Fast-track drug development

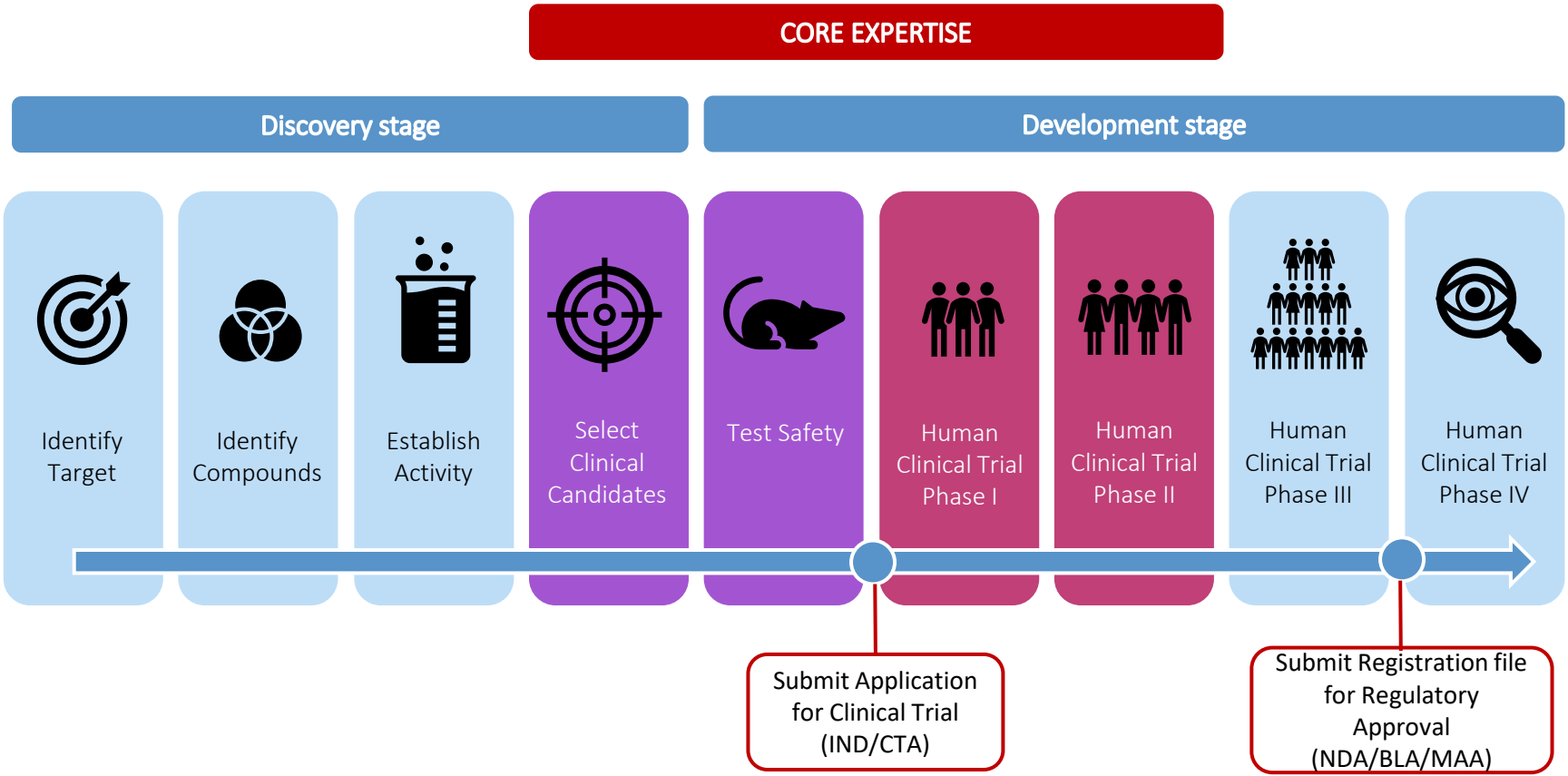
taking the highway or the roundabout?

Ronald van der Geest, Co-founder

For: *Molecule to Business*

NovioTech Campus - May 25, 2023

3D-PHARMXCHANGE CONSULTANCY & PROJECT MANAGEMENT



BRIDGING THE VALLEY OF DEATH

WHAT IT IS:

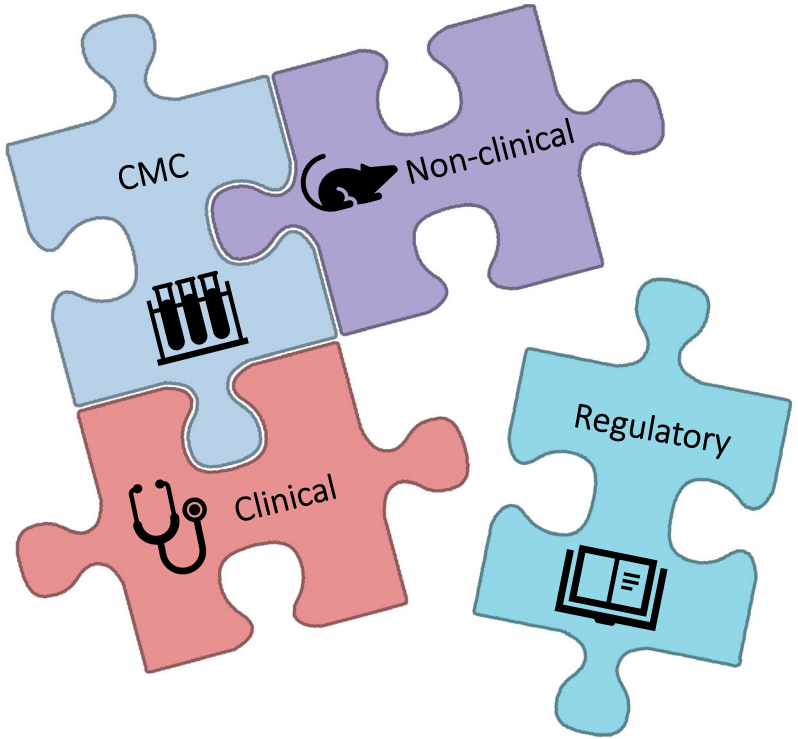
High risk phase between discovery and (partially) derisked late-stage development & commercialisation

”From bench to bedside”

Translational R&D

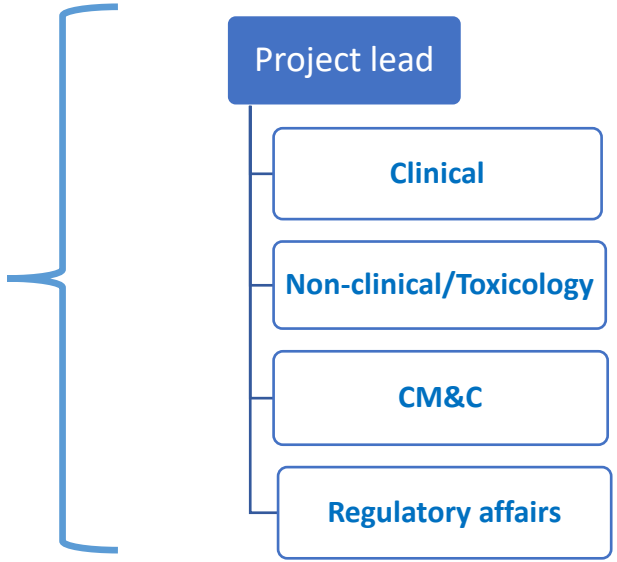
B. Mellor, Nature 2008

ORGANISATIONAL ASPECTS: CROSS-FUNCTIONAL TEAMWORK



ORGANISATIONAL ASPECTS: THE CORE PROJECT TEAM

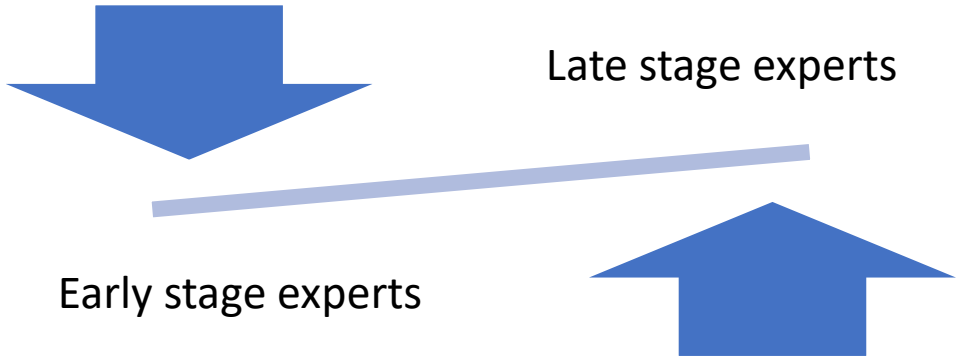
WHO NEEDS TO BE IN?



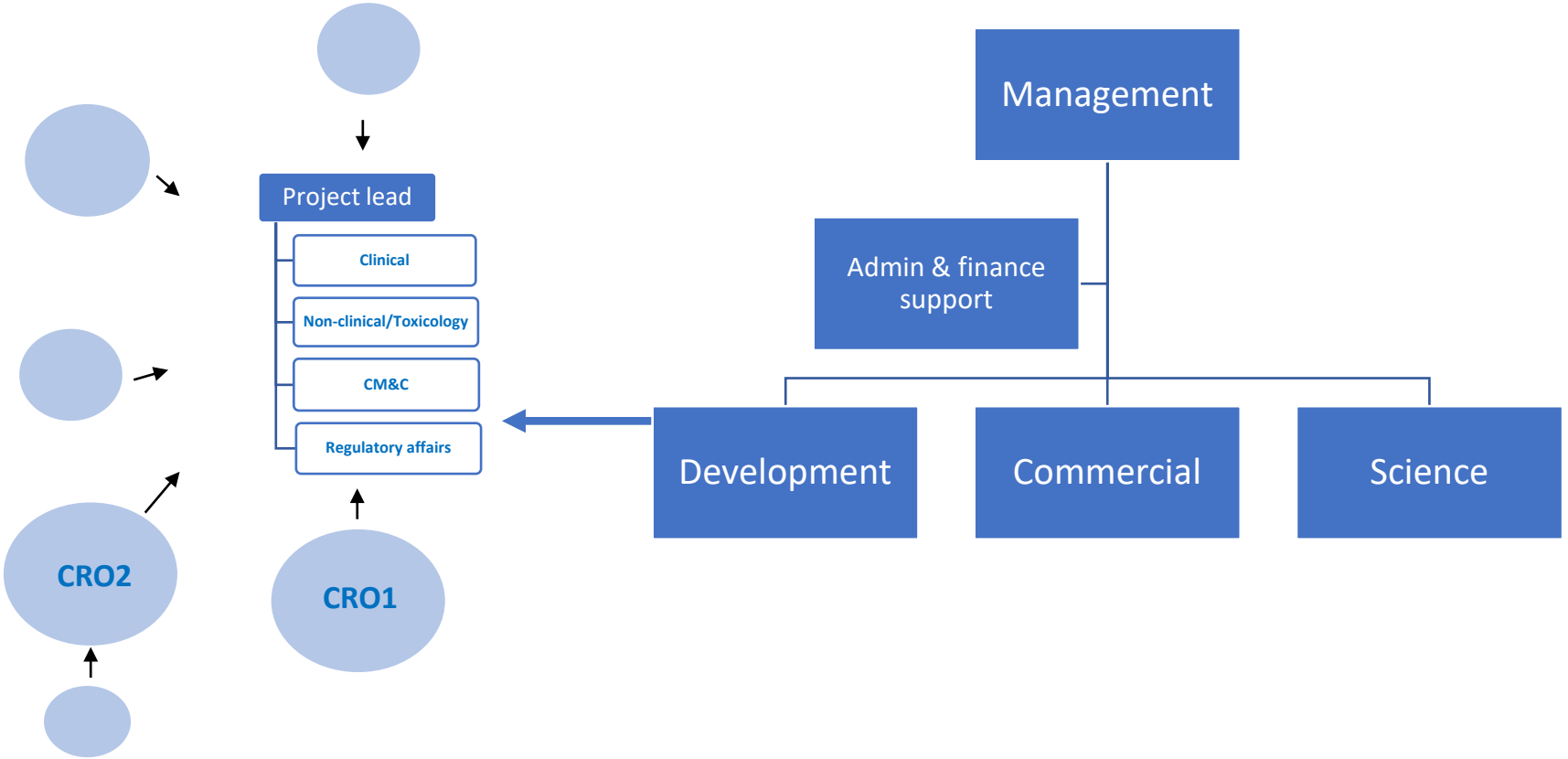
ORGANISATIONAL ASPECTS: CORE TEAM GOOD PRACTICES

Staff the core project team as early as possible and assure:

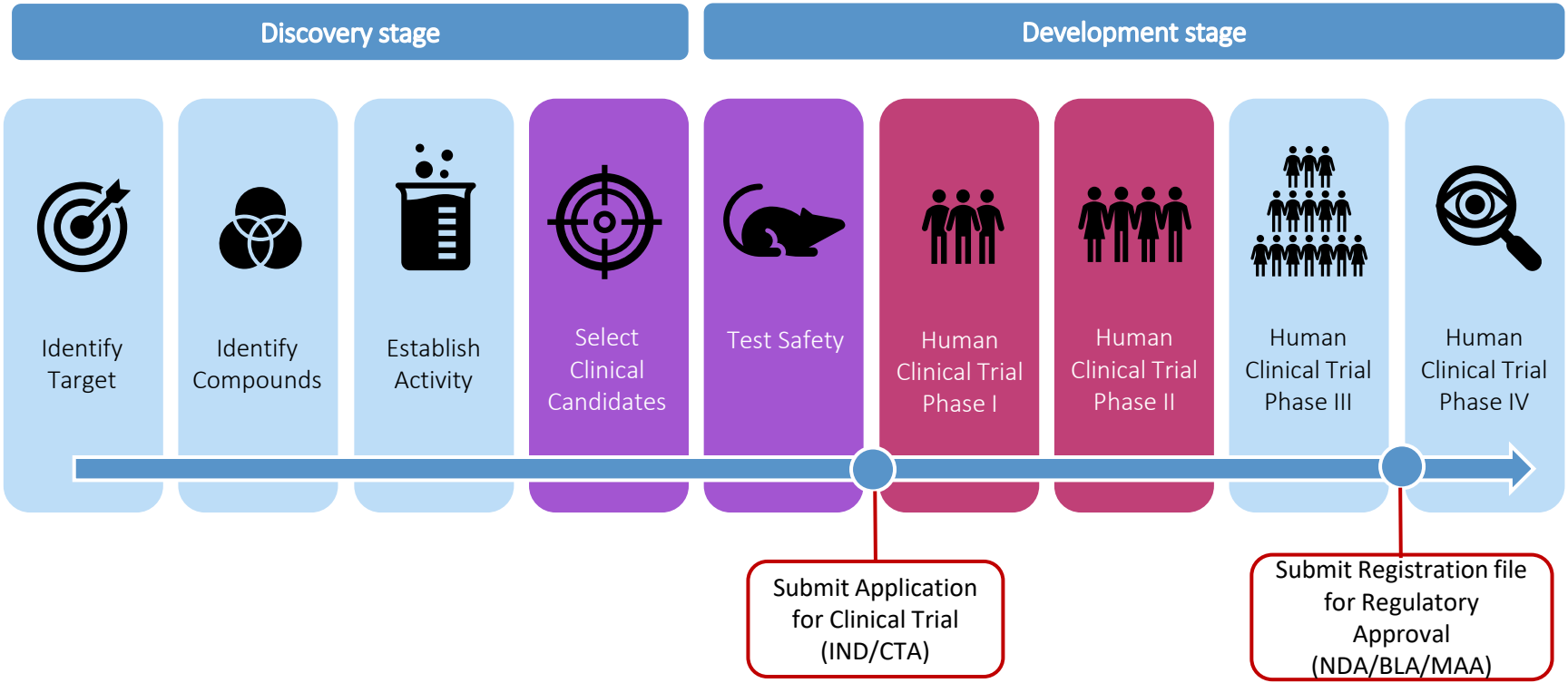
- completeness
- availability
- continuity within the team
- alignment with the company goals
- allow flexibility within the team



FIT OF THE TEAM IN THE ORGANISATION

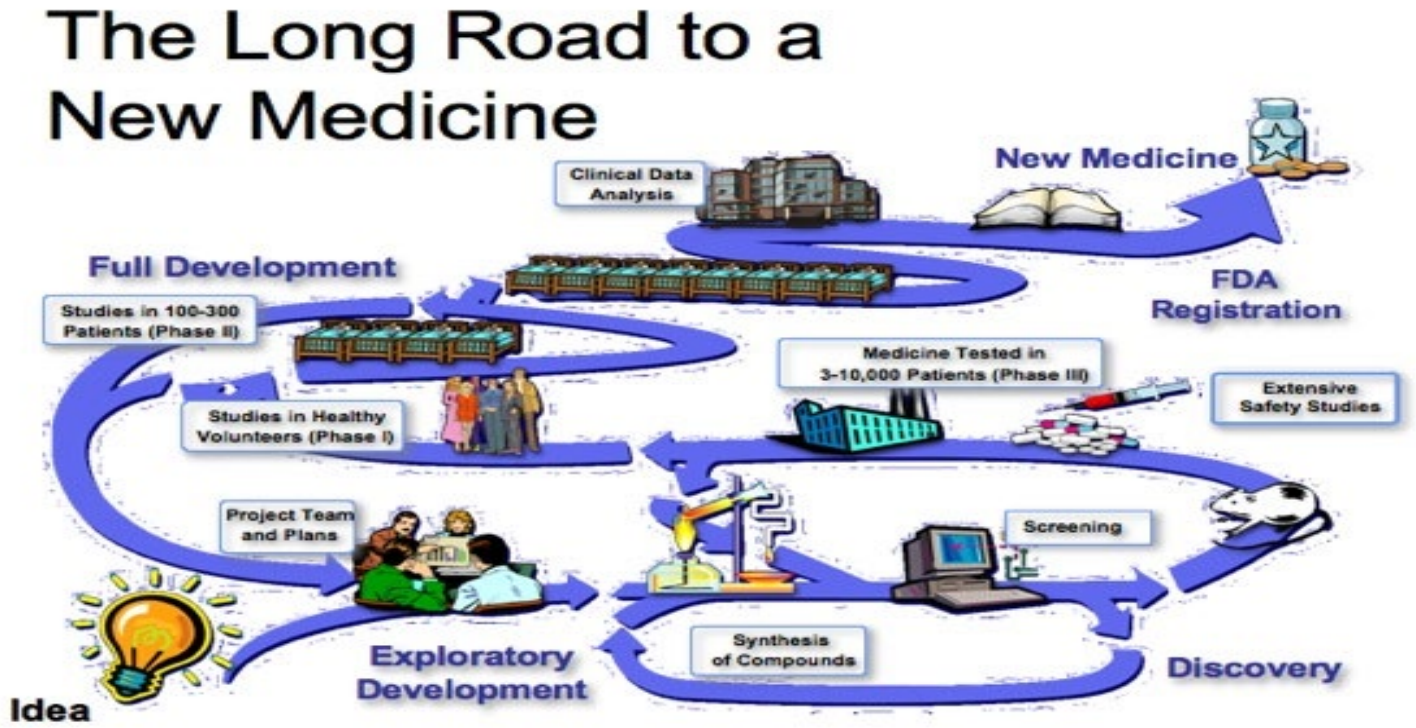


DRUG DEVELOPMENT PHASES – TEXTBOOK EXAMPLE

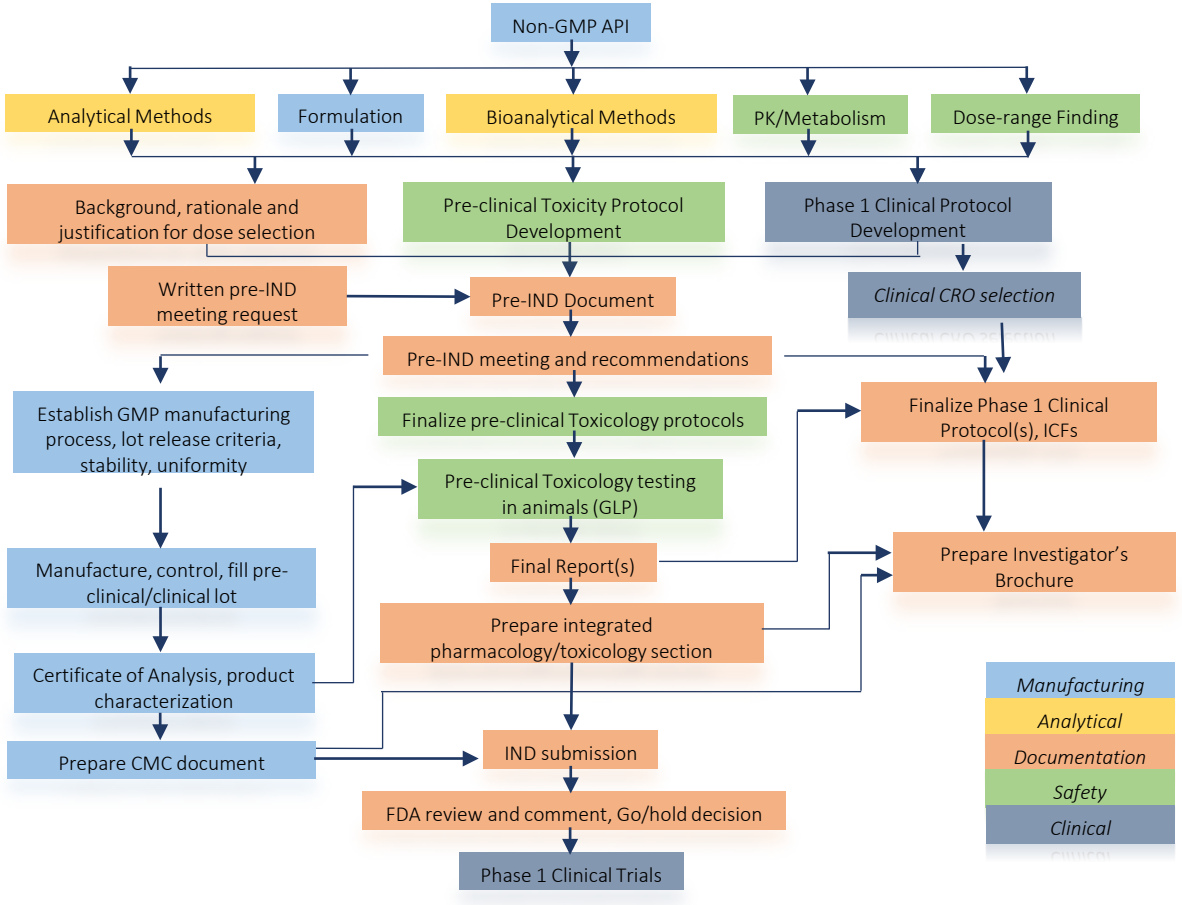


BUT IN PRACTICE …

TAKING A MORE CLOSER LOOK AT REALITY …



WHAT NEEDS TO BE IN PLACE PRIOR TO A FIRST-IN-HUMAN TRIAL?



WHAT DOES AN INTEGRATED DEVELOPMENT PLAN LOOK LIKE?

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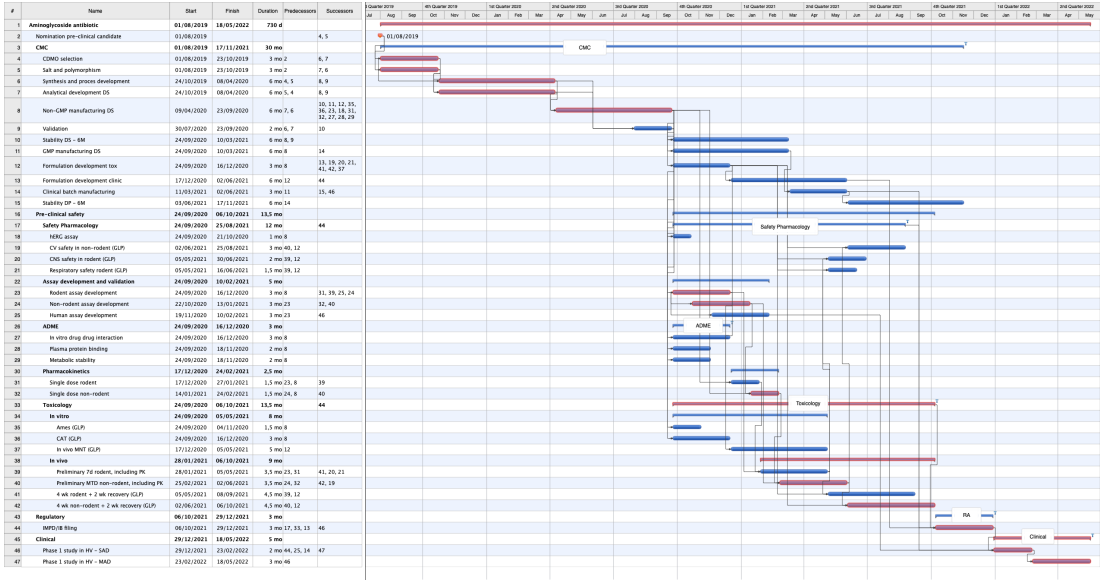

#	Name	Start	Finish	Duration	Predecessors	Successors
1	**Aminoglycoside antibiotic**	**01/08/2019**	**18/05/2022**	**730 d**		
2	Nomination pre-clinical candidate	01/08/2019				4, 5
3	**CMC**	**01/08/2019**	**17/11/2021**	**30 mo**		
4	CDMO selection	01/08/2019	23/10/2019	3 mo 2		6, 7
5	Salt and polymorphism	01/08/2019	23/10/2019	3 mo 2		7, 6
6	Synthesis and proces development	24/10/2019	08/04/2020	6 mo 4, 5		8, 9
7	Analytical development DS	24/10/2019	08/04/2020	6 mo 5, 4		8, 9
8	Non-GMP manufacturing DS	09/04/2020	23/09/2020	6 mo 7, 6		10, 11, 12, 35, 36, 23, 18, 31, 32, 27, 28, 29
9	Validation	30/07/2020	23/09/2020	2 mo 6, 7		10
10	Stability DS - 6M	24/09/2020	10/03/2021	6 mo 8, 9		
11	GMP manufacturing DS	24/09/2020	10/03/2021	6 mo 8		14
12	Formulation development tox	24/09/2020	16/12/2020	3 mo 8		13, 19, 20, 21, 41, 42, 37
13	Formulation development clinic	17/12/2020	02/06/2021	6 mo 12		44
14	Clinical batch manufacturing	11/03/2021	02/06/2021	3 mo 11		15, 46
15	Stability DP – 6M	03/06/2021	17/11/2021	6 mo 14		
16	**Pre-clinical safety**	**24/09/2020**	**06/10/2021**	**13,5 mo**		
17	**Safety Pharmacology**	**24/09/2020**	**25/08/2021**	**12 mo**		**44**
18	hERG assay	24/09/2020	21/10/2020	1 mo 8		
19	CV safety in non-rodent (GLP)	02/06/2021	25/08/2021	3 mo 40, 12		
20	CNS safety in rodent (GLP)	05/05/2021	30/06/2021	2 mo 39, 12		
21	Respiratory safety rodent (GLP)	05/05/2021	16/06/2021	1,5 mo 39, 12		
22	**Assay development and validation**	**24/09/2020**	**10/02/2021**	**5 mo**		
23	Rodent assay development	24/09/2020	16/12/2020	3 mo 8		31, 39, 25, 24
24	Non-rodent assay development	22/10/2020	13/01/2021	3 mo 23		32, 40
25	Human assay development	19/11/2020	10/02/2021	3 mo 23		46
26	**ADME**	**24/09/2020**	**16/12/2020**	**3 mo**		
27	In vitro drug drug interaction	24/09/2020	16/12/2020	3 mo 8		
28	Plasma protein binding	24/09/2020	18/11/2020	2 mo 8		
29	Metabolic stability	24/09/2020	18/11/2020	2 mo 8		
30	**Pharmacokinetics**	**17/12/2020**	**24/02/2021**	**2,5 mo**		
31	Single dose rodent	17/12/2020	27/01/2021	1,5 mo 23, 8		39
32	Single dose non-rodent	14/01/2021	24/02/2021	1,5 mo 24, 8		40
33	**Toxicology**	**24/09/2020**	**06/10/2021**	**13,5 mo**		**44**
34	**In vitro**	**24/09/2020**	**05/05/2021**	**8 mo**		
35	Ames (GLP)	24/09/2020	04/11/2020	1,5 mo 8		
36	CAT (GLP)	24/09/2020	16/12/2020	3 mo 8		
37	In vivo MNT (GLP)	17/12/2020	05/05/2021	5 mo 12		
38	**In vivo**	**28/01/2021**	**06/10/2021**	**9 mo**		
39	Preliminary 7d rodent, including PK	28/01/2021	05/05/2021	3,5 mo 23, 31		41, 20, 21
40	Preliminary MTD non-rodent, including PK	25/02/2021	02/06/2021	3,5 mo 24, 32		42, 19
41	4 wk rodent + 2 wk recovery (GLP)	05/05/2021	08/09/2021	4,5 mo 39, 12		
42	4 wk non-rodent + 2 wk recovery (GLP)	02/06/2021	06/10/2021	4,5 mo 40, 12		
43	**Regulatory**	**06/10/2021**	**29/12/2021**	**3 mo**		
44	IMPD/IB filing	06/10/2021	29/12/2021	3 mo 17, 33, 13		46
45	**Clinical**	**29/12/2021**	**18/05/2022**	**5 mo**		
46	Phase 1 study in HV – SAD	29/12/2021	23/02/2022	2 mo 44, 25, 14		47
47	Phase 1 study in HV – MAD	23/02/2022	18/05/2022	3 mo 46		

Gantt chart

HOW TO DO CRO SELECTION & BUDGETTING?

	CRO 1	CRO 2	CRO 3	CRO 4
1 Study Initiation	**10000**	**13160**	**24609**	**36510**
1.1 Protocol				
1.2 Investigator's Brochure				
1.3 Volunteer Information				
1.4 CRF				
1.5 IMPD				
1.6 Submissions to EC and CA				
2. Clinical execution	**72429**	**132272**	**194710**	**234012**
2.1 Recruitment (incl. volunteer fee + screening)				
2.2 Volunteer insurance				
2.3 Handling of supplies (include destruction, if possible)				
2.4 Clinical Conduct				
2.5 Lab safety				
2.6 CRF Handling				
3. Data management	**3186**	**10600**	**49092**	**14919**
3.1 Database Set-up				
3.2 Data Preparation / Handling				
3.3 Data Entry				
3.4 Checks / Validation				
3.5 Coding				
3.6 SAE-Reconciliation				
3.7 Data transfer				
4. Analytics and Pharmacokinetics	**284**	**2972**	**51004**	**45520**
4.1 Sample Handling / Shipment				
4.2 Generation of analytical protocol				
4.3 Assay Development / Validation				
4.4 Sample Analysis				
4.5 Analytical Report				
5. Statistics	**0**	**15780**	**17758**	**14038**
5.1 Statistical Analysis Plan				
5.2 Randomization				
5.3 Data Preparation / Handling				
5.4 Listings, Figures, Tables				
5.5 PK Evaluation				
5.6 Statistical Tests				
6. Medical Report	**0**	**10600**	**14191**	**9350**
7. Other	**3115**	**7340**	**14420**	**9880**
GRAND TOTAL	**89014**	**192724**	**365784**	**364229**

QUESTION: THE CONTRIBUTION OF “THE HUMAN FACTOR” ON SUCCESS?

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70/30 RATIO

SIMILAR DRUG-DEVICE COMBO & INDICATION - DIFFERENT PROGRAMS/SCENARIO's

The human factor in practice

Program I	Program II	Program III
4 phase I trials 1 phase II trial 2 phase III trials 2 open label trials	6 phase I trials 0 phase II trials 2 phase III trials	1 phase I trial 1 small phase II trial
development duration: Est. 5-6 yrs	development duration: Est. 4 yrs	development duration: **Est. 2 yrs**
Est. budget: 105 M	Est. budget: 60 M	Budget: **5-6 M**


WORDS MAY INSPIRE
BUT ONLY ACTIONS CREATE VALUE