Assembling the Best Team to Navigate Through Preclinical Development

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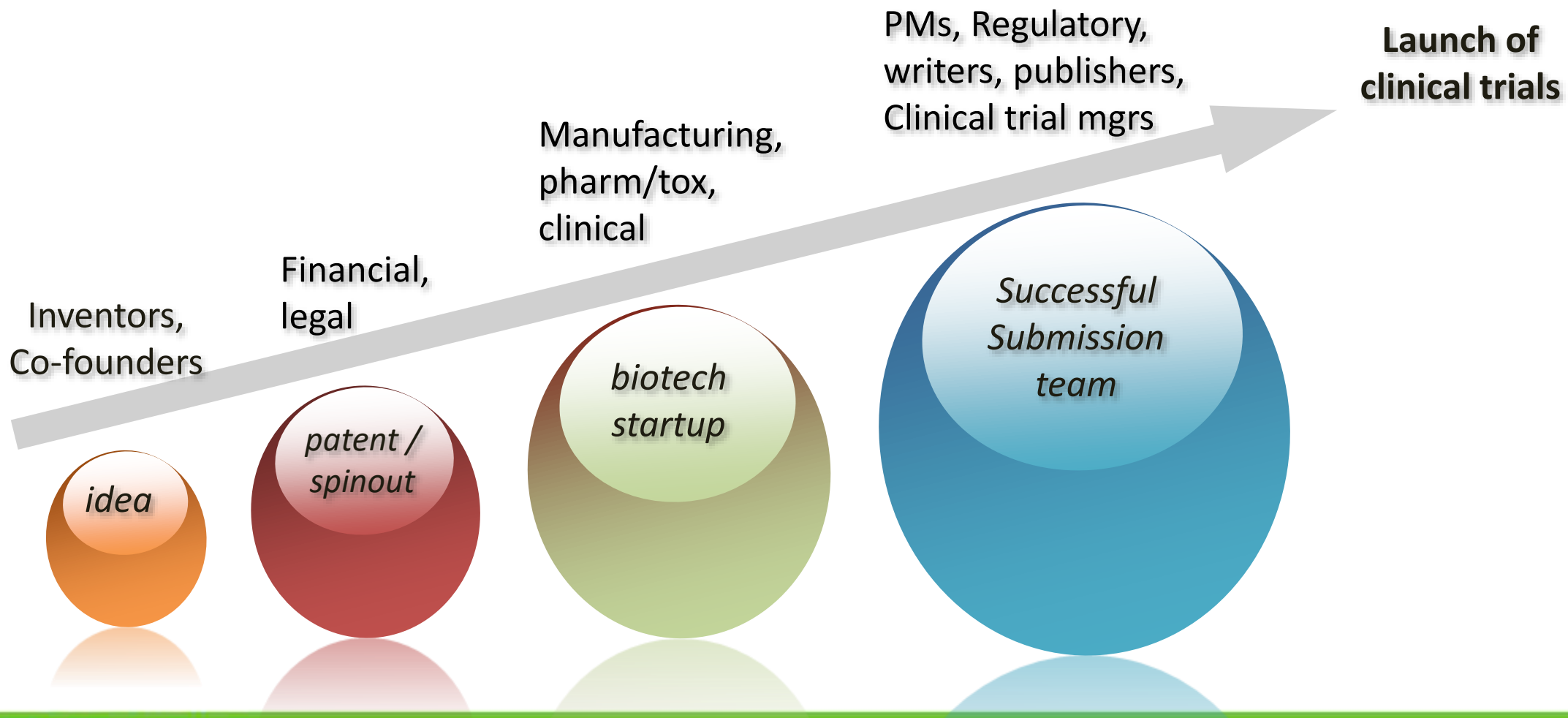
Preclinical development requires new partners



The transition from academic research to preclinical development:

Study Planning

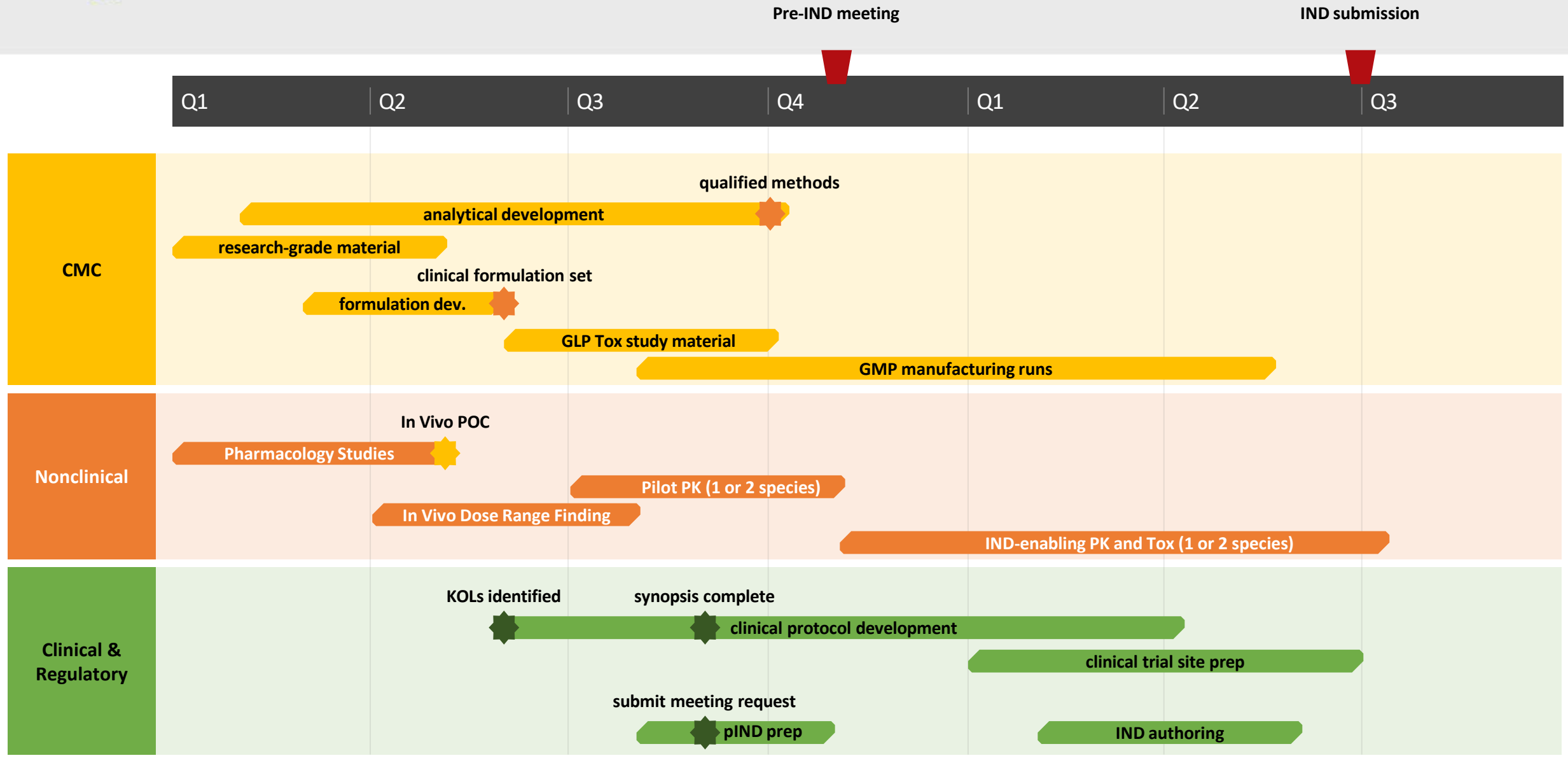
Preclinical Study Planning: Common Pitfalls

"Our work was already published in Nature, so the FDA should have everything they need in our papers…"

"Let's just wait and not plan on doing any more studies, - the FDA will tell us what we have to do…"

"Let's skip the pre-IND meeting. If we meet with the FDA in advance, they'll make us do a bunch of studies we don't want to do…."

What studies do I need for an IND?



When can we have a pre-IND meeting? What about an INTERACT meeting?

For a pre-IND:

- Is lead optimization complete? Is the clinical candidate set?
- Is the manufacturing process set? Has it been reviewed by a GMP-compliant manufacturer?
- Are all pharmacology and toxicology studies planned?
- How concrete are plans for the clinical trial?
  - Patient population, eligibility criteria
  - Dosing regimen, combination with any other therapies

Pharm/Tox Study Planning:

Make a table of all studies that will be needed in the IND

	In vitro Pharmacology	In Vivo Pharmacology	Pilot PK / biodistribution	Toxicology
Objectives	Binding / specificity	Efficacy	Species cross-reactivity, pilot safety	safety
Model	Ligand-binding or cell-based assays	Rodent and non-rodent models of disease	Varies	Healthy animals, if product is biologically active
Laboratory	In-house	In-house	CRO	CRO
Compliance	Non-GLP	Non-GLP	Varies	GLP
Material	Research grade	Research grade (lead candidate)	research grade (clinical candidate)	clinical grade (or representative)
Timing	Before meeting with FDA	Before meeting with FDA	Before pre-IND	After pre-IND

Executing IND-Enabling Studies

- Who will write the protocol?
  - For in vivo studies, IACUC protocol is not the same as study protocol
- Who will be the study director?
- Who will write the study report?
  - study reports for regulatory submission are very different from manuscripts for publication
  - Consider sub-reports
- Which CRO is most appropriate?
  - GLP compliance, test article characterization, assay qualification

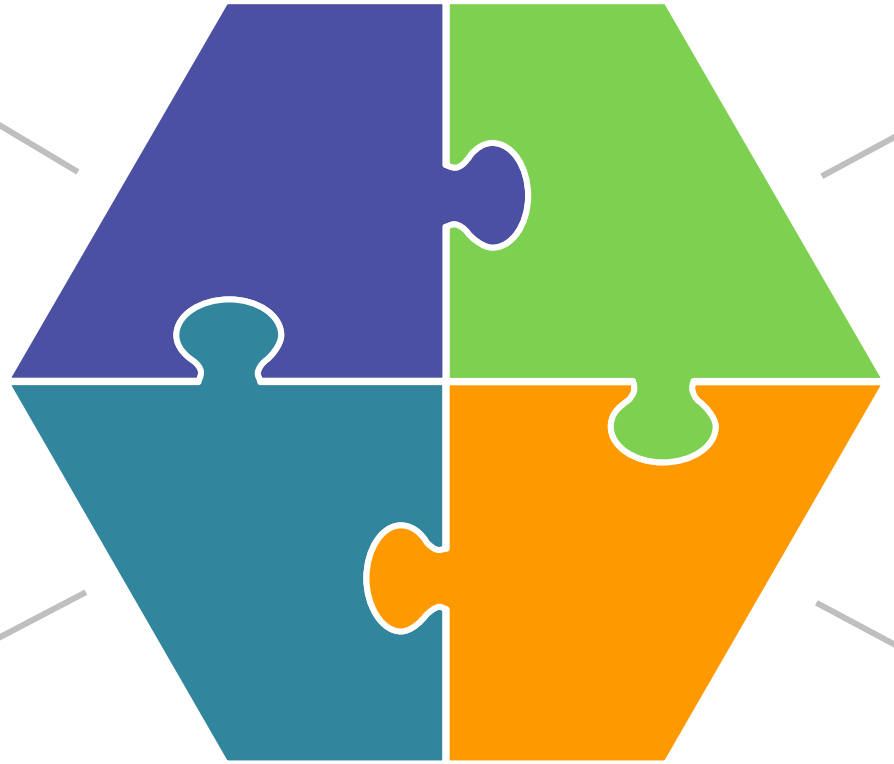
Preclinical development costs

	Potential range	Contributing factors
Pharmacology studies (efficacy, dose-range finding)	$20K - $100k+	Species (rodent, non-rodent) Duration, # doses
Assay development (e.g. for detection of product in animal matrices)	$25K-100K+	Number of matrices, analytes Level of qualification required
Safety studies	$100K – 400K (rodent) $300K – 1M+ (non-rodent)	Species (rodent, non-rodent) Duration, # doses Compliance (GLP)
Writers and publishing/submission support	$20K - $100K+	# reports # pages # datasets Use of eCTD templates US Agent

Common preclinical issues with regulatory implications

- Initial pharm/tox studies were not done with the same product
- Consideration of regulatory feedback in study designs
- Change in formulation (buffer, temperature)
- Genetic engineering:
  - Change in coding sequence
  - Change in plasmid design
- <u>Incorrect assumptions (without supporting data):</u>
  - Species cross reactivity and immune response
  - Repeat dosing
- Delivery device: approval/compatibility for use with investigational product

Key Players on the Preclinical Team



Sponsor, inventors,
Clinical investigators

Preclinical experts
Manufacturing experts
CROs

Financial /
legal support

Project managers, regulatory
writers, publishers, US agent

Final thoughts

Team	Start assembling your team early!
Experience	Seek out experts with experience with your product type, including successful regulatory submissions
Focus	Build submission teams around a singular product and/or clinical trial

Thank you!!

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