R E G I S T E R N O W !

1,000,000,000 *CHF investment*

7,000,874 *hours of work*

6,587 *experiments*

423 *researchers*

1 *medicine*

Health Hackathon
4.12 & 11.12.2025

THE MAKING OF AN INNOVATIVE MEDICINE

Introductory workshops on translational biomedical research, drug discovery and development

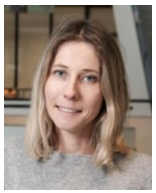
Judge Prof Dr med Olaia Naveiras

BIO-698 resumes Thursday September 11. 2025
4:15 PM @ CM013

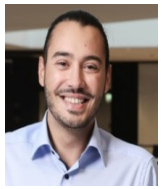
With Timothee Ferrari MD PhD cand

EPFL

Sciences de la Vie -SV



With Justine Epiney MD PhD cand



Mehdi AliGadiri MD PhD cand

Prof Roger G. Clerc

The Making Of An Innovative Medicine – class schedule

Thursday's @ 4-6 PM except 04.12/11.12.25 @2-6 PM

Session 1: **Scope of the course _ general organization _ case study**
11.09.25 *Embracing a career at the heart of biomedical research !?*
CM013

Session 2: **Historical perspective: the modern pharmacy**
18.09.25 *Advent of modern medicines - placebo controlled drug development*
CM013

Session 3: **Introduction to translational research: crossing the bridge**
25.09.25 *A chasm has opened wide between biomedical research and patients in need*
CM013

Sessions 4-5: **Therapeutic target identification I & II**
02-09.10.25 *"me too" vs a wealth of innovative targets _ small MW cpds vs biologicals*
CM013 *Early front loading of biomarker identification for cohort stratification*

Session 6: **Structure based drug design _medicinal chemistry_low/high throughtput**
16.10.25 **screening assays_ multiple parallel optimization_ML-powered screens**
CM013 *Setting up screening assays, the robotics, the million cpds librairies*

Session 7: **Therapeutic modalities biologicals–peptides : today's - tomorrow's**
30.10.25 **pharmacy NBEs**
CM013 *Challengies (cost of goods - healthcare payers) and opportunities*

The Making Of An Innovative Medicine - class schedule

Thursday's @ 4-6 PM except 04.12/11.12.25 @2-6 PM

Session 8: **Personalized Healthcare PHC _ precision medicine**
06.11.25 *How PHC started: from a single case to a paradigm change*
CM013

Session 9: **Pharmacogenetic polymorphisms, Pharmacogenomics**
13.11.25 *Interindividual variability toxicity in response to medicines*
CM013

Session 10: **In vivo pharmacology, investigative toxicology with Nathalie Brandenberg PhD eMBA CEO Doppl Ltd**
20.11.25 *Preclinical research ends up with IDB's, FDA guidelines for FIH*
CM013

Session 11: **Clinical research_ phase 0, phase I, II, III, IV with Raphael Sommer PhD Bristol Myers Squibb**
27.11.25 *The long and complex experimental procedures with human patients*
CM013
Intellectual property_ integrity in research_my genome vs our genomes
Why are patents essential to new medicine/biotech development

Session 12: **Health Hackathon – Hacking medicine I with T. Ferrari & M. Ali Gadiri MD PhDs confirmed !**
04.12.25 *Pitches –building teams – hacking problem - 5Ws – brainstorm*
starts @ 2PM ! CO017

Session 13: **Health Hackathon – Hacking medicine II with judges Prof Olaia Naveiras - Prof James Habib**
11.12.25 *Building up solutions – make it better - final presentations*
starts @ 2PM ! CO017

WORKSHOP LISTING - THE MAKING OF AN INNOVATIVE MEDICINE BIO 698-HS2025 in CM013			
! NON EXHAUSTIVE LISTING - SUGGESTIONS WELCOME !			
sessions		workshops	speaker/s
S02 (18-09-25)			
historical medicines		penicilin: impact, whose invention ?	
hopping on giant shoulders		prozac at the core of psychiatry	
		vaccine discovery:smallpoxJennerTodaymRNAvaccine	Eugenio
		artemisinin and malaria	
		insulin-Banting Best et al. beagle dog	
		slide51-X-ray image DNA--Rosalind Franklin	
		cyclosporin from soil sample to life saver	
S03 (25-09-25)			
translational research		expanding scope of translational therapies	
from bench to bedside and back		chronotherapy,circadian clock,sex,longevity	Solomon
		CAR-T, TCR-T cell therapies in "cold" tumors	
		Y chrom loss in immune cells drives cancer	
S04 (02-10-25)			
therapeutic target identification		th. target identification using a phenocopy screen	Justine
S05 (09-10-25)		nocosomial inf/MRSA/phage antibacterials	
therapeutic target identification		Crispr/Cas9 gene editing huntington disease	
		AI in drug discovery / ML-powered medicine	Lou
		AIDS - Lenacapavir : end of plague ?	
S06 (16-10-25)			
structure based drug design		macrocycles and non druggable targets	Benedikt
		chemoproteomics - NMEs	
		AIDS HIV from deadly virus to chronic disease	
S07 (30-10-25)			
therapeutic modalities - NBEs		rare diseases repurposing medicines	Jana
		biologics on the rise-MABs medicines & more	Eleni
		RNA therapeutics, antisense medicines	
		Wnt pathway - PROTACs vs molecular GLUEs	
S08 (06-11-25)			
PHC personalized healthcare		BRCA1/2 preventive surgery/tumor board	
Human genomics		4P medicine-GWAS-Personalized Health Care	Frederico
		disease enabling biomarkers/micro RNAs	
		AZ-biomarker BD-tau yet still no curative drug	
		centenarian host isoallo-LCA bile acid bacteria	
S09 (13-11-25)			
pharmacogenetic polymorphism		Pharmacogenomics	Greta
		deCODE Inc pharmgenomic/iceland genealogy	
		ageing and thanatophobia	
S10 (20-11-25)			
in vivo pharmacology		guest speaker : profiling MABs on organoids	Nathalie B
toxicology		organoids-drug discovery - CF patients	Tianhao + Alice
		thalidomide repurposing mulitple myeloma	
S11 (27-11-25)			
clinical research		SMA gene therapy - pay for performance	
		most common genetic defect : cystic fibrosis	
		guest speaker: profiling biologics in clinical research	Raphael S
		guest speaker profiling cell therapies	
		gender medicine comes of age ?	
S11 (27-11-25)			
intellectual property/integrity		23andMe - my genome	
		biopatents - biosimilars	
		SMA gene therapy - pay for performance	
		patenting natural products ?	
S12 (04-12-25) starts @ 2PM		Hacking medicine	all + invitees
S13 (11-12-25) start @ 2 PM		Hacking medicine	all + invitees

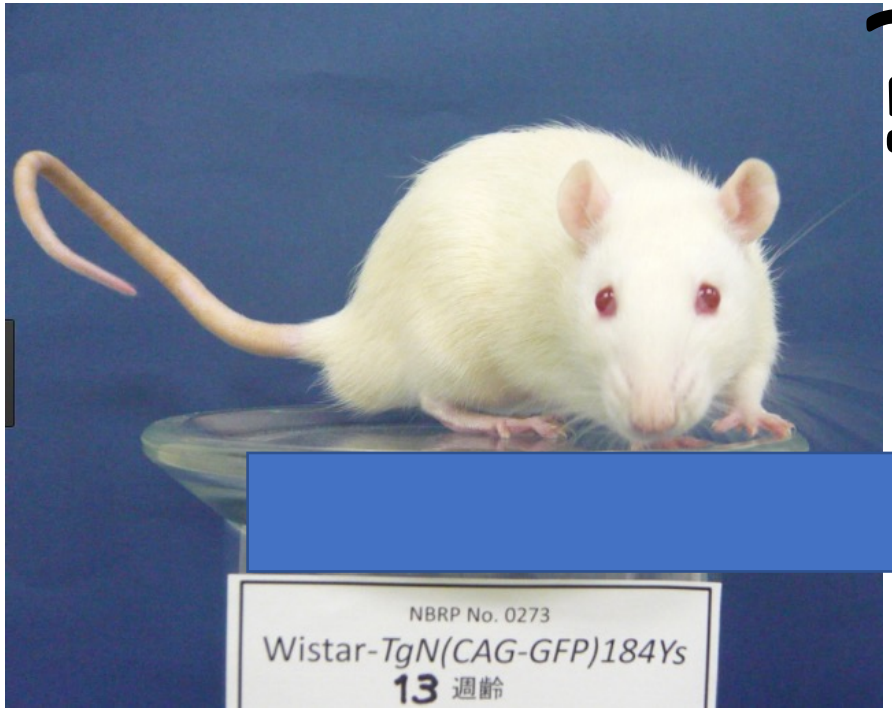
Workshops
The Making Of An Innovative Medicine
(today's class)

Prof O Naveiras

Prof J Habib

- Clinical research_early and late clinical trials of novel medicines (internal conference website ICH)
- Submit the IND (to authority and ethics body)investigational new drug application IDB
- First-in-human FIH trials
- Placebo - Nocebo

- Now that it works in the rat, will it work in human ? individualized cohorts ?
- Or the converse : no beneficial effects – even reversed therapeutic index (TI) in rodents and benefit in human cohorts



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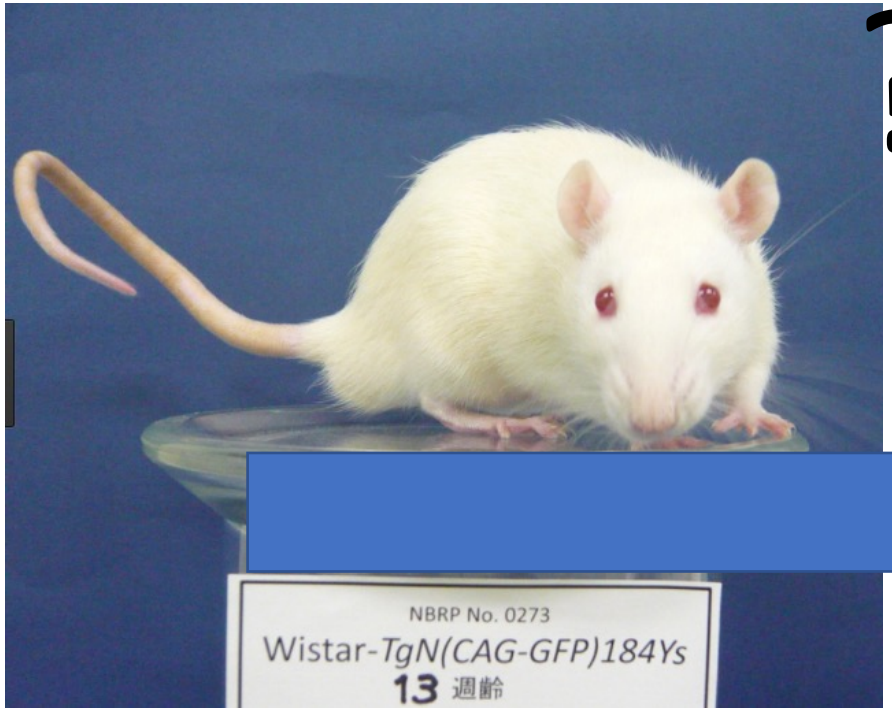
?

Clinical development – an experiment with human subjects

- Or else...all these efforts only good for the rats ?!



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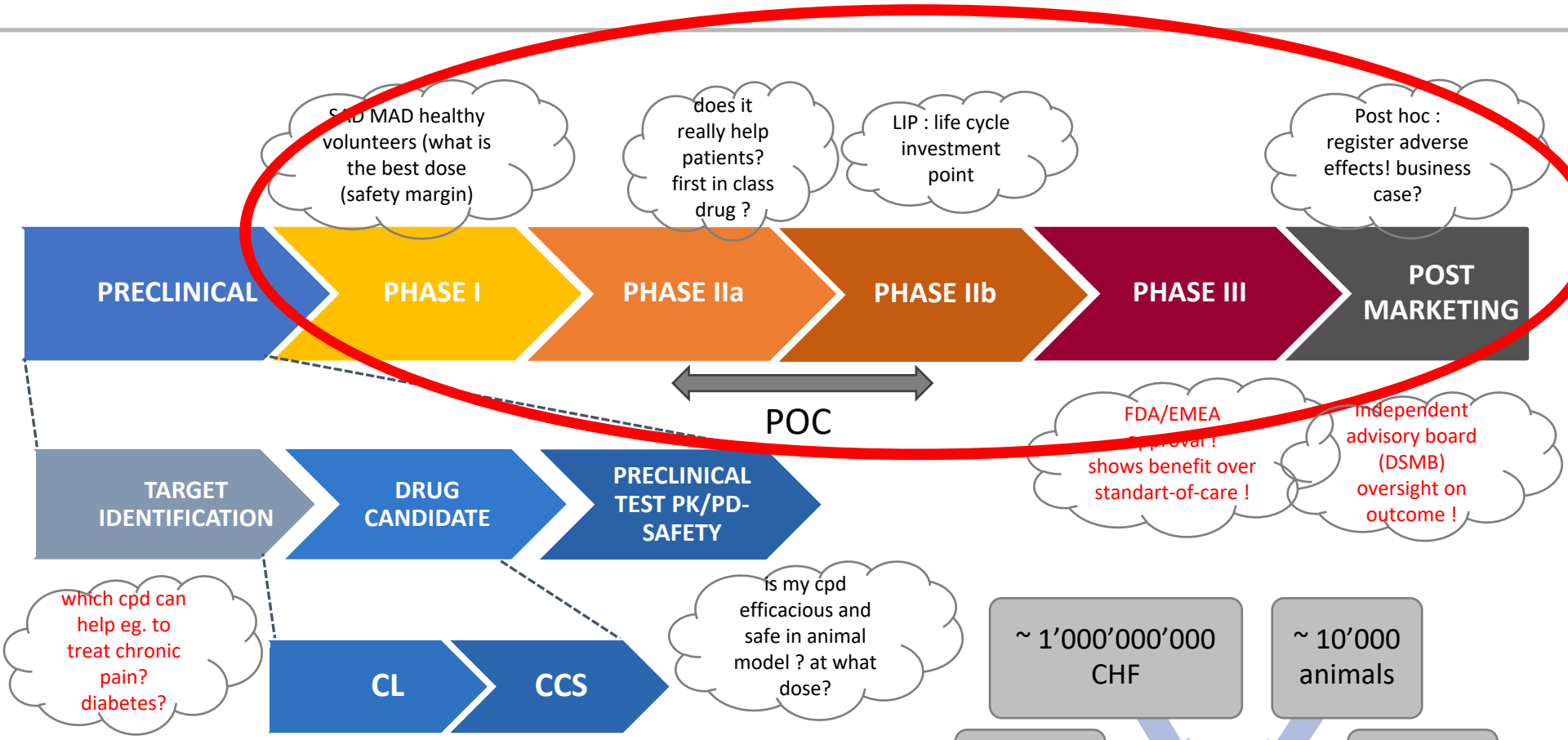
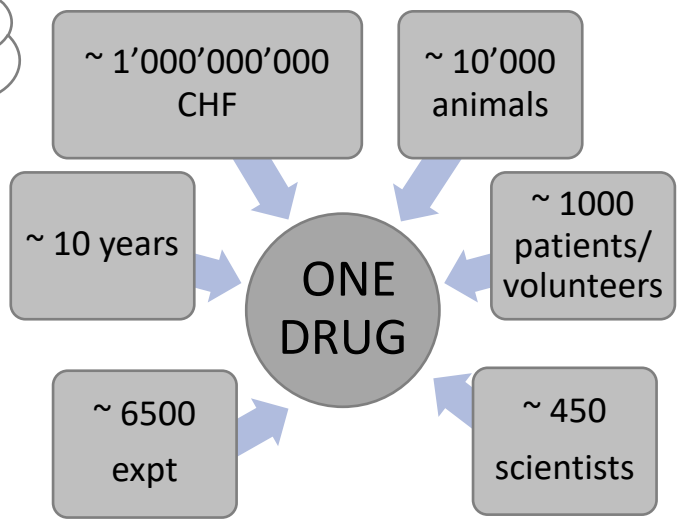
Drug discovery : the value chain _ clinical development





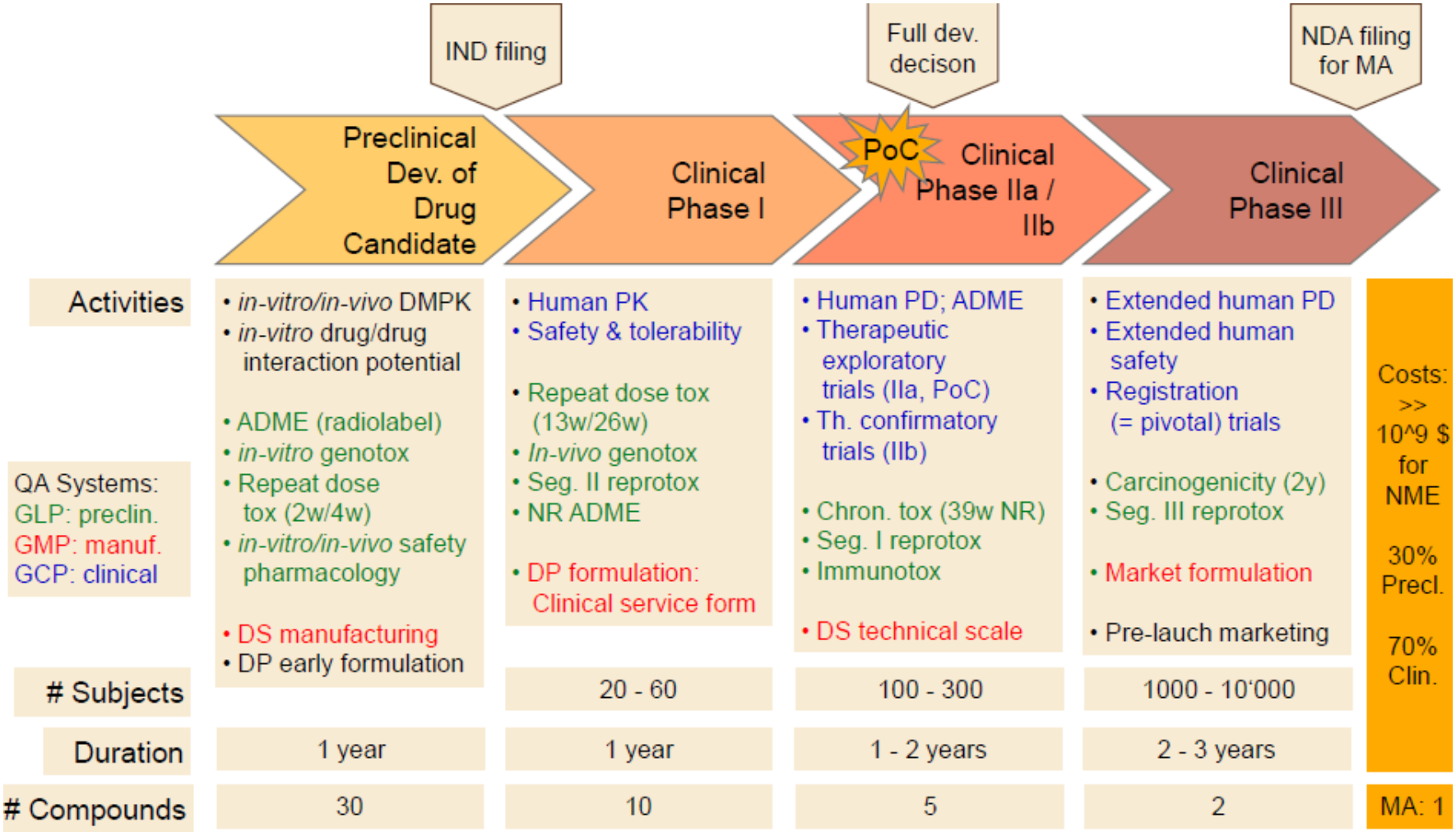
The Making Of An Innovative Medicine:
From Idea to Medicine

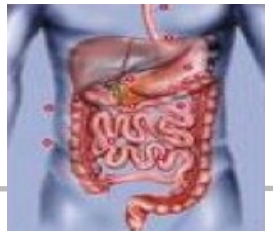
Session 10 : preclinical tests, PK PD and SAFETY

- In vitro pharmacology
- In vivo animal pharmacology, PK, PD AUC, Cmax, DMPK, IDB, IND filing
- Safety assessment for FIH trials
- Investigative toxicology (toxicogenomics)
- Drug-drug interaction
- “off target”

THE BIGGEST RISK FOR HUMAN BEEINGS IS NOT TO GET A MEDICINE !

Preclinical-clinical pharmacology : the value chain

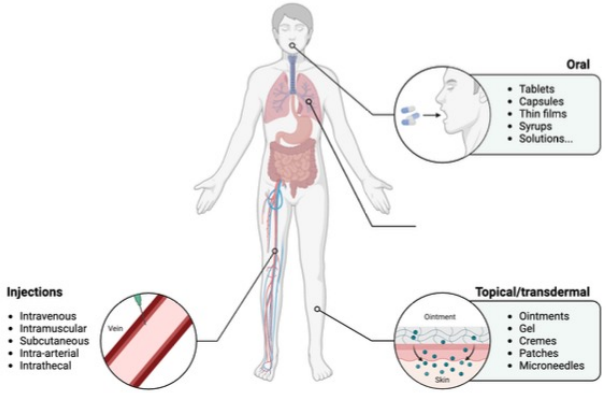




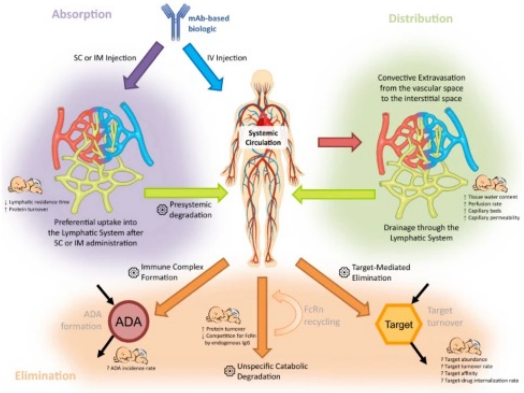
Pharmacology, DMPK, ADME

DMPK -drug metabolism and pharmacokinetics : considers the biotransformation of a drug and assessment of its pharmacokinetics

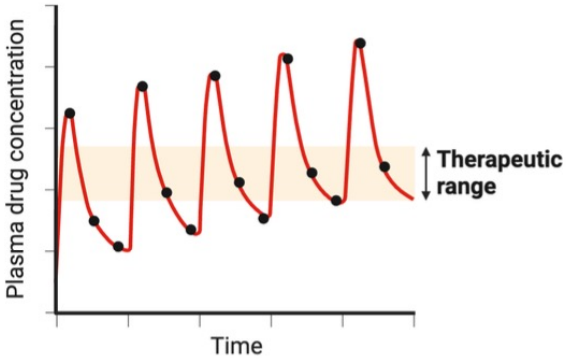
Pharmacokinetics is the description of a the drug journey from its administration to the elimination «body on drug»



Administration

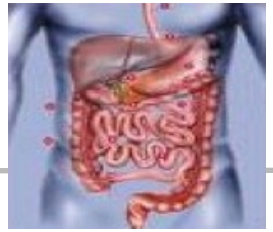


Disposition and elimination of the compound from the body



Plasma drug concentration allows to monitor and understand drug disposition

The biggest risk for human beings is not to get a medicine : when benefits outweigh the known risks



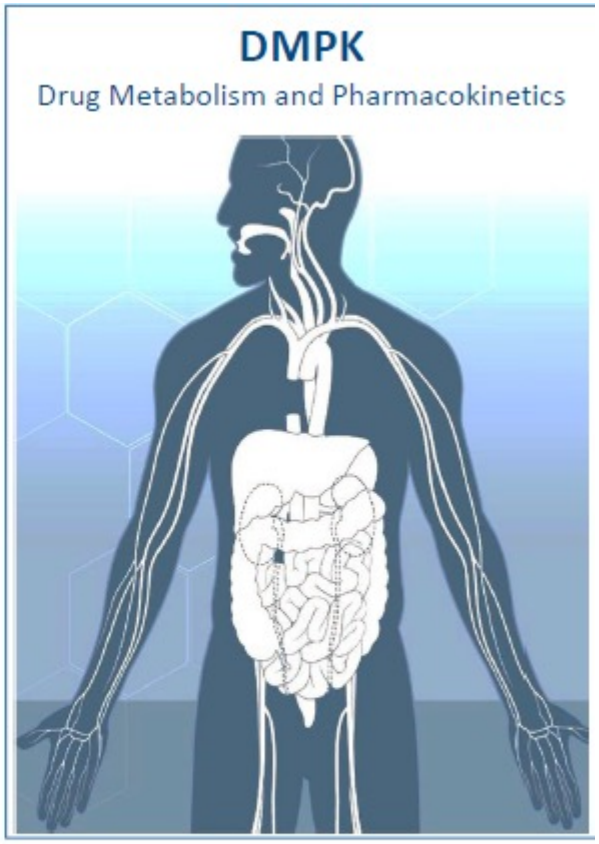
Pharmacology, DMPK, ADME

- **Pharmacokinetics (PK)** and **pharmacodynamics (PD)** are important fields of pharmaceutical sciences for investigating disposition profiles and the pharmacological efficacy of drugs under various experimental and/or clinical conditions.

- **Pharmacodynamics (PD)** is the study of the relationships between the concentration of a drug and the effect site (where target enzymes or receptors are located) and the magnitude of its pharmacological efficacy **(drug → body).**

- **Pharmacokinetics (PK)** is the study of the way drug molecules behave in the body after administration **(body → drug).**

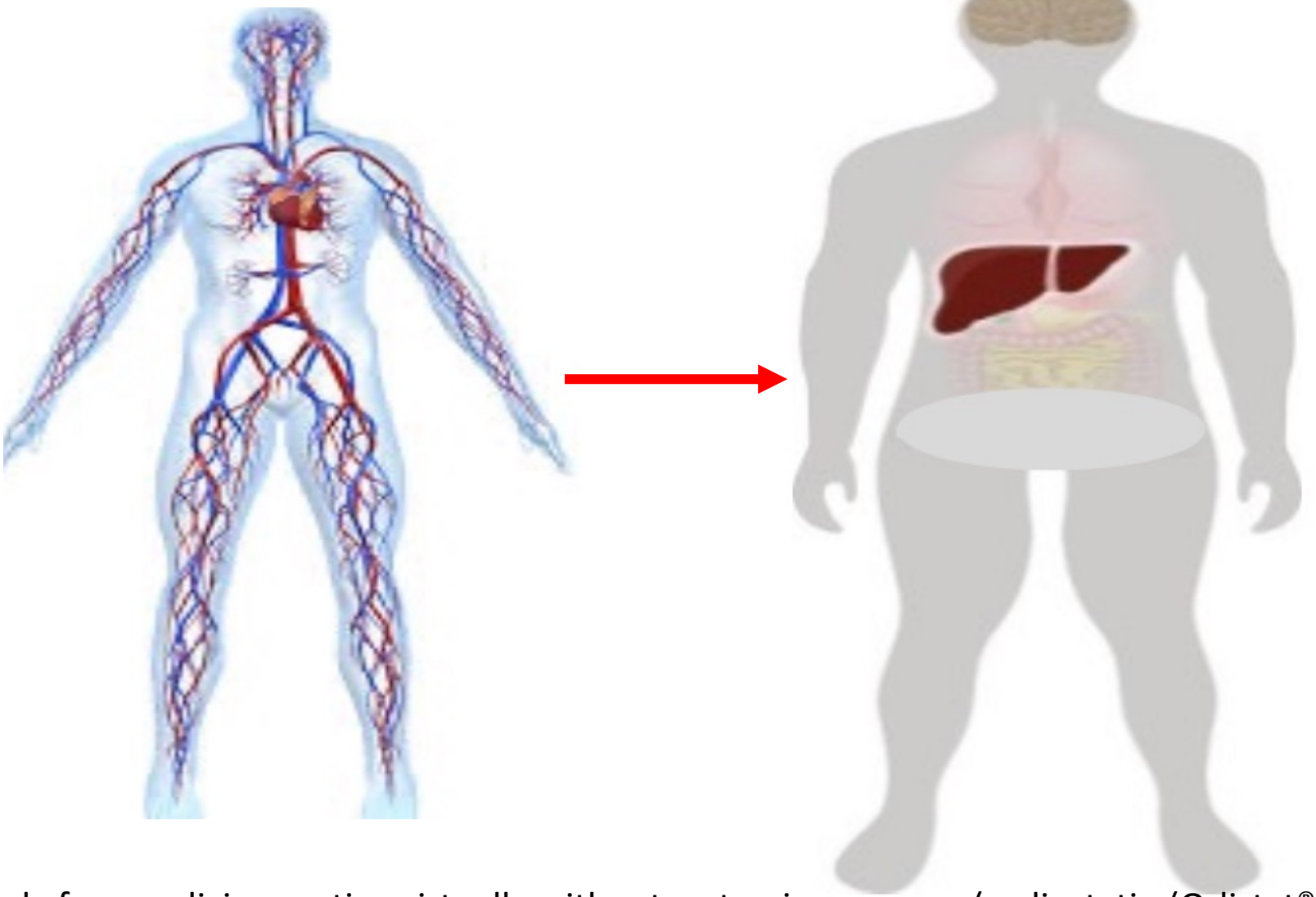
- Four distinct and interrelated processes occur between the administration and elimination of drugs from the body. These sequential events are called **ADME process**, i.e., **absorption, distribution, metabolism, and excretion.**



PK : ADME (or DMPK) process

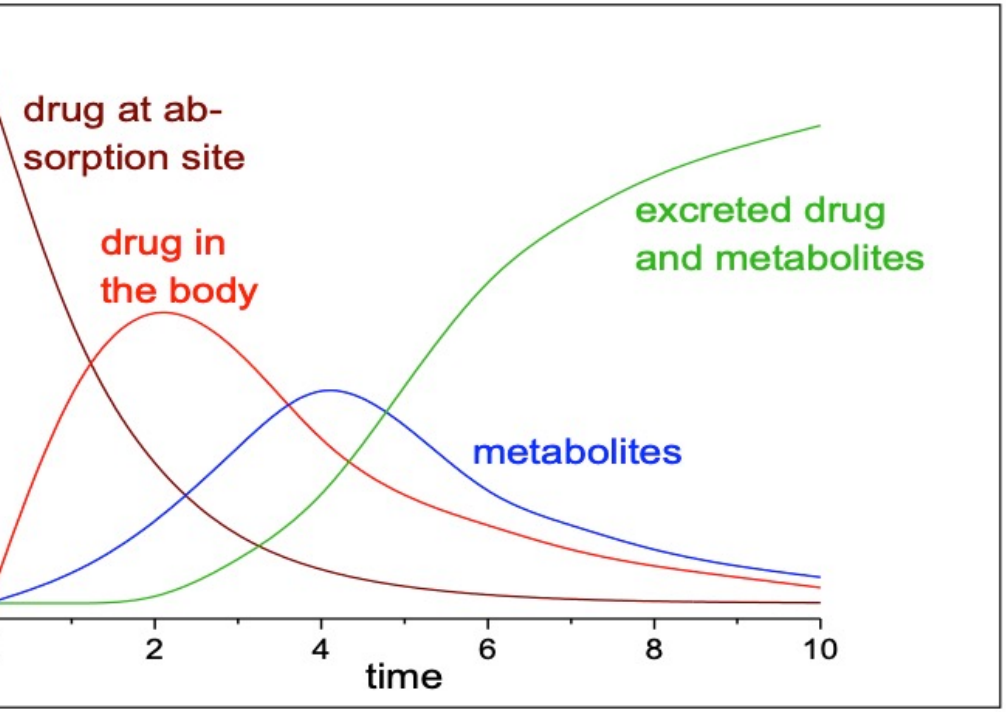
A	**Absorption:** The process (rate and extent) of compounds or drugs entering the blood circulation from their site of administration.
D	**Distribution:** The dispersion or dissemination of compounds or drugs throughout the fluids and tissues of the body.
M	**Metabolism (biotransformation):** The transformation of (lipophilic) parent compounds or drugs into more hydrophilic metabolites that can be excreted into bile or urine.
E	**Elimination/excretion:** The removal of compounds or drugs from the body either unchanged and/or as metabolites.

From plasma PK to tissue PK : drug exposure is key to efficacy



only few medicines active virtually without systemic exposure (eg lipstatin (Orlistat®)

PK : drug exposure is key to efficacy



AUC = area under the concentration-time curve

$\mathbf{C_{max}}$ = maximum concentration

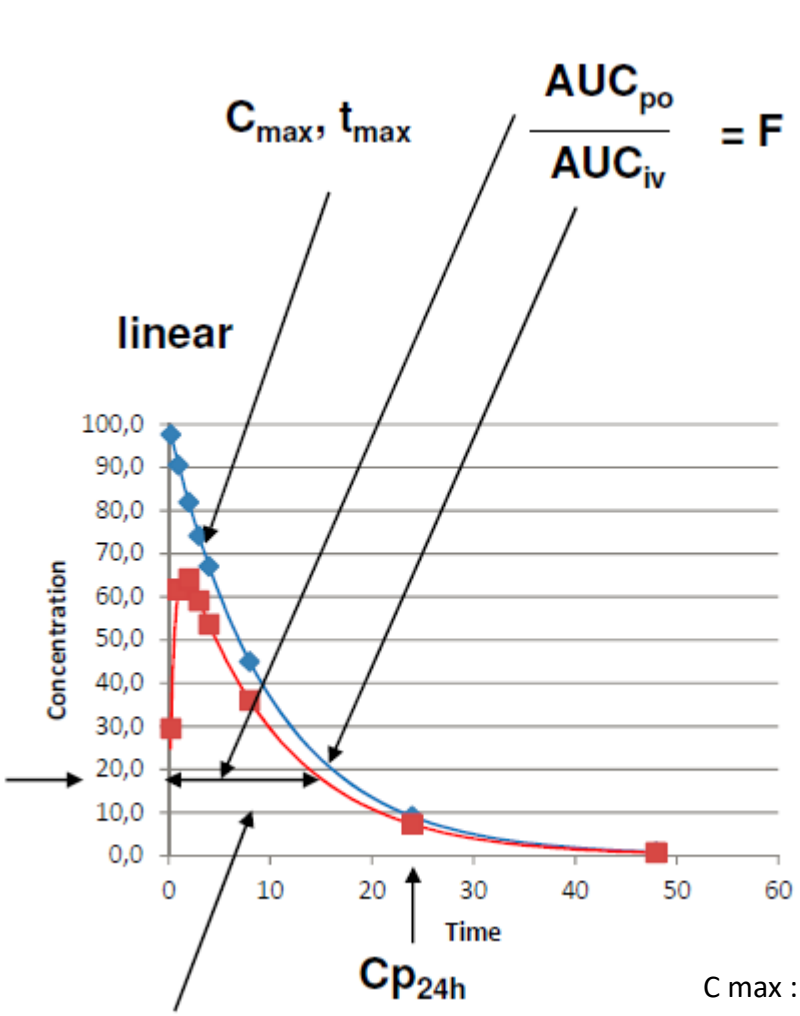
Clearance (CL) = Dose/AUC

Volume of distribution ($\mathbf{Vd_{ss}}$) = MRT*CL

Half-life ($\mathbf{t_{1/2}}$) = ln2 / lambda

Bioavailability (F) = (Dose IV * AUC_{po})/ (Dose PO * AUC_{iv})

PK *in vivo* – "body on drug"



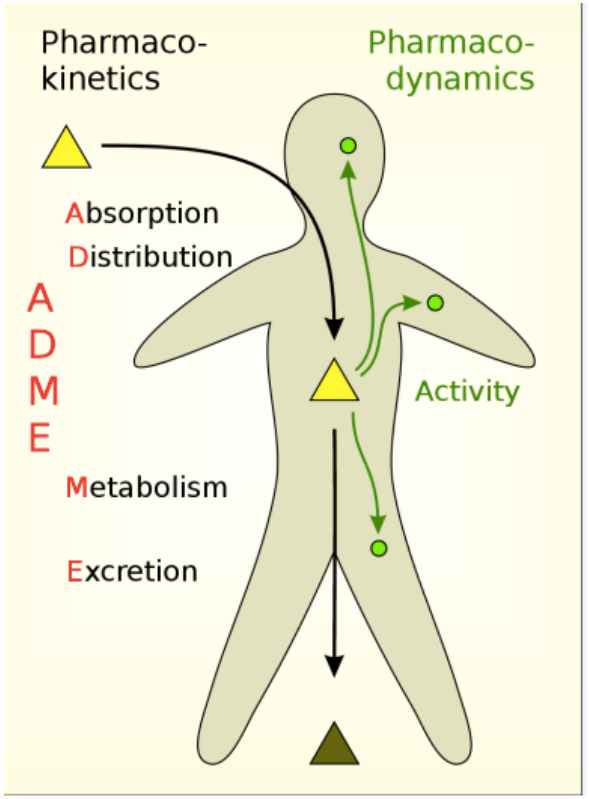
- AUC Area under the curve (from PK data analysis)
- C_{max} Peak Concentration (from PK data analysis)
- T_{max} Peak time (from PK data analysis)
- Elimination Rate Constant (λ_z , from PK data analysis)
- Elimination Half-live $t_{1/2} = \ln(2)/\lambda_z$
- F Bioavailability = AUC (po)/AUC (iv)
- Volume of Distribution V(t)
  - $V_z = CL/\lambda_z$
  - Vc = D/C(0)
- CL: Total Body Clearance D / F = AUCpo * CL = AUCiv * CL

C max : the peak serum concentration of a therapeutic drug
T max: The amount of time that a drug is present at the maximum concentration in serum.

PK, ADME, PD - in silico simulation

Fraction unbound $fu = \frac{A_{unbound}}{A_{total}}$

A_ amount of drug
C=concentration of drug



Tissues
23.8 l water
10 kg protein
15 kg lipids

bound ⇄ unbound ⇄ receptor → Effect

Plasma
2.8 l water
0.2 kg protein

bound ⇄ unbound

Interstitium
14.7 l water

Liver

unbound ⇄ bound

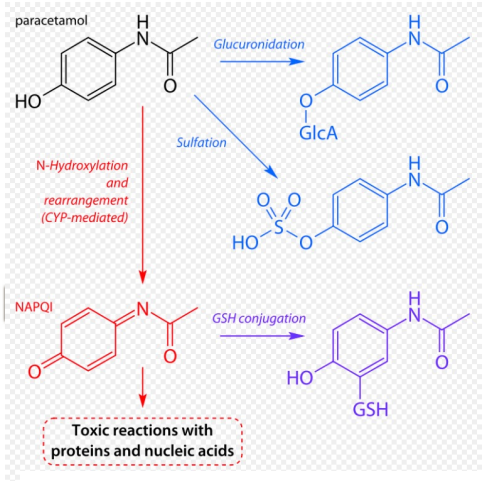
renal excretion

bilary excretion

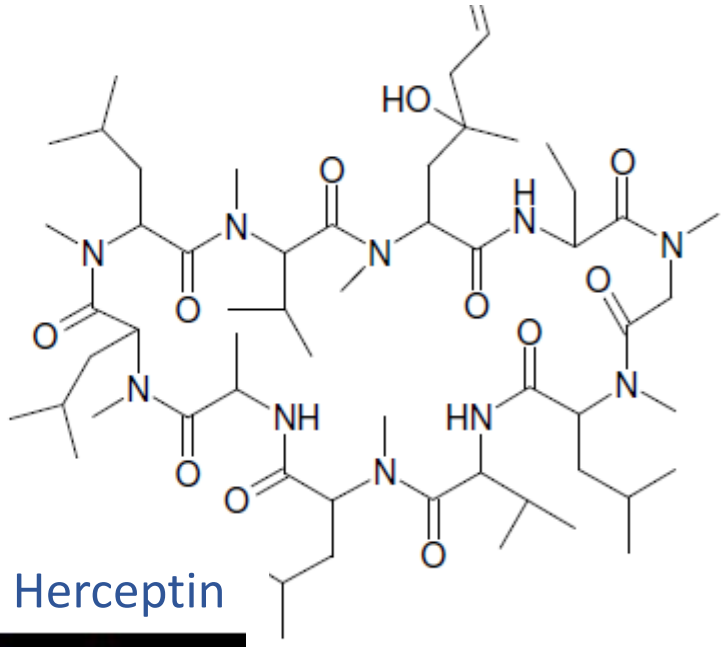
biotransformation

PK PD ADME : SMC and biologicals

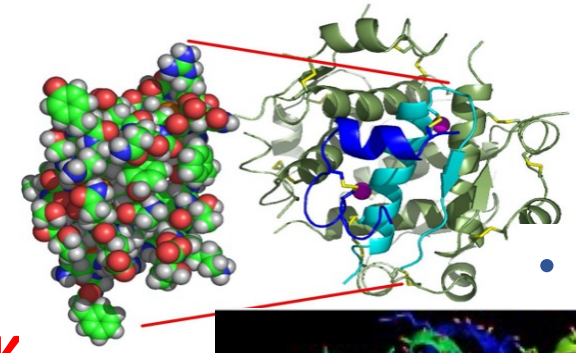
- Paracetamol



- Cyclosporin



- Sandimmun
- Insulin

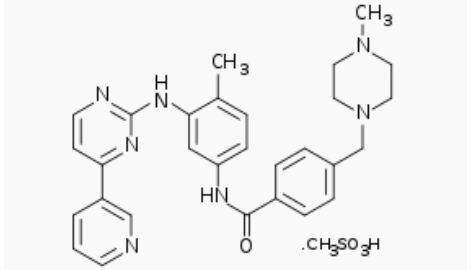


- MABs
- Herceptin

Modélisation de la molécule de trastuzumab

WILL IT WORK IN THE CONTEXT OF A LIVING ORGANISM ?

- Gleevec



Structure chimique du mésilate d'imatinib

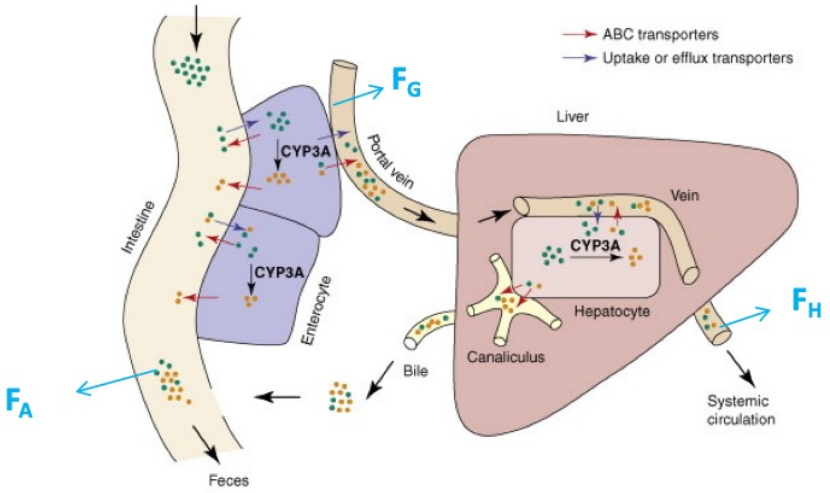
PK : ADME process

Pharmacokinetic Aspect	Small Molecules	Monoclonal Antibodies (mAbs)
Absorption and Bioavailability	Typically administered **orally**; absorbed through the gastrointestinal tract with varying bioavailability based on physicochemical properties.	Administered **parenterally** (e.g., intravenous or subcutaneous injection); poor absorption via the gastrointestinal tract; bioavailability depends on administration route and target antigens.
Distribution	Can diffuse across cell membranes to reach intracellular targets; small size facilitates widespread distribution, including the ability to **cross the blood-brain barrier**.	Predominantly remain in the extracellular space due to large size; **cannot cross cell membranes**; limited to vascular and interstitial compartments, restricting access to intracellular targets.
Metabolism	Primarily **metabolized in the liver** by cytochrome P450 enzymes, leading to active or inactive metabolites.	Undergo **catabolic processes** rather than traditional metabolic pathways; broken down into peptides and amino acids by proteolytic enzymes with minimal liver enzyme involvement.
Elimination	Eliminated mainly through **renal excretion** or **biliary secretion**, based on size, charge, and lipophilicity.	Eliminated via **target-mediated drug disposition** (TMDD); drug-target complex is internalized and degraded, leading to nonlinear pharmacokinetics with varying clearance rates.
Half-Life	Generally have **shorter half-lives**, often requiring multiple daily doses to maintain therapeutic levels.	Exhibit **longer half-lives** (days to weeks), due to size, Fc receptor interactions, and recycling mechanisms, allowing for less frequent dosing.

PK : Absorption process

Drug specific factors affect eg. oral absorption of small molecuales eg pK

- Solubility/ Dissolution (pKa, lipophilicity, size)
- Stability in the GI tract
  (chemical/enzymatic stability)
- Permeability (pKa, lipophilicity, size)
- Active and facilitated transport mechanisms



$F = F_A * F_G * F_H$

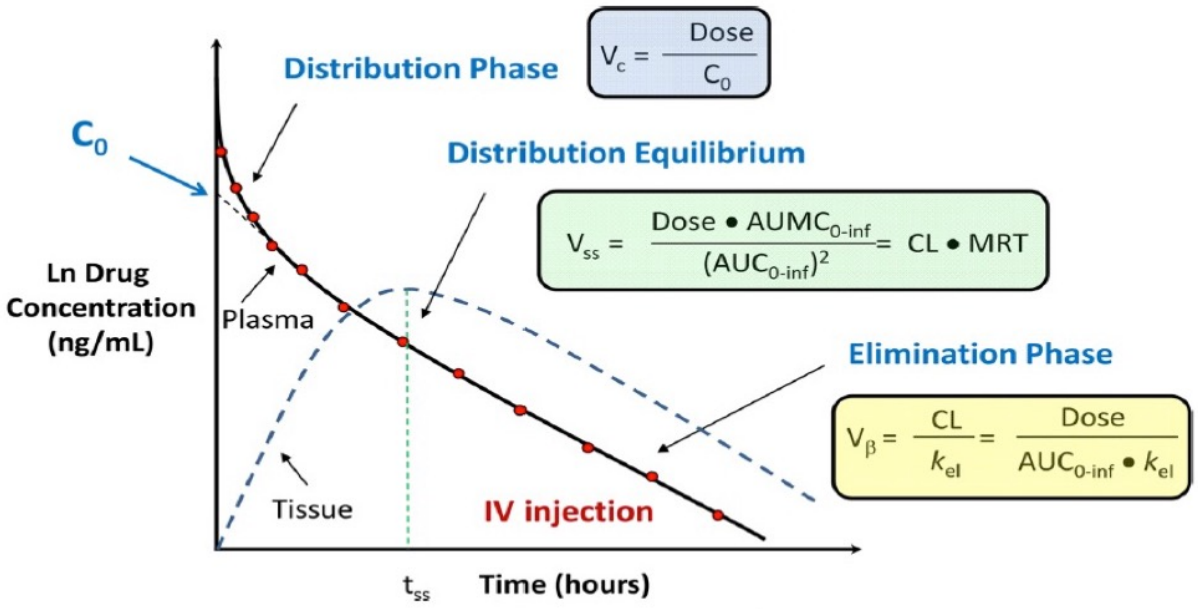
Absorption in vitro models

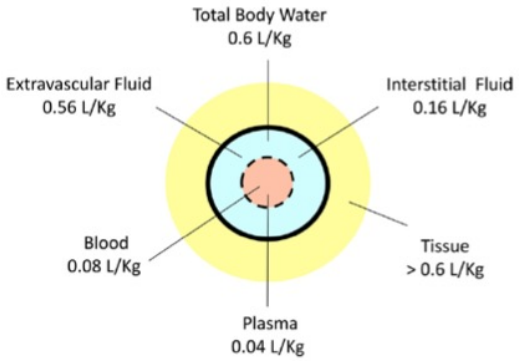
- Caco-2 cells
- MDCK cells
- PAMPA

ORGANOIDS

System specific parameters affecting (oral) absorption:
pH, intestinal transit time, motility, transporter, enzyme expression

ADME : distribution process





$$V_{ss} = V_p + \sum \left(\frac{fu_p}{fu_t} \right) V_t$$

Definition: Vd = $\frac{\textit{Amount of drug in body at equilibrium}}{\textit{Plasma drug concentration}}$

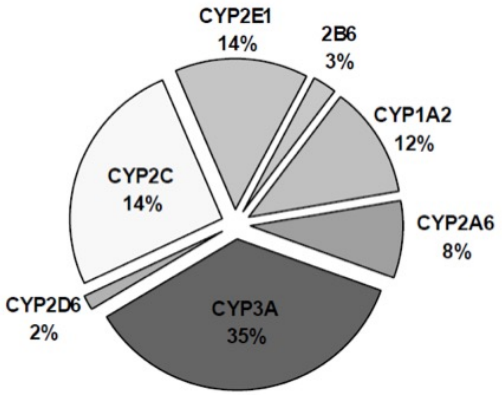
Journal of Medicinal Chemistry Vol 58/Issue 15

ADME – metabolism and excretion process

Metabolism (chemically converted metabolites (may serve as biomarkers ! Geneticaldifferences (polymorphisms) can lead to overdose !

Hepatic metabolism

- **Oxidative metabolism**
  - Referred to as **Phase I** metabolism as frequently the first metabolic step
- **Cytochrome P450** enzymes are key contributors to small molecule metabolism
  - **CYP3A4** is the main enzyme



- **Conjugation**
  - Referred to as **Phase II** metabolism as frequently following oxidative metabolism
  - However, conjugation may also occur as first step
  - UGT (glucuronidation) or SULT (sulfation) are primary conjugating enzymes
- **Other metabolically active enzymes**
  - FMO (flavin mono-oxygenase), AD or XO (aldehyde or xantine oxidase), ADH (alcohol dehydrogenase), carboxylesterases

Small molecules

1, Paine et al. (2006) Drug Metab and Dispos 34: 880-6

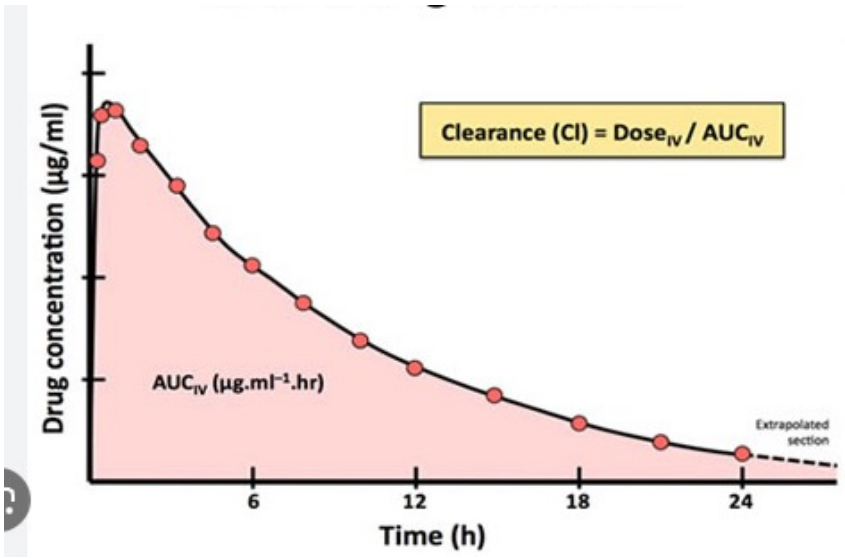
Excretion : route dependent on size and physicochemical properties ; eg. alcool expired as gas, larger less polar medicine in bile, small polar moieties in urine etc.

ADME – drug clearance
elimination rate over concentration

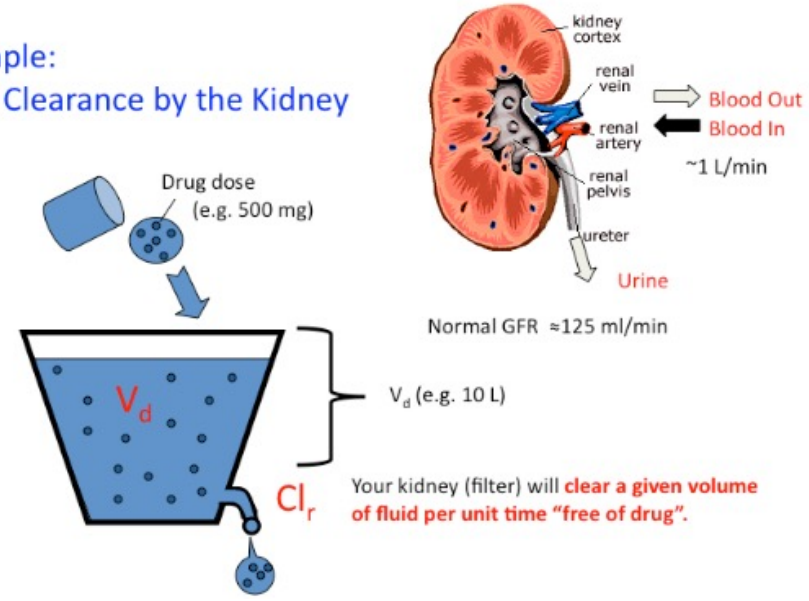
$$CL = \frac{Dose}{AUC}$$

CL represents the proportionality constant between concentration and rate of elimination or upon integration dose and AUC

- **Apparent CL** refers to the observable clearance in blood or plasma (CL_b or CL_p)
- The apparent CL may be a composite of the contribution of various organs (**frequently liver and kidneys**)
  - Elimination of drug occurs by excretion and metabolism
- **Unbound intrinsic CL** (CLu_{int}) refers to the actual cellular clearance without any limitations caused by tissue perfusion
  - CLu_{int} is not directly observable *in vivo*



Example:
Drug Clearance by the Kidney



Pharmacology during preclinical and clinical development: pharmaceutical formulation (galenics) is key

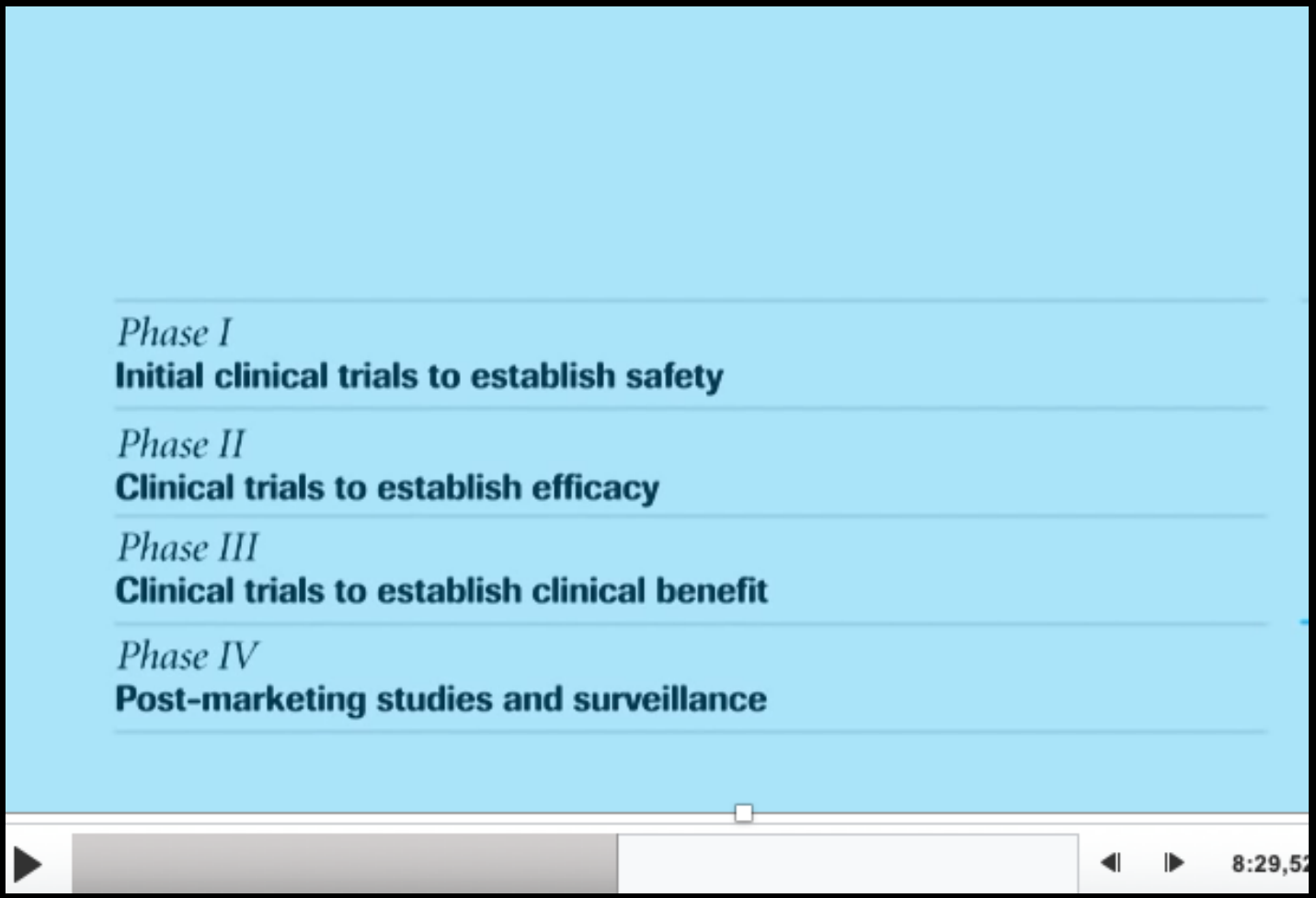
An active ingredient has to be incorporated into a suitable form of administration so that it can be transported to the part of the body where it is needed.

Medicines are required to:

- Contain an accurate dose
- Make active substance available for absorption
- Be stable
- Be convenient to administer and easy to take
- Be produced economically according to Good Manufacturing Practice (GMP)

The biggest risk for human beings is not to get a medicine : when benefits outweigh the known risks

The Making Of An Innovative Medicine: a look at the real world

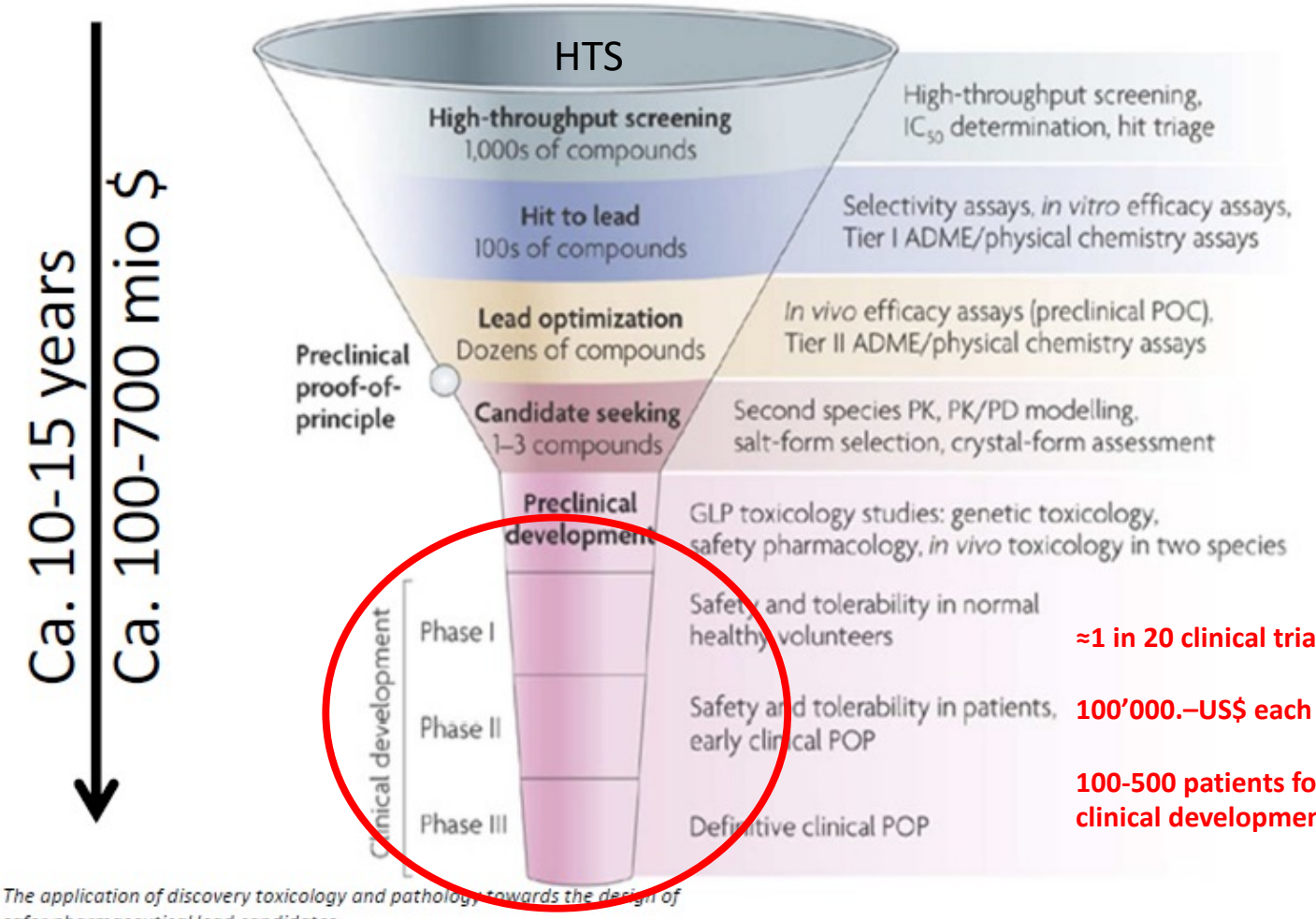


Basel - the largest Life Science Hub of the world **dixit Gilbert Ghostine, board president of Sandoz Ltd**

The Making Of An Innovative Medicine: a look at the real world Phase 0 Phase I Phase II Phase III clinical research (8:12)

https://www.youtube.com/watch?v=attNofZ7AnY

The new medicine development process 1:20 000 makes it !



The application of discovery toxicology and pathology towards the design of safer pharmaceutical lead candidates
Jeffrey A. Kramer, John E. Sagartz & Dale L. Morris
Nature Reviews Drug Discovery 6, 636-649 (August 2007)

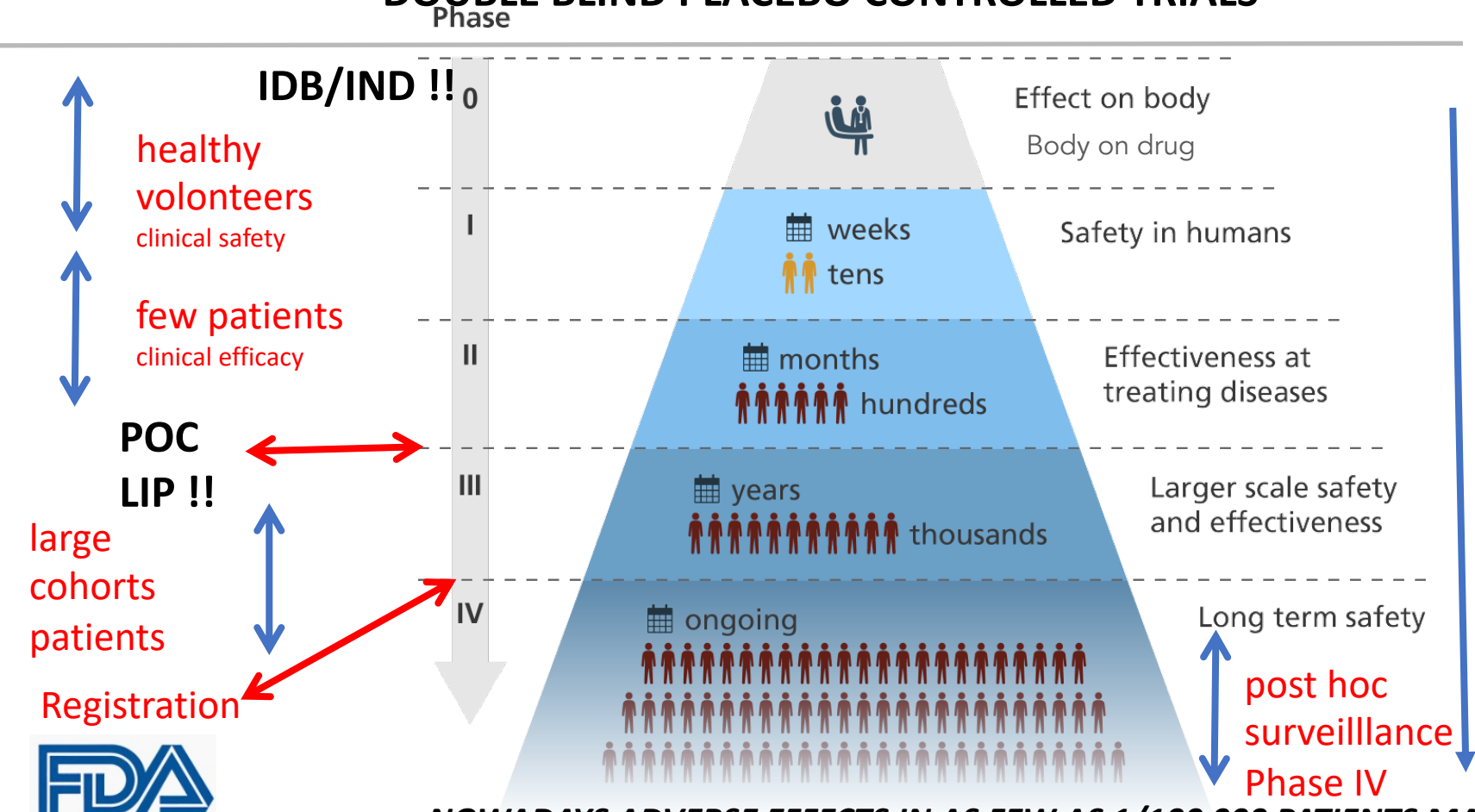
Nature Reviews | Drug Discovery

≈1 in 20 clinical trials get FDA approval

100'000.–US$ each patient in Ph2/Ph3

100-500 patients for each medicine full clinical development

Clinical development = clinical research
DOUBLE BLIND PLACEBO CONTROLLED TRIALS



NOWADAYS ADVERSE EFFECTS IN AS FEW AS 1/100 000 PATIENTS MAY FORCE WITHDRAWING OF A NOVEL MEDICINE FROM THE CLINIC !

healthy affected

ETHICS COMITEES ARE INVOLVED IN EACH CLINICAL TRIALS PROTOCOLS - EACH CLINICAL TRIAL IS HANDLED NATIONALY (SEPARATELY FOR EACH COUNTRY)

FDA

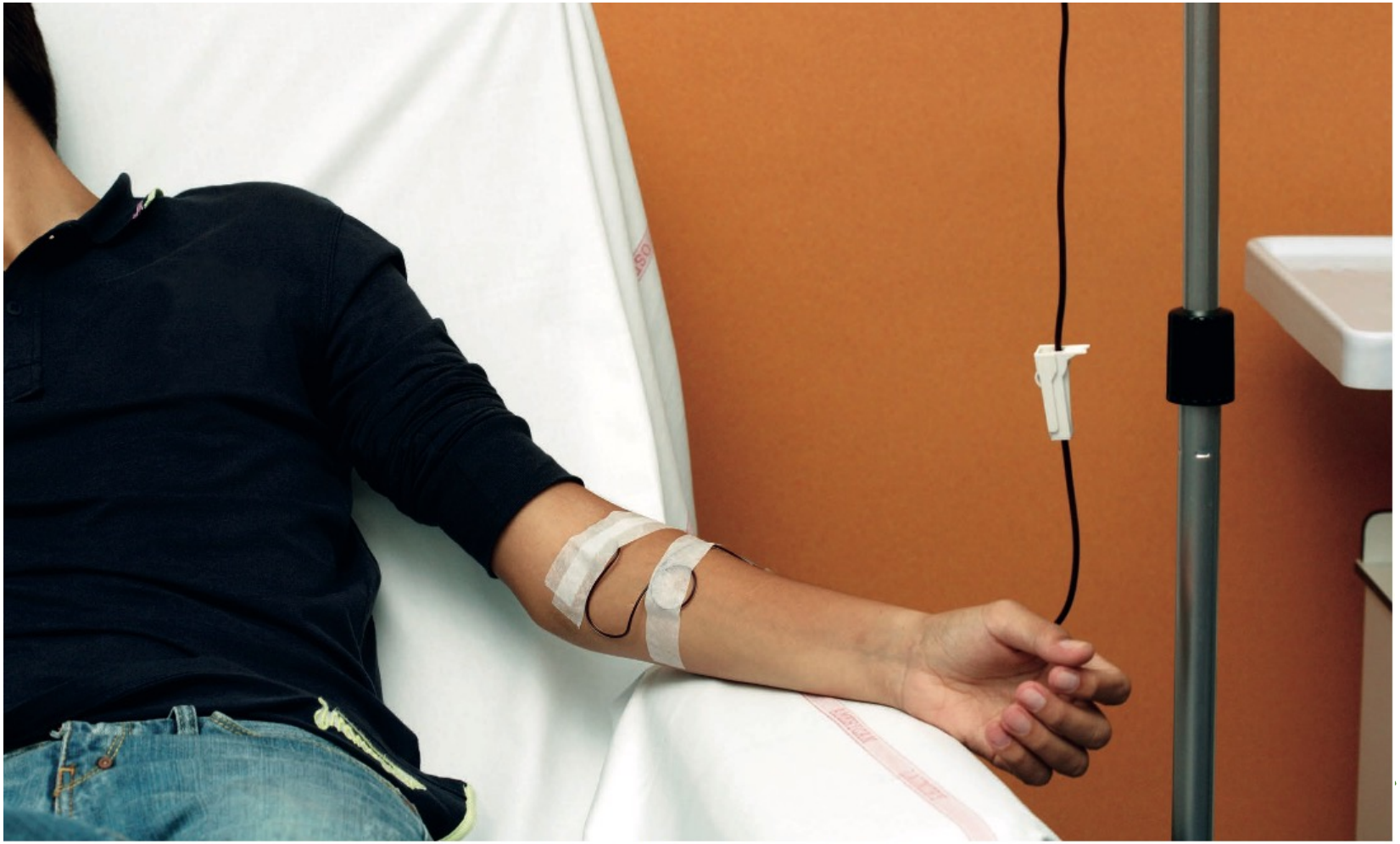
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

swissmedic

Efficacy and safety (adverse effects) is what patients care first !

Consider drug efficacy and safety before first-in-human trials - FIH

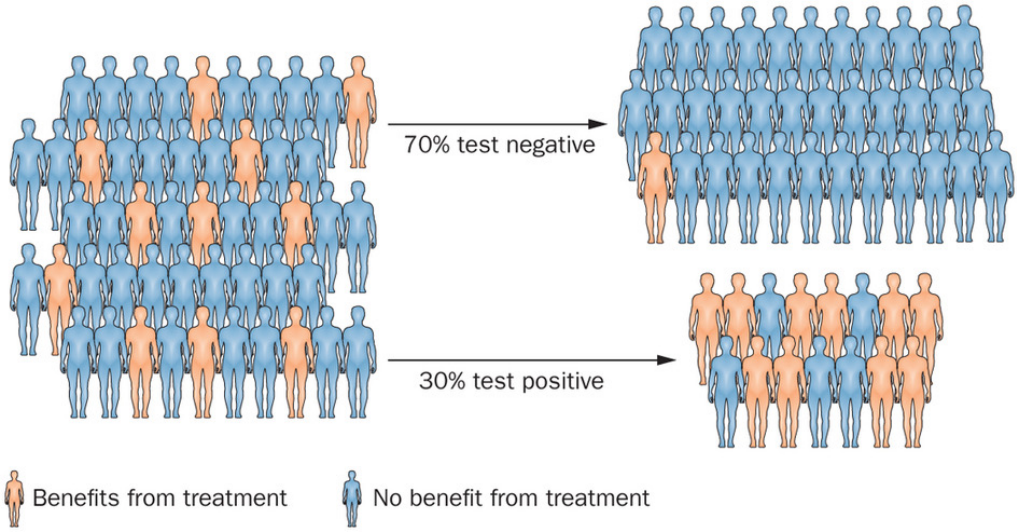
Clinical development in medical practice
Phase 0-I (FIH) with medic students @ ERs

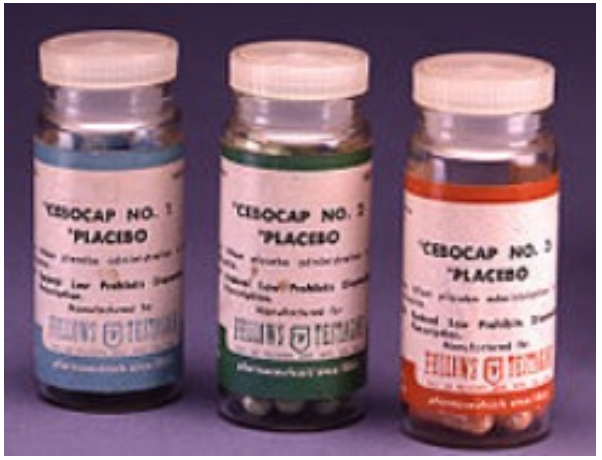


Angela Madurga (2018)

Clinical research revisited, the responders vs non responders

- **STRATIFICATION OF THE COHORTS IN GROUP OF RESPONDERS – NON RESPONDERS - PERSONALIZED HEALTHCARE !**
- **DOUBLE BLIND PLACEBO CONTROLLED TRIALS HAVE EMERGED AS STANDART APPROVED PROCEDURES FOR CLINICAL TRIALS**





Placebo are inert tablets, sugar pills

"NEGATIVE CONFOUNDING EFFECTS" MAY BLURRED EFFICACY OF AN INNOVATIVE MEDICINE !

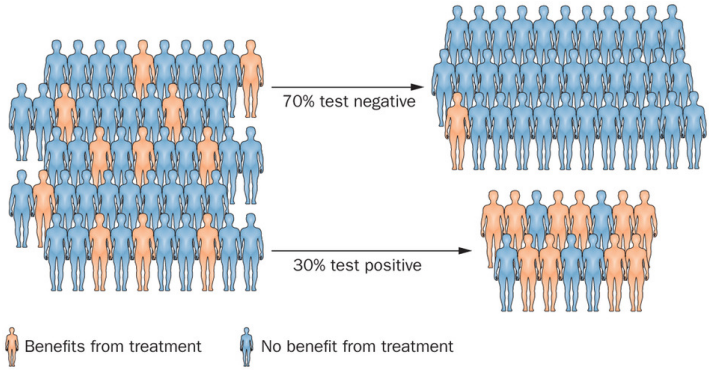
The "one pill fits all" concept no longer supported as each group of individuals carry a different blueprint !
An extraneous variable that wholly or partially accounts for the observed ***effect*** *on disease status*

Clinical research facing replicability crisis

DOUBLE BLIND PLACEBO CONTROLLED TRIALS HAVE EMERGED AS STANDART APPROVED PROCEDURES FOR CLINICAL TRIALS BUT WHY DO WE STILL PERFORM/DEVELOP INNOVATIVE MEDICINES WITH IRREPRODUCIBLE ANIMAL PHARMACOLOGY ? IRREPRODUCIBILITY MEANS HIGHER HEALTH CARE COST !

95% OF PRECLINICAL RESULTS/DATA DO NOT REPRODUCE IN CLINICAL TRIALS (EXCEPTION FABRICATED DATA BOTH PRE-CLINICAL RESEARCH)

CLINICAL RESEARCH ITSELF SUFFERS FROM REPRODUCIBILITY (MULTICENTRIC SAMPLING INCONSISTENT– AGE – SEX – ETHNIES RANDOMISATION INCONSISTENT-POLISHED UP DATA REPORTING .ETC



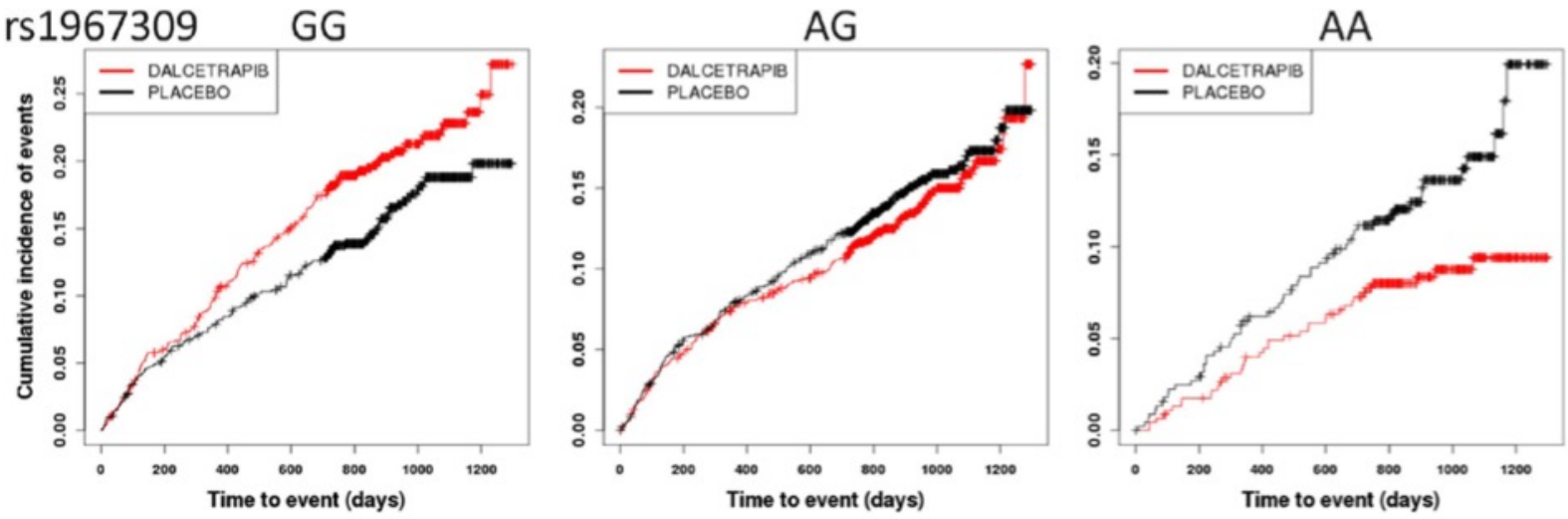
Concerns about a crisis of mass irreplicability across scientific fields ("the replication crisis") have stimulated a movement for open science, encouraging or even requiring researchers to publish their raw data and analysis code. Recently, a rule at the US Environmental Protection Agency (US EPA) would have imposed a strong open data requirement.

- **PUBLISH THE RESEARCH PLAN BEFORE TRIALS BEGINS (NO OPPORTUNITY TO CHANGE DURING THE APPROVED PROTOCOL (>5Y STUDIES)**
- WHY HUMAN CLINICAL TRIALS ? WE CANNOT USE HUMAN BEINGS AS GUINEA PIGS !
- **INTERNATIONAL COLLABORATIONS INCREASE VISIBILITY HENCE REPRODUCIBILITY**

Hicks DJ. 2023. Accountability in research 30:34-62

CVD - HDL medicine – phase 3 outcome trial (pharmacogenomics)

Treatment Effect by *ADCY9* Genotypes in dal-OUTCOMES



N at risk/days	*0*	*200*	*400*	*600*	*800*	*1000*	*1200*
Dalcetrapib	978	914	864	822	648	373	118
Placebo	1006	947	916	880	698	388	124

	0	*200*	*400*	*600*	*800*	*1000*	*1200*
	1379	1308	1255	1225	1003	570	186
	1417	1326	1284	1243	1019	577	192

	0	*200*	*400*	*600*	*800*	*1000*	*1200*
	485	475	458	449	378	223	74
	476	459	438	424	353	208	55

Events: Composite of CHD death, resuscitated cardiac arrest, non-fatal myocardial infarction, unstable angina with objective evidence of ischemia, atherothrombotic stroke and unanticipated coronary revascularization

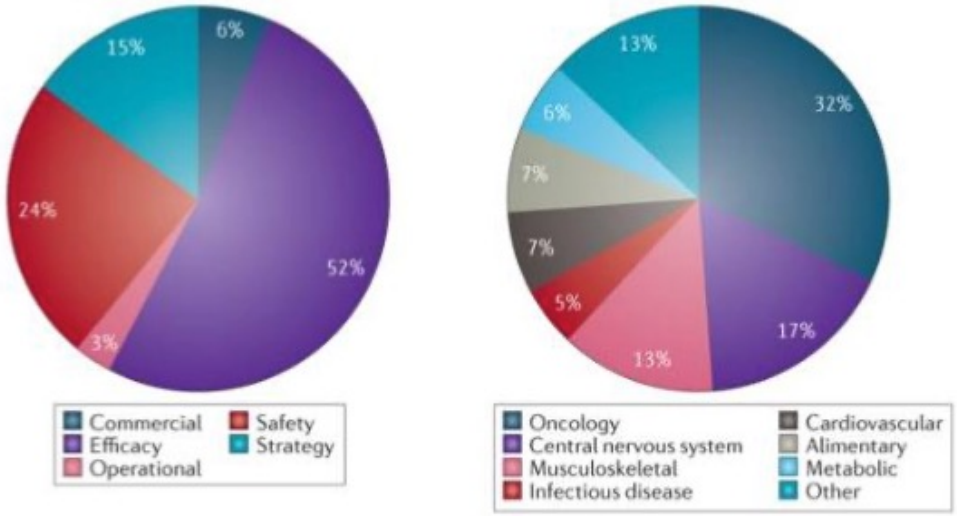
Figure. Kaplan–Meier curves of accumulating cardiovascular events in the dalcetrapib and placebo arms broken down according to the genotypes at rs1967309 in the *ADCY9* (adenylate cyclase type 9) gene. CHD indicates coronary heart disease.

Tardiff et al. (2016) Cir Cardiovasc Genet 116: 340-348

Clinical research portfolio : the attrition rate - is AI-guided clinical research the solution ?

Translational failure in clinical phases

R. K. Harrison, *Nat. Rev. Drug Discov.* 2016, *15*, 817.



76% of clinical programs fail due to efficacy or safety.

Clinical research portfolio : the attrition rate - the advent of AI-guided clinical research as improvment

The High Price Of Failed Clinical Trials: Time To Rethink The Model

By Ralf Huss, MD, Chief Medical Officer, Definiens

Back in 2014, a study in Nature Biotech showed that only 32% of drugs have a probability of making it to Phase 3 trials, and only one in 10 drugs overall actually makes it to market. Things haven't improved since then.

BIO recently put out a study reporting that the average overall likelihood of approval (LOA) by FDA from Phase I was 9.6 percent – a 1 in 10 chance. The rate is even lower for major disease areas like oncology. Phase II clinical programs continue to experience low success rates as well, with only 30.7 percent of candidates advancing to Phase III, a slightly worse rate than it was a few years ago.

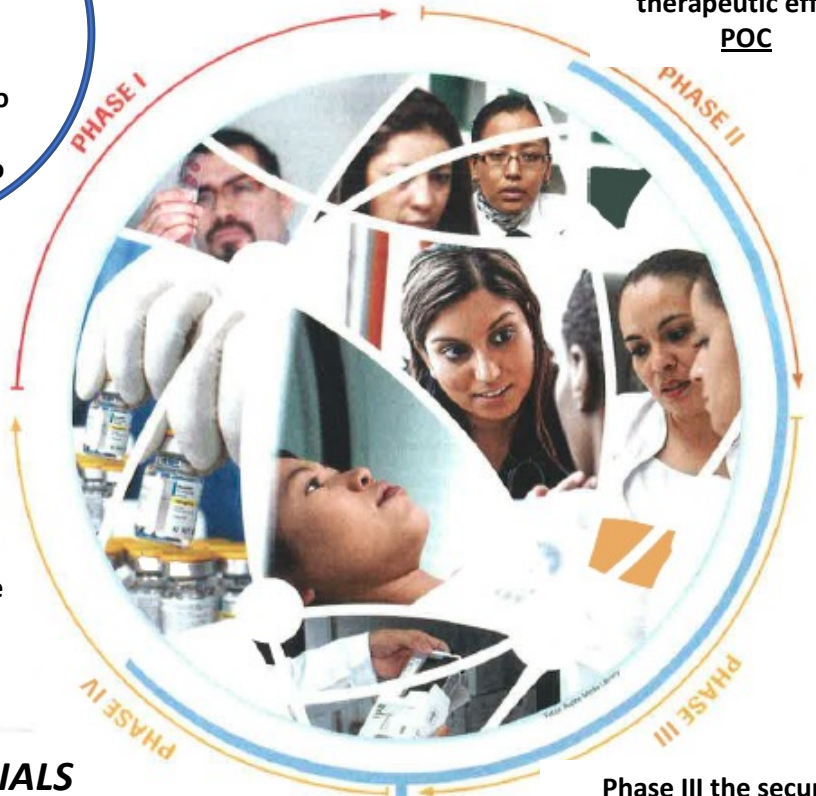
The cost of failed clinical trials is high, and the industry needs to focus on ways to reduce the

Clinical research : a 360 degrees view of a clinical scientist

- WHO IS DOING THIS ?
- AN EXPERIMENT WITH HUMAN SUBJECTS !
  (healthy volonteers)
- MAINLY CARRIED OUT IN CLINICAL SETTING, CLOSE TO THE EMERGENCY ROOM
- DATA SHOULD/HAVE TO BE REPORTED TO A SPONSOR INDEPENDANT MONITORING BODY (DSMB)

Phase 0-I is the most risk associated clinical phase as the medicine is going to be administrated for the first time to human

Phase II requires the technical infrastructure to test the beneficial therapeutic effect <u>POC</u>



Phase IV the safety profile of the new medicine Pharmacovigilance !

Phase III the security efficacy profile of the new medicine should be well characterized

ETHICS COMITEES ARE INVOLVED IN EACH CLINICAL TRIALS PROTOCOLS - EACH CLINICAL TRIAL IS HANDLED NATIONALY (SEPARATELY FOR EACH COUNTRY)

Ranking of the hospitals in the world according to Newsweek 2025

Die besten Spitäler der Welt 2025

Rang	Institution	Land	Standort
1	Mayo Clinic	USA	Rochester
2	Cleveland Clinic	USA	Cleveland
3	Toronto General - University Health Network	Kanada	Toronto
4	The Johns Hopkins Hospital	USA	Baltimore
5	Karolinska Universitetssjukhuset	Schweden	Stockholm
6	Massachusetts General Hospital	USA	Boston
7	Charité	Deutschland	Berlin
8	Sheba Medical Center	Israel	Ramat Gan
9	Singapore General Hospital	Singapur	Singapur
10	Universitätsspital Zürich	Schweiz	Zürich
11	AP-HP Hôpital Universitaire Pitié Salpêtrière	Frankreich	Paris
12	Universitätsspital Basel	Schweiz	Basel
13	UCLA Medical Center	USA	Los Angeles
14	Universitätsklinikum Heidelberg	Deutschland	Heidelberg
15	CHUV	Schweiz	Lausanne

Tabelle: Basler Zeitung; Quelle: «Newsweek»

Die besten Spitäler der Welt 2025.

Clinical research portfolio is public available - eg Incyte Inc.

https://clinicaltrials.gov

Our Portfolio

Incyte | SOLVE ON.

MPNs and GVHD

		Clinical Proof of Concept	Pivotal	Approved
Jakafi® (ruxolitinib)[1] JAK1/JAK2	Myelofibrosis[2], polycythemia vera[2], GVHD[2]			●
ruxolitinib QD JAK1/JAK2	*Bioequivalence and stability testing*		●	
parsaclisib PI3Kδ	Myelofibrosis | + ruxolitinib		●	

General Hematology/Oncology

		Clinical Proof of Concept	Pivotal	Approved
Pemazyre® (pemigatinib) FGFR1/2/3	Cholangiocarcinoma[10]			●
Monjuvi® (tafasitamab-cxix)[11] **Minjuvi® (tafasitamab)**[11] CD19	r/r DLBCL[2,12,13]			●
Iclusig® (ponatinib)[14] BCR-ABL	Chronic myeloid leukemia[12], Ph+ ALL[12]			●

NIH U.S. National Library of Medicine

ClinicalTrials.gov

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ClinicalTrials.gov is a database of privately and publicly funded clinical studies conducted around the world.

baricitinib[4] JAK1/JAK2	Alopecia areata, COVID-19[9]			●
capmatinib[7] MET	Liver cancer		●	

INCB81776 AXL/MER	Solid tumors		●	
INCB106385 A2A/A2B	Solid tumors		●	
INCA00186 CD73	Solid tumors		●	
INCB123667 CDK2	Solid tumors		●	

21 Molecular Targets | **25** Clinical Candidates | **7** Approved Products

incyte biosciences | usine | yverdon | incyte corporation

incyte biosciences | usine | yverdon | incyte corporation

Clinical research ends up with FDA submission and marketing : a survey of big Pharma pipelines

Expected Submission Timeline

Pipeline charts as communicated at full-year results meeting dated February 7, 2019

	2019(2)	2020(2)		2021(2)	2022(2)		2023 and beyond(2)	
NMEs	**isatuximab** anti-CD38 mAb 3L RRMM (ICARIA)	**fitusiran** RNAi therapeutic targeting anti-thrombin Hemophilia A/B	**avalglucosidase alfa** Neo GAA Pompe Disease	**venglustat** Oral GCS inhibitor ADPKD(6)			**SAR156597** IL4/IL13 bi-specific mAb Systemic Scleroderma	**SAR422459(**)** ABCA4 gene therapy Stargardt Disease
	SAR341402 Rapid acting insulin Type 1/2 Diabetes - EU(3)	**sutimlimab(4)** Anti Complement C1s mAb Cold Agglutinin Disease	**olipudase alfa** rhASM ASD(5)	**efpeglenatide(**)** Long acting GLP1-R agonist Type 2 Diabetes	**SP0232 mAbs(7)(**)** Respiratory syncytial virus		**SAR440340(**)** Anti-IL33 mAb Atopic dermatitis	**HIV** Viral vector prime & rgp120 boost vaccine
Additional Indications	**dupilumab(**)** Anti-IL4Rα mAb Nasal Polyposis Adult	**sarilumab(**)** Anti-IL6R mAb Polyarticular Juvenile Idiopathic Arthritis	**Aubagio®** teriflunomide Relapsing MS – Ped.	**isatuximab** Anti-CD38 mAb (IMROZ) 1L Newly Diagnosed MM Ti	**Dupixent®(**)** dupilumab AD 6 months - 5 years old	**sarilumab(**)** Anti-IL6R mAb Giant Cell Arteritis	**SAR440340(**)** Anti-IL33 mAb COPD	**isatuximab** Anti-CD38 mAb Newly Diagnosed MM Te (GMMG)
	Fluzone® QIV HD Quadrivalent inactivated Influenza vaccine - High dose	**Dupixent®(**)** dupilumab AD 6 - 11 years old -	**Zynquista™(**)** Oral SGLT-1&2 inhibitor Type 2 Diabetes	**cemiplimab(**)** PD-1 inhibitor mAb 2L Cervical Cancer	**dupilumab(**)** Anti-IL4Rα mAb Eosinophilic Esophagitis	**sarilumab(**)** Anti-IL6R mAb Polymyalgia Rheumatica	**SAR440340(**)** Anti-IL33 mAb Asthma	**venglustat** Oral GCS inhibitor GrPD(8)
	Men Quad TT Adv. generation meningococcal U.S.: 2y+ & EU: Toddlers+	**isatuximab** Anti-CD38 mAb 1-3L RRMM (IKEMA)	**Shan 6** DTP-HepB-Polio-Hib Pediatric hexavalent vaccine	**cemiplimab(**)** PD-1 inhibitor mAb 1L NSCLC	**dupilumab(**)** Anti-IL4Rα mAb Asthma 6 - 11 years old	**sarilumab(**)** Anti-IL6R mAb Systemic Juvenile Arthritis	**dupilumab (**)+ AR101** Anti-IL4Rα mAb Peanut Allergy - Pediatric	**venglustat** Oral GCS inhibitor Fabry Disease
	Pentacel® vIPV DTaP-IPV/Hib	**cemiplimab(**)** PD-1 inhibitor mAb Advanced BCC		**Zynquista™(**)** Oral SGLT-1&2 inhibitor Worsening Heart Failure in Diabetes	**venglustat** Oral GCS inhibitor Gaucher Type 3	**Cerdelga®** eliglustat Gaucher Type 1, switch from ERT – Pediatric	**Pediatric pentavalent vaccine** DTP-Polio-Hib (Japan)	**Rabies VRVg** Purified vero rabies vaccine
					SP0173 Tdap booster US Tdap booster	**Praluent®(**)** alirocumab LDL-C reduction - Pediatric		

Immuno-inflammation
Oncology
Rare Diseases
Rare Blood Disorders
MS & Neuro
Diabetes
Cardiovascular & metabolism
Vaccines

(1) Excluding Phase 1
(2) Projects within a specified year are not arranged by submission timing
(3) Submission strategy for the U.S. under evaluation
(4) Also known as BIVV009
(5) Acid Sphingomyelinase Deficiency
(6) Autosomal Dominant Polycystic Kidney Disease
(7) Also known as MEDI8897
(8) Gaucher Related Parkinson's Disease
(**) Partnered and/or in collaboration – Sanofi may have limited or shared rights on some of these products

SANOFI

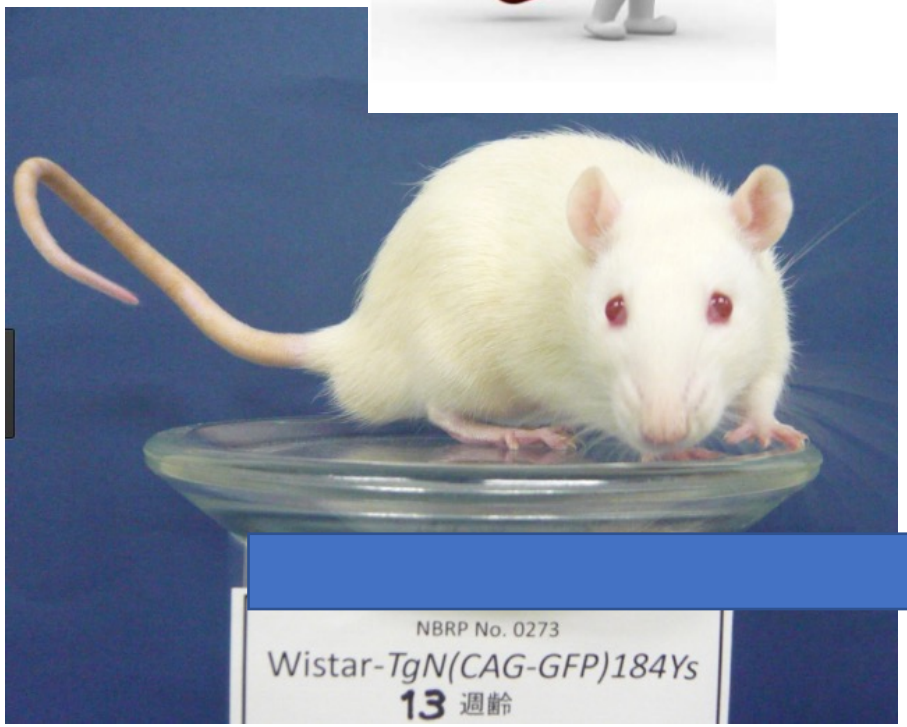
1

The "one pill fits all" concept no longer supported as each group of individuals carry a different blueprint !
An extraneous variable that wholly or partially accounts for the observed ***effect*** *on disease status*

Clinical development not possible without animal pharmacology

THANK YOU…….

DO YOU HAVE ANY QUESTIONS ?



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