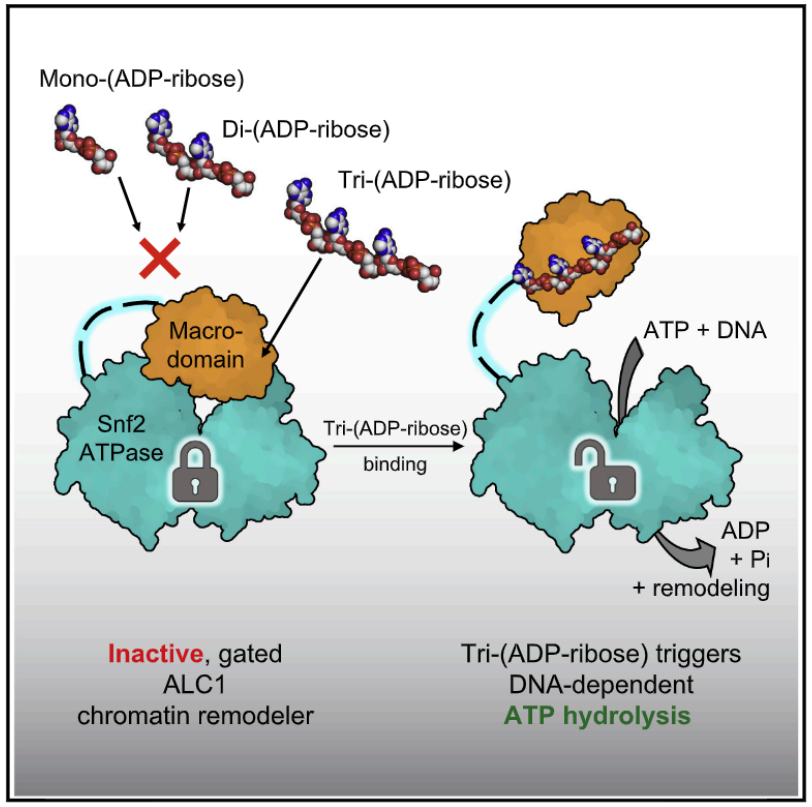
Key LMU expertise – basis for company creation

Article

Molecular Cell

A Poly-ADP-Ribose Trigger Releases the Auto-Inhibition of a Chromatin Remodeling Oncogene

Graphical Abstract



Authors

Hari R. Singh, Aurelio P. Nardozza, Ingvar R. Möller, ..., Gyula Timinszky, Kasper D. Rand, Andreas G. Ladurner

Correspondence

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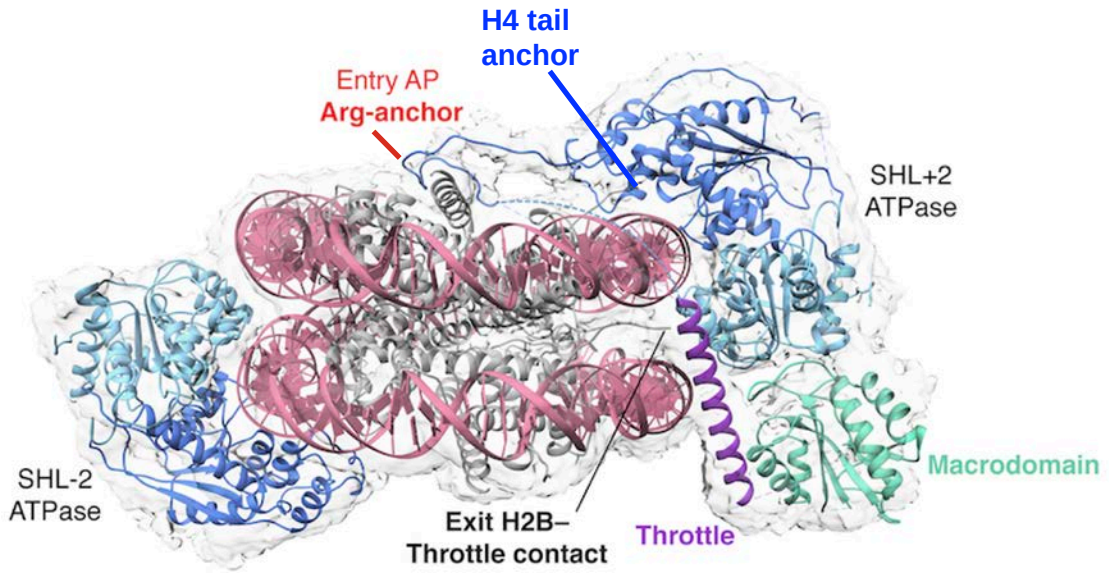
In Brief

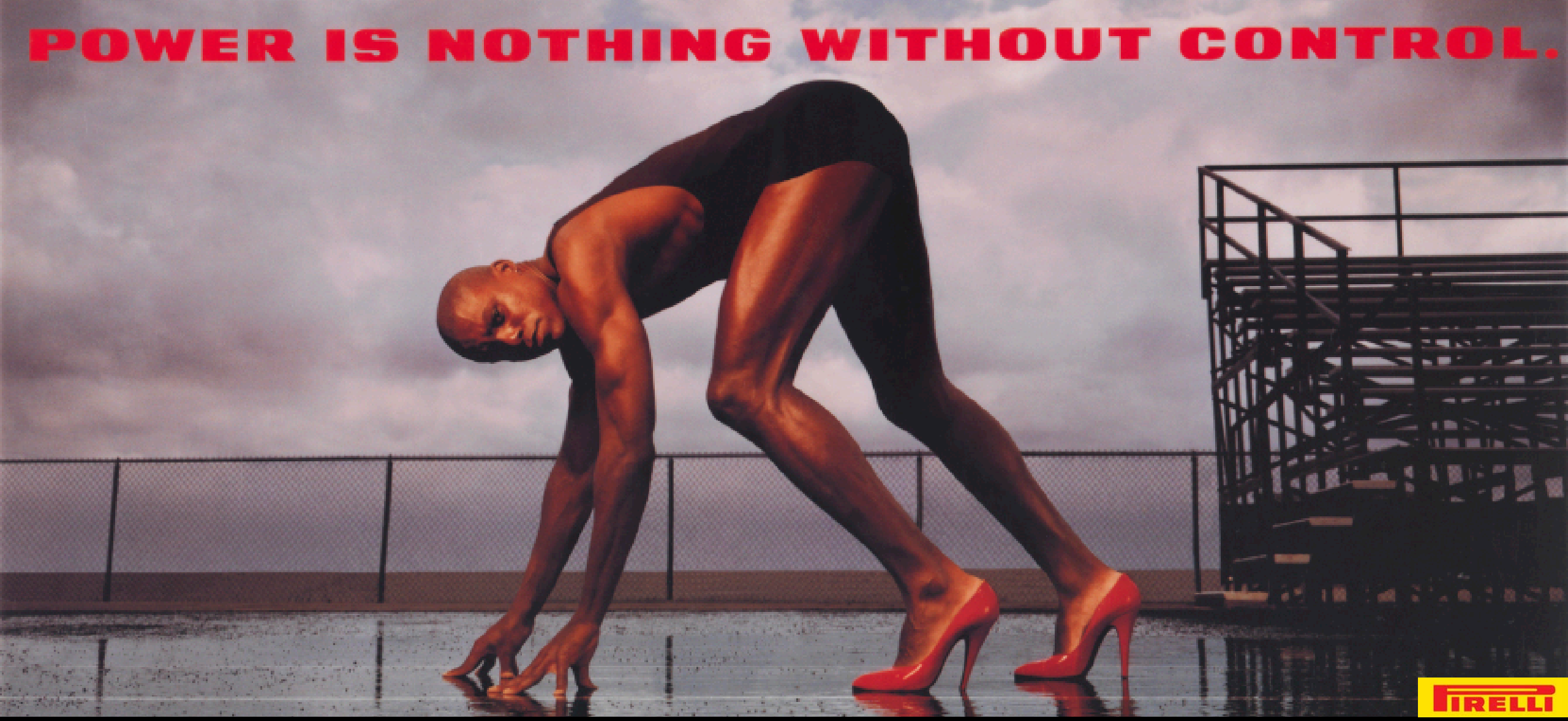
The activity of the human oncogene and chromatin remodeler ALC1/CHD1L is strictly regulated by PARP1 activation. Singh et al. reveal how oligomers of ADP-ribose trigger the activation of ALC1 from an auto-inhibited state and identify cancer mutations that disrupt the NAD+-metabolite-regulated allosteric mechanism.

LMU Munich

Munich (published 2017)

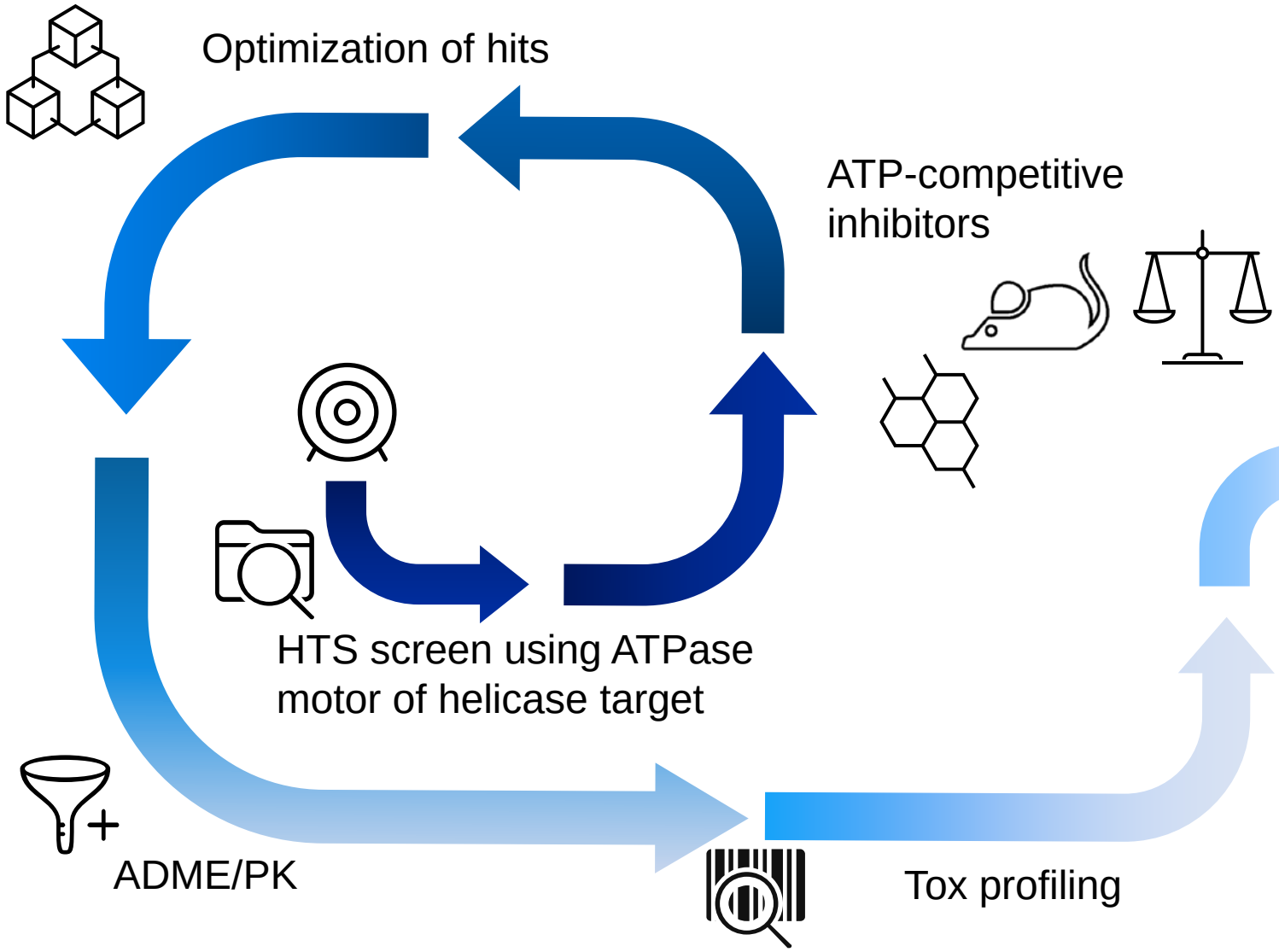
Allosterically-activated ALC1
on the nucleosome
(CryoEM, solved at Eisbach
unpublished observations)





Substrates and mechanisms, together,
inform and reveal the target's druggable vulnerability

Conventional Drug Discovery is ill-suited to Identify Selective Helicase Inhibitors



Efficacy limited by toxicity due to off-target effects (e.g. SMARCA2 inhibitors)

Only low doses/ intermittent dosing possible

Few/no combination therapies possible

We Discover how the Powerful Activity of Molecular Machines is Strictly Regulated

"Power is nothing without control" (Pirelli)

Power

Control

Conventional drug discovery targets the engine and measures fuel consumption

"Poisoning the fuel" → ATP competitive inhibitors. Dose-limiting toxicity.

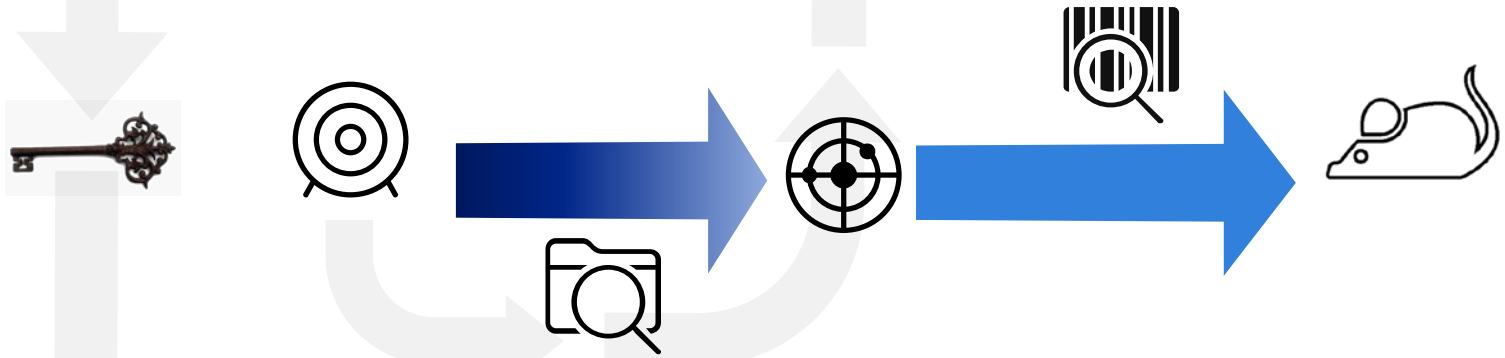
Eisbach uses natural substrates (nucleosome, protein complexes) + allosteric key

"We disrupt the controls" → Allosteric inhibitors. Oral, selective and safe drugs.

Physiological HTS Screening, Allosteric Drugs & “Tox-first” Enable 1st-in-class Drugs

Full-length helicase **+** Allosteric key **=**
FULL CONTROLS in our HTS & validation

Highest feasible oral dosing,
tox-assessment first,
then ADME/PK



We only obtain selective, **allosteric inhibitors**
Stringent, orthogonal, cellular and structural validation (AI, cryo-EM)

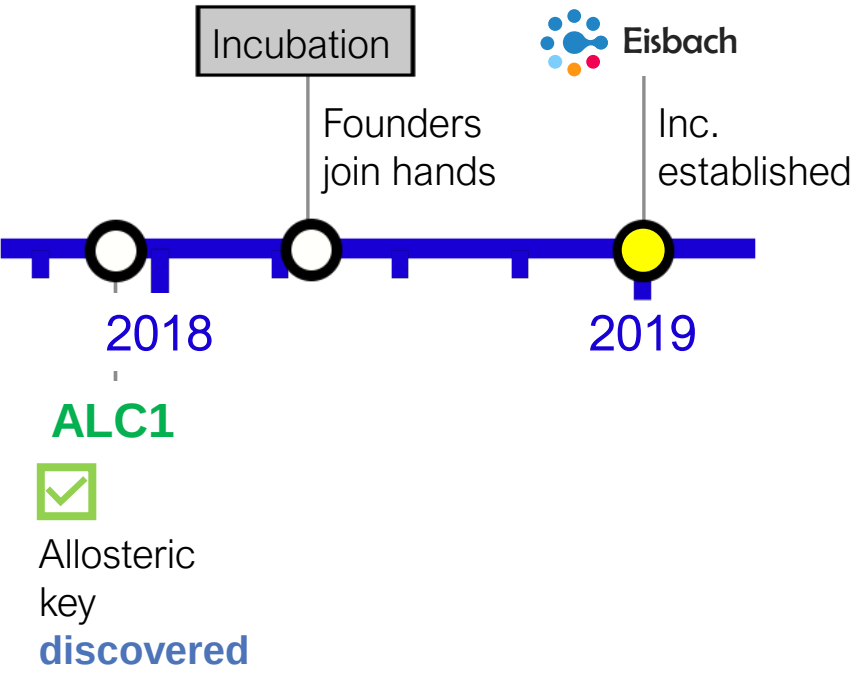
High therapeutic window, high doses, high efficacy

Orally bio-available drugs

Enabled powerful mono-/ combination therapies

1st-in-class, non-ATP-competitive Helicase INHIBITORS

Key challenges – “Incubation” period



Article

Molecular Cell

A Poly-ADP-Ribose Trigger Releases the Auto-Inhibition of a Chromatin Remodeling Oncogene

Eisbach has no:

→Business plan
→Budgets
→Reporting structure
→Milestones
→Controlling
→Organigram

But we have a vision to make medicines

Agreement between founders

Annotated non-binding Term Sheet

between

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Biomedical Center, Faculty of Medicine
Ludwig Maximilians University of Munich, Munich, Germany
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E-mail: andreas.ladurner@bmc.med.lmu.de
and ladurner.andreas@gmail.com

and

Adrian Schomburg, Dr. rer. nat
Current CTO of Proteros GmbH, Martinsried-Planegg, Germany

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E-mail: adrianschomburg@gmail.com

1. **Peamble:**

This document outlines preliminary terms to establish, develop, operate and manage an independent biotechnology and biopharmaceutical company that researches and develops innovative anti-cancer medicines. The focus of the company will be on developing a range of novel therapeutics that exploit the vulnerability of cancer cells to the interference of epigenetic and chromatin remodeling processes in the context of synthetic lethal genetic and functional interactions, oncogene activation and the sensitization of patients and/or individual tumor types toward cancer immunotherapy.

Cooperation agreement LMU

Kooperationsvereinbarung

zwischen

der Ludwig-Maximilians-Universität München, Geschwister-Scholl-Platz 1, 80539 München, für ihren Lehrstuhl für Physiologische Chemie (Prof. Dr. Andreas Ladurner) am Biomedizinischen Centrum der Medizinischen Fakultät („LMU")

und der

Firma Eisbach Bio GmbH, Am Klopferspitz 19, 82152 Martinsried („Eisbach")

Die Kooperationspartner vereinbaren eine wissenschaftliche Zusammenarbeit. Ziel ist es, innovative neue Wirkstoffkandidaten in der Krebsforschung zu identifizieren und zu validieren.

§ 1 Leistungen der LMU

Die LMU stimmt einer anteiligen Nutzung der dem LS Physiologische Chemie zugewiesenen Räume N.B.02.024 und N.B.02.024A in der Großhaderner Str. 9 einschließlich der Laboreinrichtung zu. Dies ist in einer entsprechenden Nutzungsvereinbarung mit der Universität München zu regeln.

§ 2 Leistungen der Firma Eisbach GmbH

Die Firma ermöglicht den Mitarbeiterinnen und Mitarbeitern des Lehrstuhls sowie den Studierenden des Departments direkte Einblicke in der Etablierung und Forschungsaktivität eines translationalen Biotechnologieunternehmen in der Onkologie zu erhalten. Zudem stellt die Firma Eisbach Bio GmbH wichtige Forschungs- und Geräteinfrastruktur dem Lehrstuhl kostenfrei zur Nutzung, z.B. Äkta Explorer Proteinaufreinigungsapparatur und Infors Inkubator.

Lab lease within the LMU

EINGEGANGEN 27. Feb. 2019

LMU · Geschwister-Scholl-Platz 1 · 80539 München

An die
Eisbach Bio GmbH
Herrn Dr. Adrian Schomburg
Am Klopferspitz 19
82152 Martinsried

ABDRUCK

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Geschwister-Scholl-Platz 1
80539 München

München, 25.02.2019

Ihr Zeichen, Ihre Nachricht vom

Unser Zeichen
IV -

Staatseigenes Anwesen Großhaderner Str. 9, 82152 Martinsried-Planegg

hier: Zusendung Vertragsunterlagen

Anlagen: 1 Nutzungsvereinbarung von 07.01./28.01.2019
1 Kooperationsvereinbarung von 07.01.2019

Sehr geehrter Herr Dr. Schomburg,

anliegend erhalten Sie je ein Original der vorbenannten Unterlagen zum Verbleib.

Für den Monat Januar 2019 ergibt sich vereinbarungsgemäß folgende Zahlung:

Anteiliges Nutzungsentgelt für 24 Tage:	528,11 €
zzgl. USt. 19 %	100,34 €
Nutzungsentgelt brutto:	628,45 €

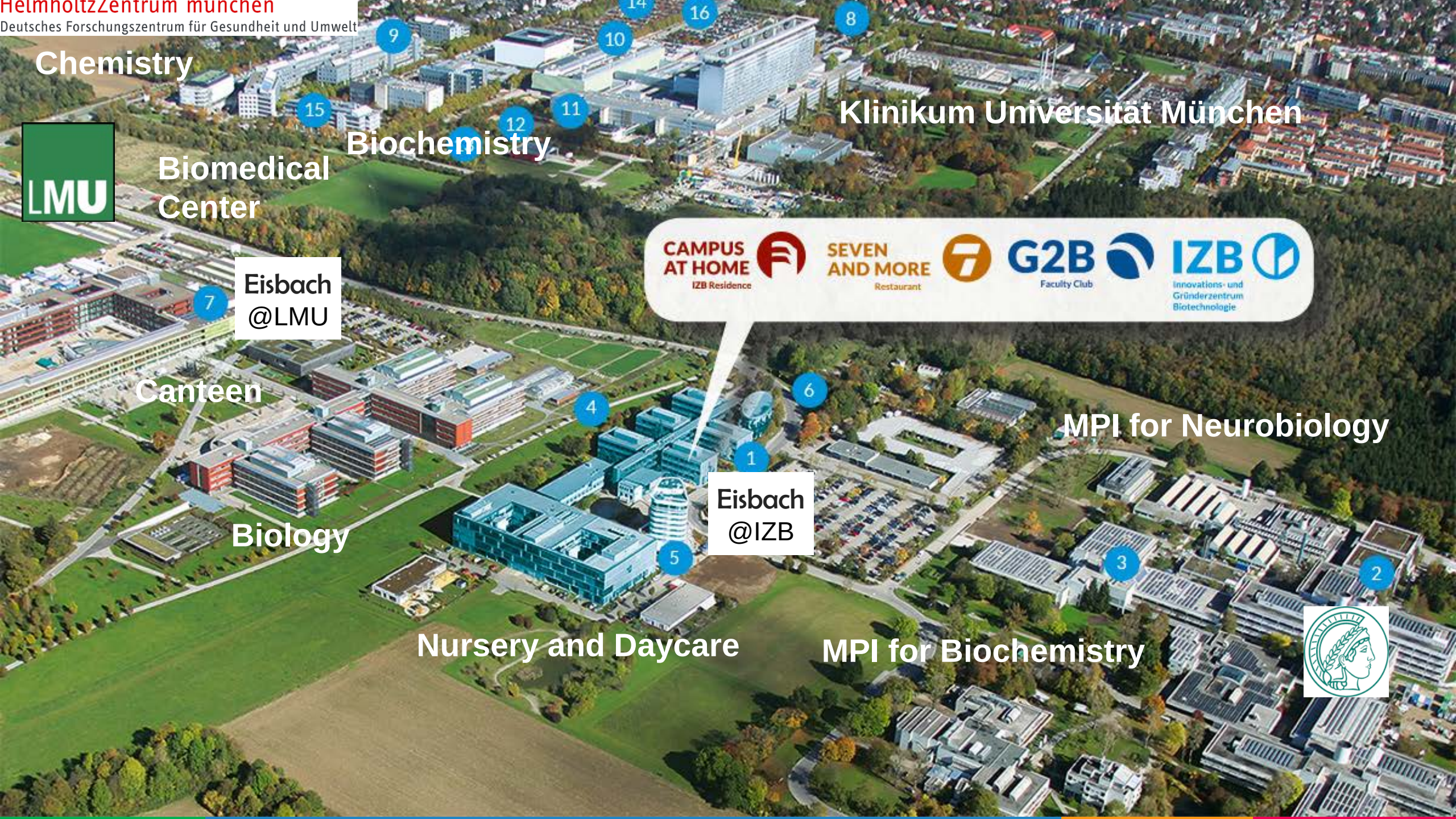
Eisbach

Academic / Startup drug discovery
In a strong and innovative **environment**

200 life science companies & CROs.
10 startups/yr. Mostly preclinical.

Innovations- & Gründerzentrum Biotechnologie (IZB)

Ludwig-Maximilians-Universität, Biomedical Center


HelmholtzZentrum münchen
Deutsches Forschungszentrum für Gesundheit und Umwelt
Chemistry
Biochemistry
Klinikum Universität München
LMU
Biomedical Center
Eisbach @LMU
CAMPUS AT HOME
IZB Residence
SEVEN AND MORE
Restaurant
G2B
Faculty Club
IZB
Innovations- und Gründerzentrum Biotechnologie
Canteen
MPI for Neurobiology
Eisbach @IZB
Biology
Nursery and Daycare
MPI for Biochemistry
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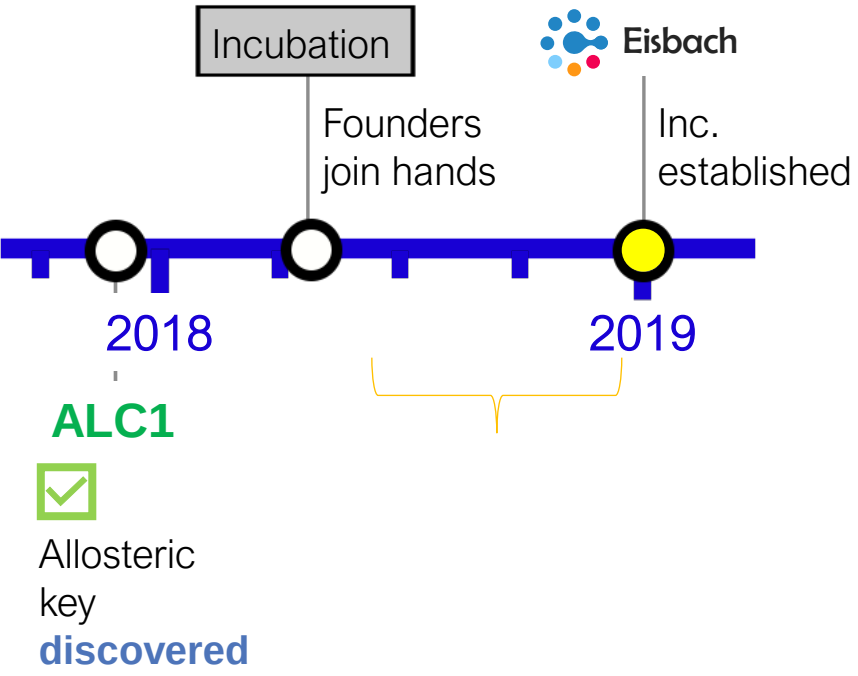
Key challenges – “Incubation” period - Financing



”Translational” grants - challenges:

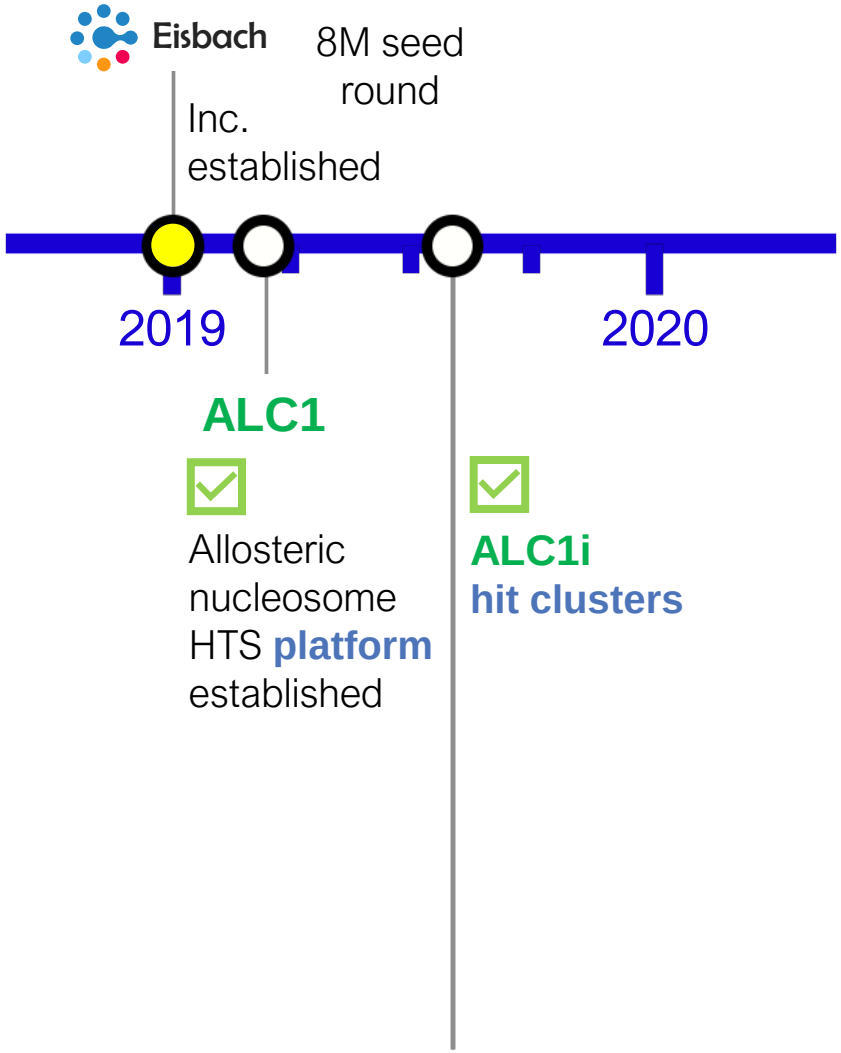
Go-Bio, VIP Plus, Exist, Flügge et al.

- Extremely long review process (we applied for VIP plus, relply was 1.5y later)
- Limited funding
- Some do not allow company formation during funding period

Alternative: Private investors, VC

- Big advantage of incubation within university
- Lab infrastructure available, results are generated
- Young company can focus on science
- Results attract more $$
- Validation by performance

Development of Eisbach – “Growth” period



Next stage: “Maturing” the company:

Team:

- Hires beyond the “academic” team that was inherited with the project
- Industry experts, business / non-scientific

Company:

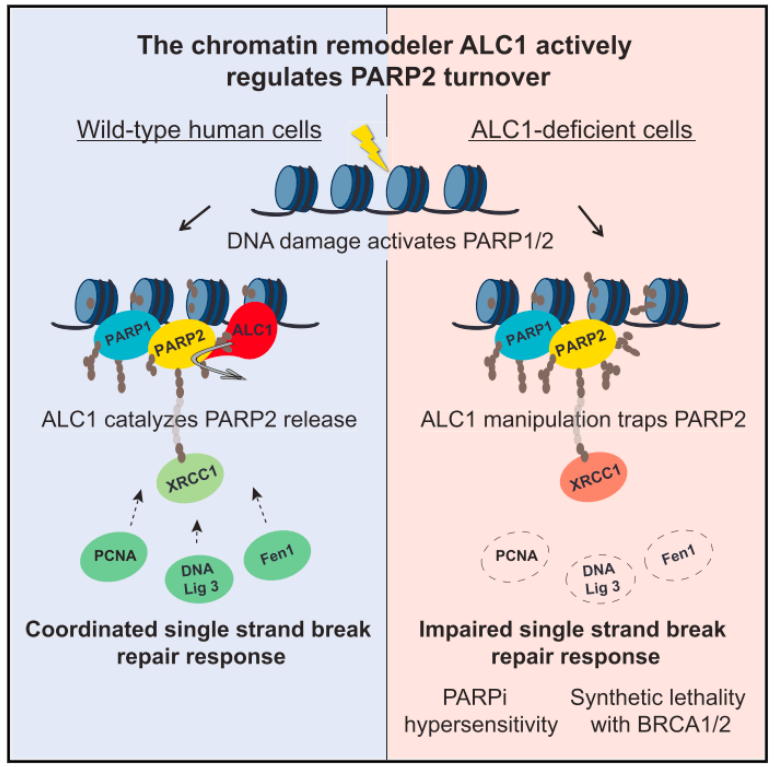
- Own lab, offices
- Generates more trust with investors
- Professionalize

Molecular Cell

Article

The Oncogenic Helicase ALC1 Regulates PARP Inhibitor Potency by Trapping PARP2 at DNA Breaks

Graphical Abstract



Authors

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Imke Karlijn Mandemaker,
Claudia Gonzalez-Leal, Julia Preisser,
Adrian Schomburg,
Andreas Gerhard Ladurner

Correspondence

andreas.ladurner@bmc.med.lmu.de

In Brief

PARP inhibitors (PARPis) are used to treat BRCA-deficient tumors. Blessing et al. reveal how they trap PARP2 on damaged chromatin and show that the chromatin-remodeling helicase ALC1 is required for its release. ALC1 manipulation impacts the single-strand DNA break repair response and potentiates PARPi-induced cancer killing through PARP2 trapping.

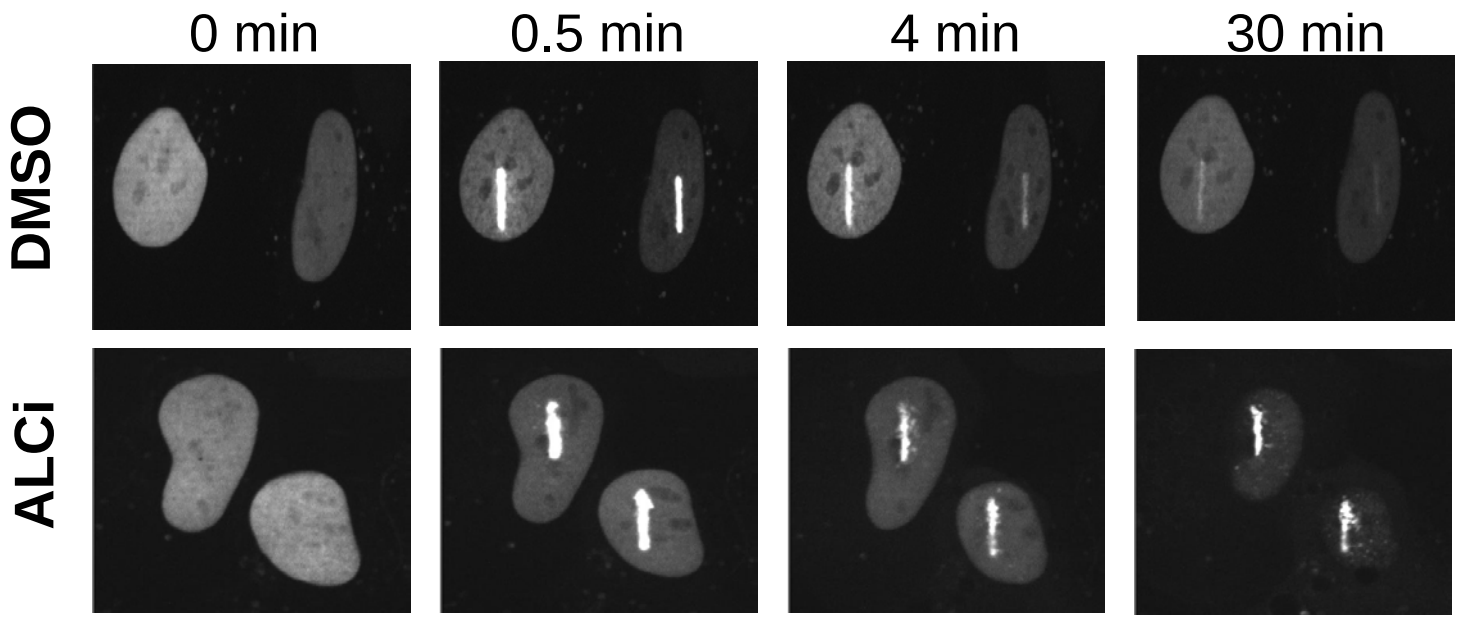
Eisbach & LMU Munich

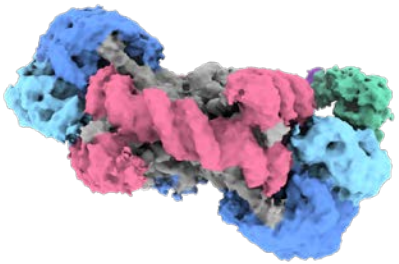
Munich

Published: December 03rd, 2020

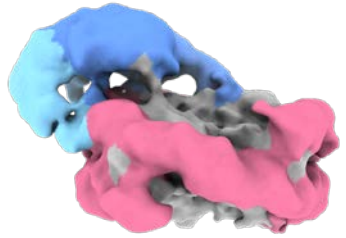
Allosteric ALC1 Inhibitors are Efficacious by Trapping the Helicase *in vitro* and *in vivo*

Laser-induced DNA damage, GFP-labeled ALC1





Activated ALC1
on the nucleosome
(cryoEM structure,
solved at Eisbach)



Inhibited, trapped &
inactive ALC1
on the nucleosome

ALC1 inhibitors trap repair complexes on chromatin
(including PARP1/2)

Molecular Cell

December 03, 2020

CellPress

Article

The Oncogenic Helicase ALC1 Regulates PARP Inhibitor Potency by Trapping PARP2 at DNA Breaks

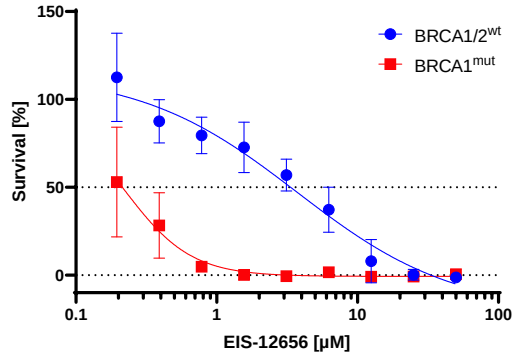
Charlotte Blessing,[1,2] Imke Karlijn Mandemaker,[1] Claudia Gonzalez-Leal,[1,2] Julia Preisser,[1] Adrian Schomburg,[1,3] and Andreas Gerhard Ladurner[1,2,3,4,*]

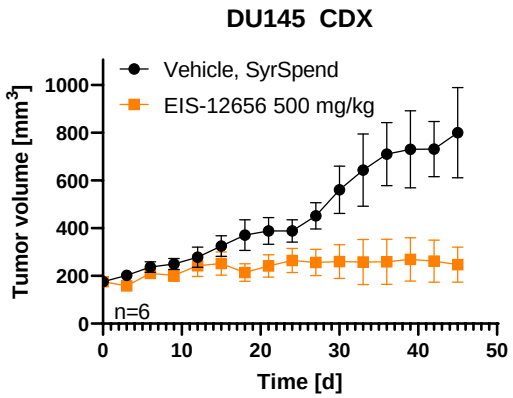
Lead ALC1 Inhibitor – Clinical Candidate EIS-12656; Efficacy

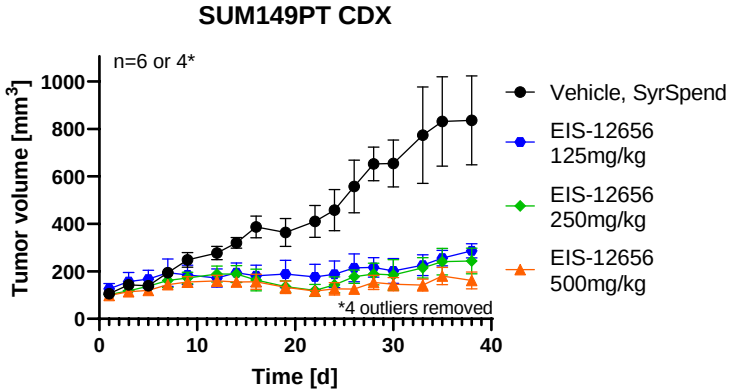
ALC1i EIS-12656

- Selectivity
- Single-agent activity in HRD CDX models
- Combinatorial efficacy in HR^{+} CDX models

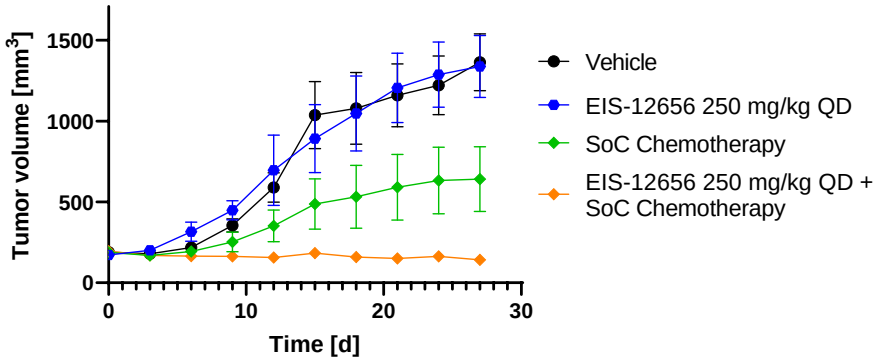
EIS-12656 displays >10-fold selectivity between HRD SUM149PT cells (PARPi resistant) and HR- proficient MDA-MB-231 cells



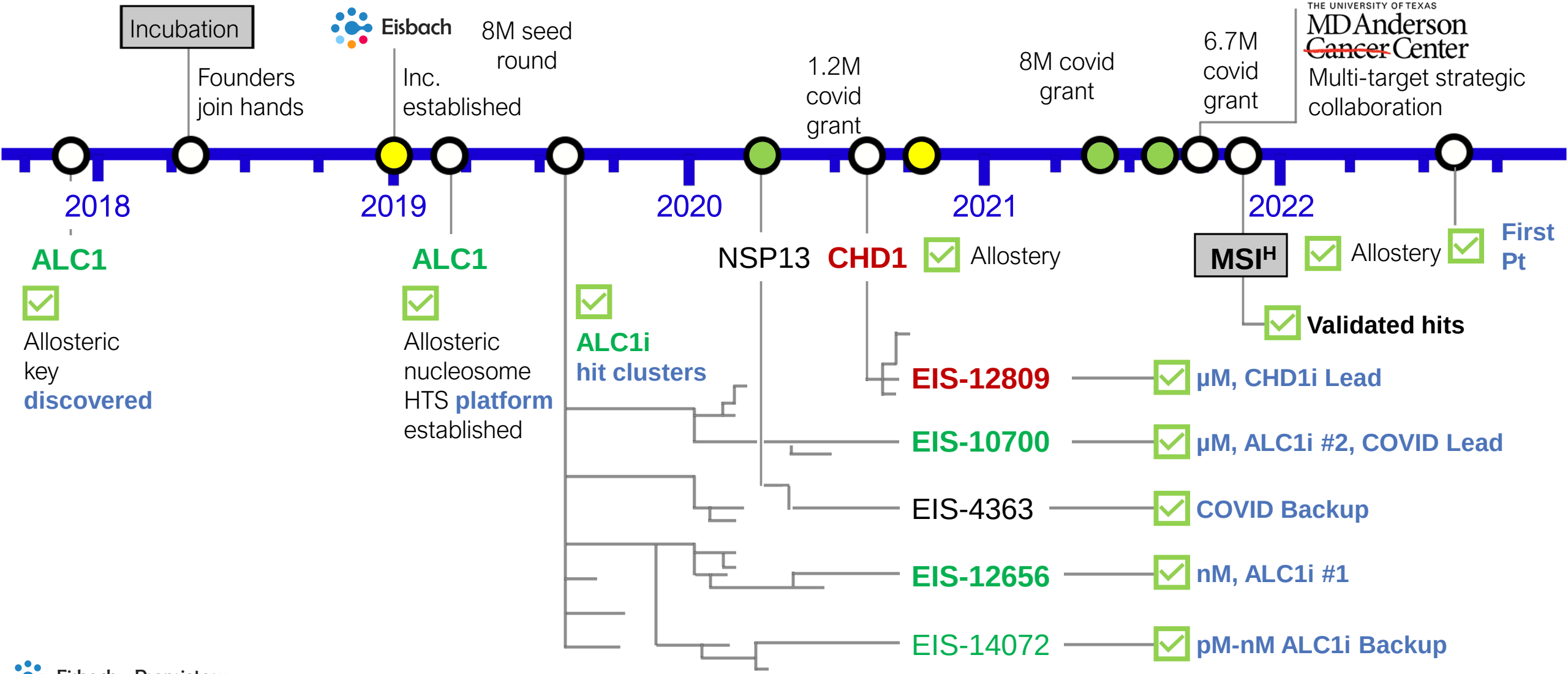




BRCA1/2^{wt} PSN1 cells respond to ALC1 inhibition after inducing BRCAness with DNA damaging chemotherapeutics



Development of Eisbach

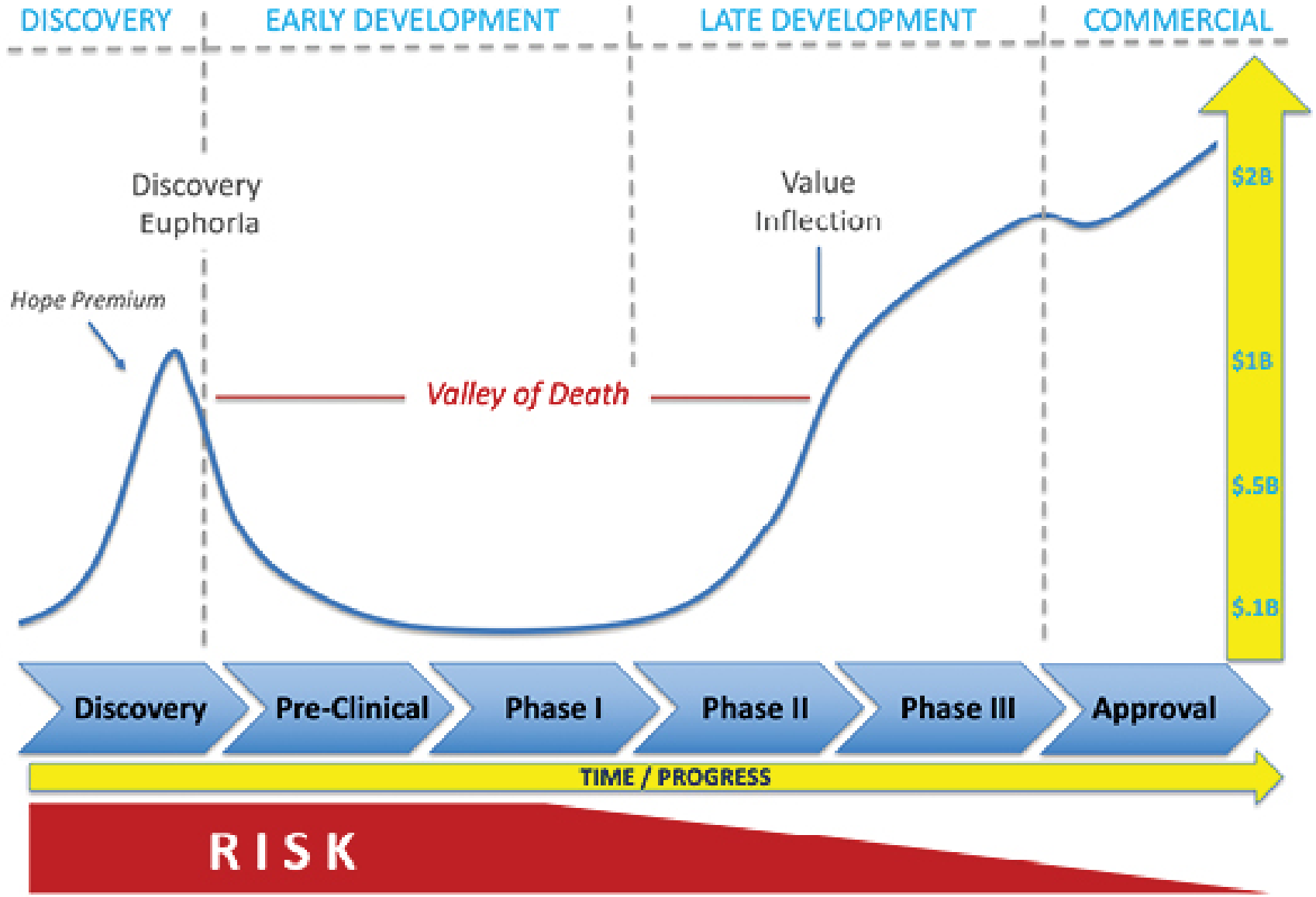


Eisbach Pipeline – 1st-in-class Allosteric Inhibitors of Synthetic Lethal Helicases

Indication	Target	Ownership	Discovery	Lead op	GLP	IND	Ph1	Next milestone
Oncology								
Eisbach pioneered								
HRD/BRCA$^{-/-}$	ALC1		EIS-10700*					FIH, 23Q1
			EIS-12656					IND, 23Q2
PTEN$^{-/-}$	CHD1							DC selection, 23Q1
DNA helicases								
MSI^{HIGH}	Helicase		Collaboration with MD Anderson Cancer Center					Lead op, 22Q3
Virology								
RNA helicases								
COVID-19	CoV-2 Nsp13		EIS-10700*					FIH, 22Q4
			EIS-4363					IND, 23Q1

(*EIS-10700 is active against ALC1 as well as viral NSP13. 17.2M EUR non-dilutive funds awarded for pre-clinical & clinical development in SARS-CoV-2)

Biotech Value Map



Thank you for your attention!

Adrian Schomburg, PhD
Founder, CEO
Managing Director

Executed **SPVs**
R&D partnering

Andreas Ladurner, PhD
Founder, CSO
Managing Director

Pioneer in dissecting
allosteric regulation

Jörk Zwicker, PhD
CLO

Managing partner
of leading IP firm

15 scientists
+ 14 chemists
+ MDACC “brains”

Investors
Industry professionals
and family offices

Thank you for your attention!

A surfer riding the standing wave of the synthetic stream Eisbach in Munich, Germany. 48° 8’ 36.9” N 11° 35’ 16.1” E

Let’s target the Achilles heel of cancer. Together.

Eisbach
Taming the forces within