Important Factors To Consider For Clinical Trial Success

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We want the best possible cancer therapy.

SAKK
WE BRING PROGRESS TO CANCER CARE

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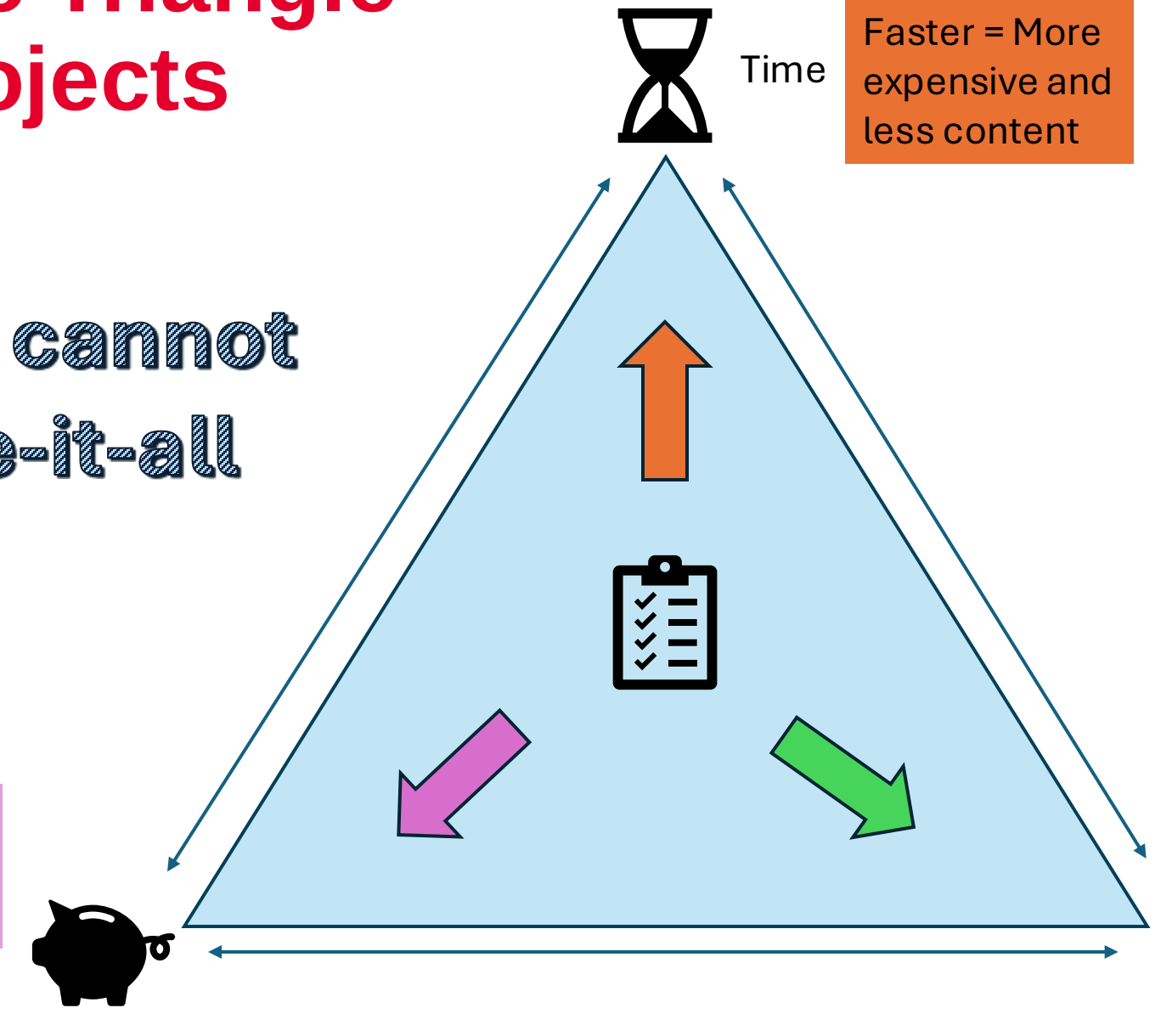
What makes a great idea?

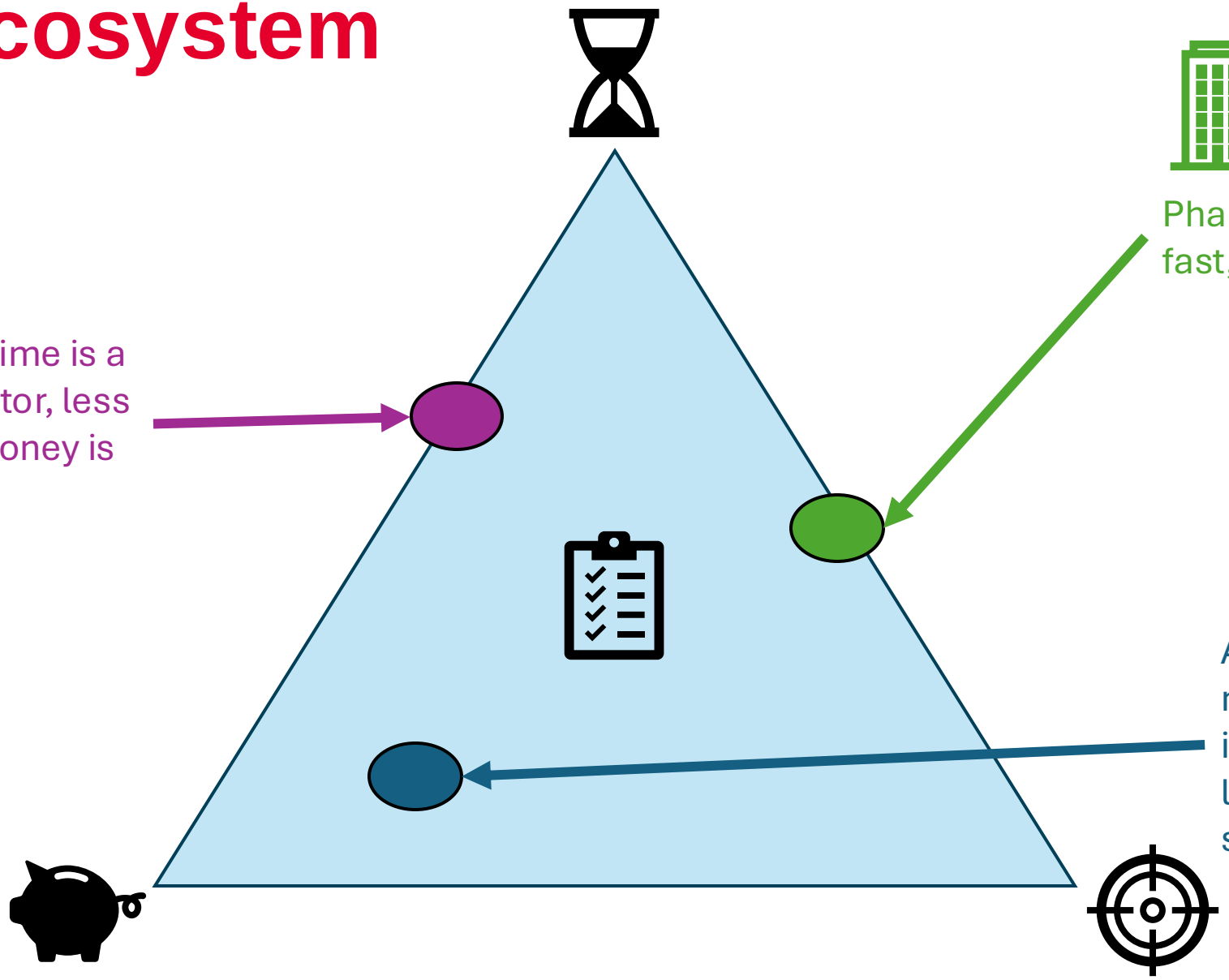
Simple	• Like everything else in life, simpler is better (EC, SwissMedic, Patients…)
Pragmatic	• Follows the standard of care (re-imbursed by insurances) • Cost efficient (less project and safety management)
Concerns many patients	• You will need to recruit/convince patients! • Dynamic is essential (if people loose steam, so does the trial)

Magic Triangle in Projects

One cannot have-it-all



Our ecosystem



Start-ups: time is a survival factor, less focused, money is an issue

Pharma: Very focused and fast, money is secondary

Academia: Money is the most critical part, focus is a concern, time is not a limiting step (for tenured-scientists)

Our ecosystem

Pharma: Very focused and fast, money is secondary

If you have more resources, invest in time, not scope

What are the failure factors

- Over specialized (scope-focused… loose time and money)
- Wanting to do-it-all (scientific question + change of practice + biobanking + translational)
- Make choices: only answer YOUR question, multiplicity is NOT a plus
- Over ambitious: while we all want “practice changing” phase 3 trials, feasibility and proof of concepts are good ways to start and leverage funding
- Pharma-like trials… in academia

Always start with a question

Scientifically sound	Supported by literature real-world data/registries Or “Lack of Knowledge”
Easy to explain	Could be summarized in 2 sentences max (e.g., Pitch elevator = 30 sec)
Anything that could be answered with a measurable hard fact.	No measurements, no statistics, no proof Anything that depends on a subjective assessment is in danger

How do Pharma design their trials?

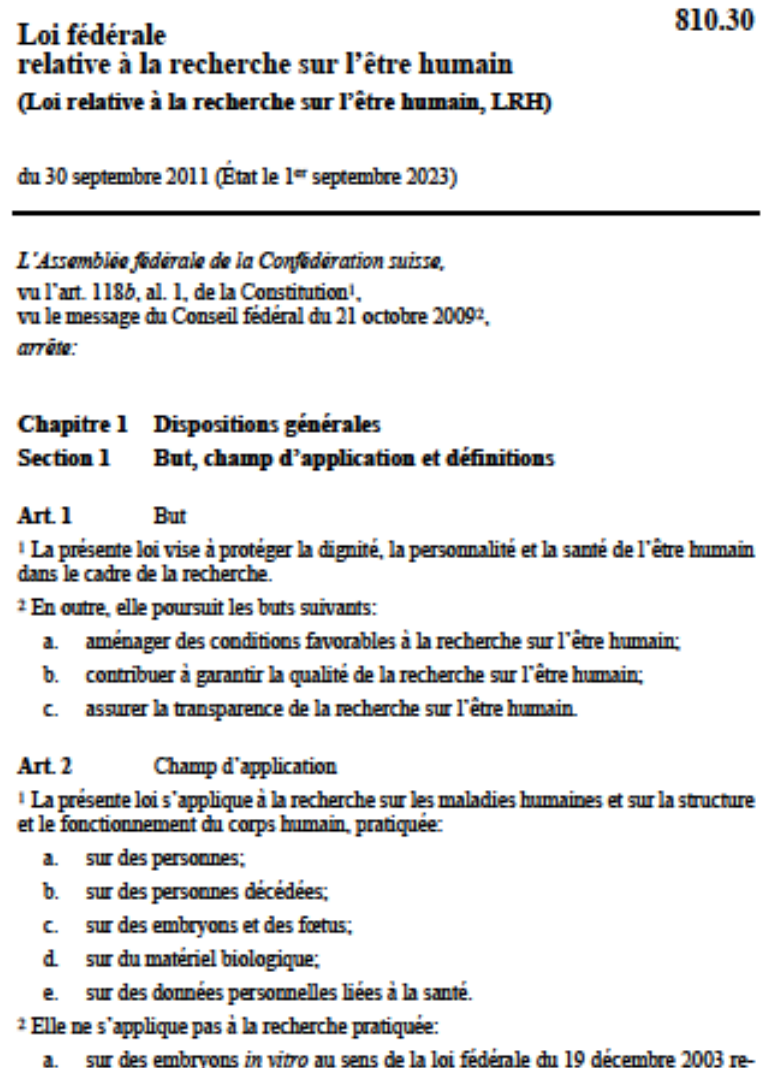
- Answer a large medical need (wide market)
- Select the best fitted patients (narrow in-/exclusion criteria)
- Short-timed end points (even non-clinical endpoints)
- Articulated around a global strategy (that took years to develop)
- Collect as much data as possible

Do not overthink about ethic or regulators

At the beginning, many question come as: what would Swissmedic say or think?

Just keep in mind that according to the HRA

1. Swissmedic has to assess the safety of the drug
2. Ethics boards have to ensure the patients' rights



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Loi fédérale
relative à la recherche sur l'être humain
(Loi relative à la recherche sur l'être humain, LRH)

du 30 septembre 2011 (État le 1er septembre 2023)

L'Assemblée fédérale de la Confédération suisse,
vu l'art. 118*b*, al. 1, de la Constitution[1],
vu le message du Conseil fédéral du 21 octobre 2009[2],
arrête:

Chapitre 1 Dispositions générales
Section 1 But, champ d'application et définitions

Art. 1 But

[1] La présente loi vise à protéger la dignité, la personnalité et la santé de l'être humain dans le cadre de la recherche.

[2] En outre, elle poursuit les buts suivants:

a. aménager des conditions favorables à la recherche sur l'être humain;
b. contribuer à garantir la qualité de la recherche sur l'être humain;
c. assurer la transparence de la recherche sur l'être humain.

Art. 2 Champ d'application

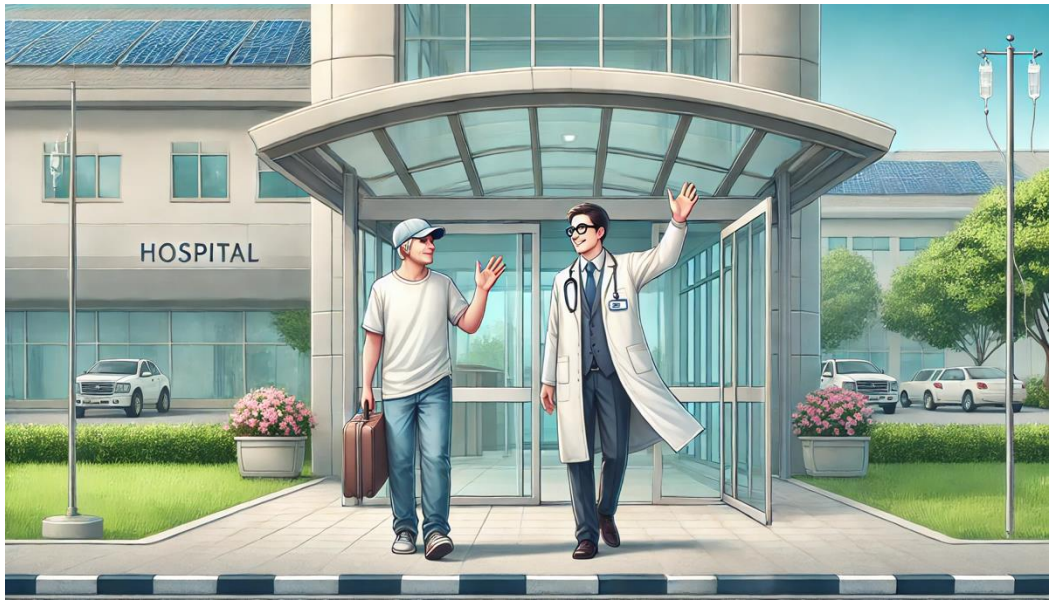
[1] La présente loi s'applique à la recherche sur les maladies humaines et sur la structure et le fonctionnement du corps humain, pratiquée:

a. sur des personnes;
b. sur des personnes décédées;
c. sur des embryons et des fœtus;
d. sur du matériel biologique;
e. sur des données personnelles liées à la santé.

[2] Elle ne s'applique pas à la recherche pratiquée:

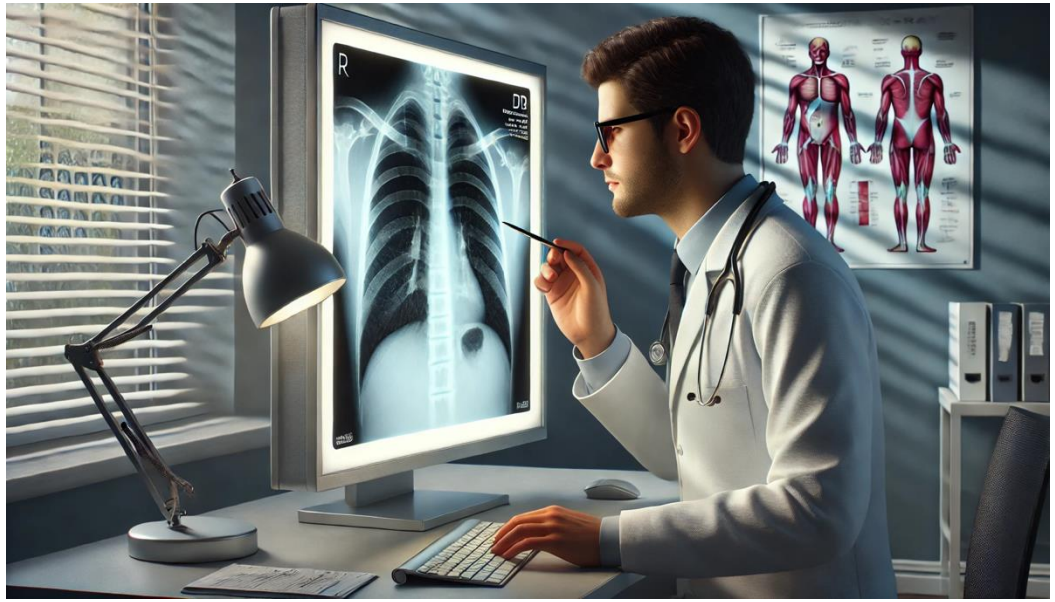
a. sur des embryons *in vitro* au sens de la loi fédérale du 19 décembre 2003 re-

Objective Vs Endpoint



Objective: cured patient

Endpoint: clean X-ray



Design Objective & Endpoints

1st: Objective

The trial idea is driven by an objective (what you want to show/demonstrate)

It ends up being successful or not (binary)

2nd Endpoint

The endpoint is the measurable that demonstrate if the objective is achieved or not.

It should be a numerical value (statistical analysis)

Powered?

More Endpoints & Objectives ?

3rd Secondary Endpoints:

What can we learn more?

Next project?

Save samples for later?

Use the data to pool with another project?

Choose your endpoint wisely

only 1 primary endpoint

Only this one will be statistically powered

Only this one will determine the success of the trial

Secondary endpoints are exploratory

Should not generate extra procedure and patients visits

Secondary endpoints are meant to open new questions, not give new answers

Your next trial!

Design your first synopsis

- Get acquainted to a synopsis
- Write a 1-pager for your colleagues/friends
- Challenge ASAP (fail fast)
- Describe your question to biostatisticians and let them design the model
- Makes assumptions, be ready to be wrong
- Get ready to pitch and be ready to hear some hard truth
- There is no perfect design, only compromise-resulting choices

Key parts of the CTP

1- Synopsis

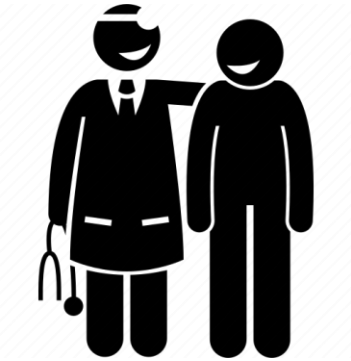
1-2 pages overview of the clinical trial presented as a table

Decisive criteria for the evaluation of success… Should be picked carefully!

Sponsor / Sponsor-Investigator
Study Title:
Short Title / Study ID:
Protocol Version and Date:
Trial registration:
Study category and Rationale
Clinical Phase:
Background and Rationale:
Objective(s):
Outcome(s):
Study design:
Inclusion / Exclusion criteria:
Measurements and procedures:
Study Product / Intervention:
Control Intervention (if applicable):
Number of Participants with Rationale:
Study Duration:
Study Schedule:
Investigator(s):
Study Centre(s):
Statistical Considerations:
GCP Statement:

Key parts of the CTP

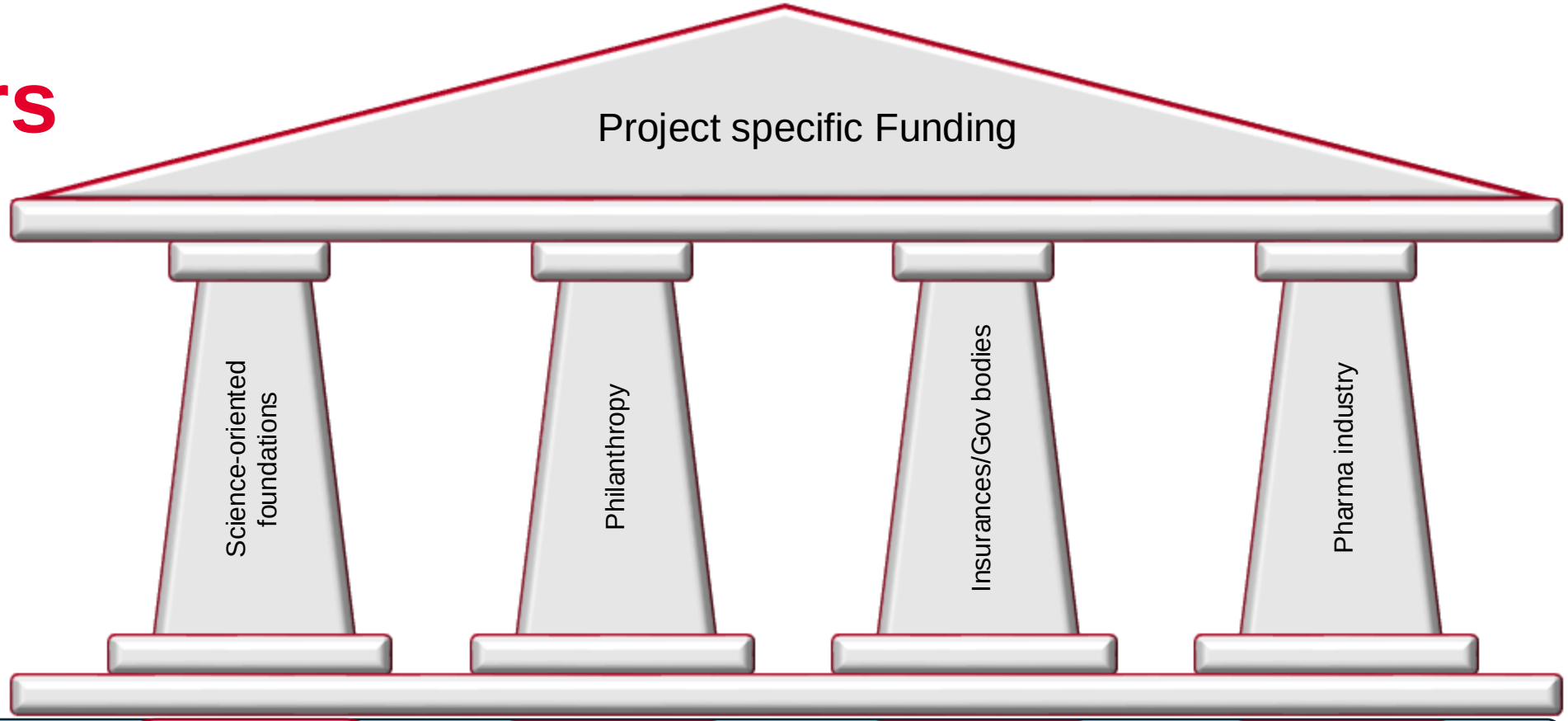
2- Study Schedule



1 page outlook of the clinical trial procedures:

Study Periods	Screening	Treatment, Intervention Period				Follow-up
Visit	1	2	3	4	5	6
Time (hour, day, week)	-7	0	1	8+/-1d	15+/-2d	22
Patient Information and Informed Consent	x					
Demographics	x					
Medical History	x					
In- /Exclusion Criteria	x	x				
Physical Examination	x					x
Vital Signs	x	x	x	x	x	x
Laboratory Tests	x				x	x
Pregnancy Test	x					(x)
Randomisation		x				
Other examinations, tests…	x			x		x
Other examinations, tests…	x					
Administer Study Medication		x	x	x	x	
Primary Variables	x	x	x	x	x	x
Secondary Variables	x	x	x	x	x	x
Concomitant Therapy, Intervention		x	x	x	x	
Adverse Events		x	x	x	x	x

4 pillars



	Science-oriented foundations	Philanthropy	Insurances/Gov bodies	Pharma industry
Examples	• Rising Tide • Krebs Liga/KFS • Smaller funds	• Banks • Family offices • Philanthropic funds	• BAG • Curafutura/ Santésuisse	• Big Ones • Biotechs • Start-ups
Their Goals	• Support research(ers) • Generate knowledge	• Improve people's lives • Positive image • Indication-centered?	• Reduce costs • Reduce interventions	• Find new indications • Show better potency • Small/risky indications
Project they might fund?	• Good scientific questions • Solid scientific background	• Patient-centered projects • Human-related outcome	• Dose de-escalation projects • Treatment selection on outcome	• Drug repurposing • Drug combinations • GAP trials

SNF, Rising Tides, Krebsliga

- Letter of intend (couple of pages)
- Patient advisory board
- Full application (50 pages)
  - Budget
  - Detailed plan

- Reviews (international?) and board
- Very competitive

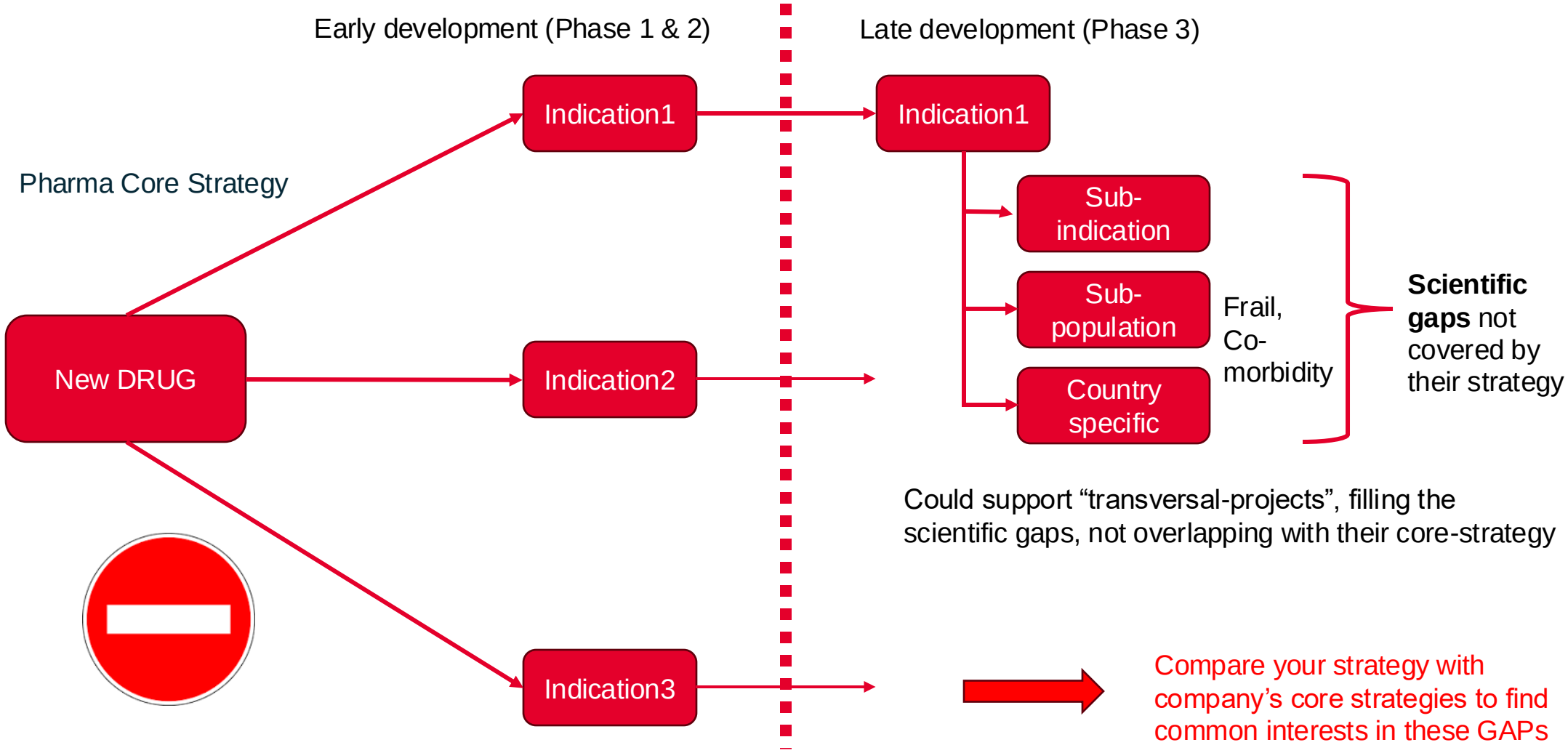
Investigator Initiated Trial (IIT) vs Collaboration

- IIT were originally, a tool for Pharma to provide a drug to a Key Opinion Leader to “play” with in order to generate habits and subsequent prescriptions
- Clinicians have total freedom, the company takes it or leave it (IP to the company, data to the scientists)
- Collaboration is the new trend
- Negotiations possible, win-win approach (Data shared between the scientists and the company)

Pharma meetings

- Be goal-oriented
  - Project Pitch
- Select the right people mix
  - Area specialist, Drug-lead, Medical Experts
  - Swiss affiliate, Regional, Global
- Set the right Timing
  - ASCO, ESMO, SOHC, HJV, Ad-Hoc
  - Life cycle of the drug (end of patent, or unmature safety profile)

GAP scientific question



(Don’t forget) Registries

- Useful tool when you feel something but cannot really point out the issue
- Usually agnostic, no in/exclusion criteria as it follows the current practice
- Consign patients' history and drug treatments (patient’s journey)
- If well structured could be used to test your intuition and generate a trial
- Cheaper and well funded by local branches of Pharma