Dermatology Innovation Forum
an Advancing Innovation in Dermatology conference

2025 Entrepreneur Bootcamp

Michael D. Howell, PhD; President & Chief Executive Officer, Mountaineer Biosciences, Inc.

Jasmina Jankicevic, MD, MSc, CCRP; Chief Medical & Scientific Officer, Indero

Vijendra Nalamothu, PhD; Founder & Chief Executive Officer, ApoStrata, LLC

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Michael D. Howell, PhD

DIF Entrepreneur Bootcamp
Orlando, Florida
March 6, 2025
9:30 – 11:00AM

MOUNTAINEER BIOSCIENCES

Scientific and Career Journey

PhD
Card Carrying
Immunologist

Spesolimab/SPEVIGO
Rizankizumab/SKYRIZI

Ruxolitinib/OPZELURA
Ruxolitinib/JAKAFI
Povorcitinib
Parsaclisib

Co-Founder/CEO
AhR Modulators

Chief Scientific Officer
Tibulizumab
Torudokimab
Crebankitug

Assistant Professor
Th2 and Epithelial Biology

Tralokinumab/ADBRY
Tezepelumab/TEZSPIRE
Tozorakimab
Brodalumab/SILIQ
MEDI9314

Chief Scientific Officer
Novel Dx Approaches

Board of Directors
SAB

Scientific Advisor
OR-101
OR-102

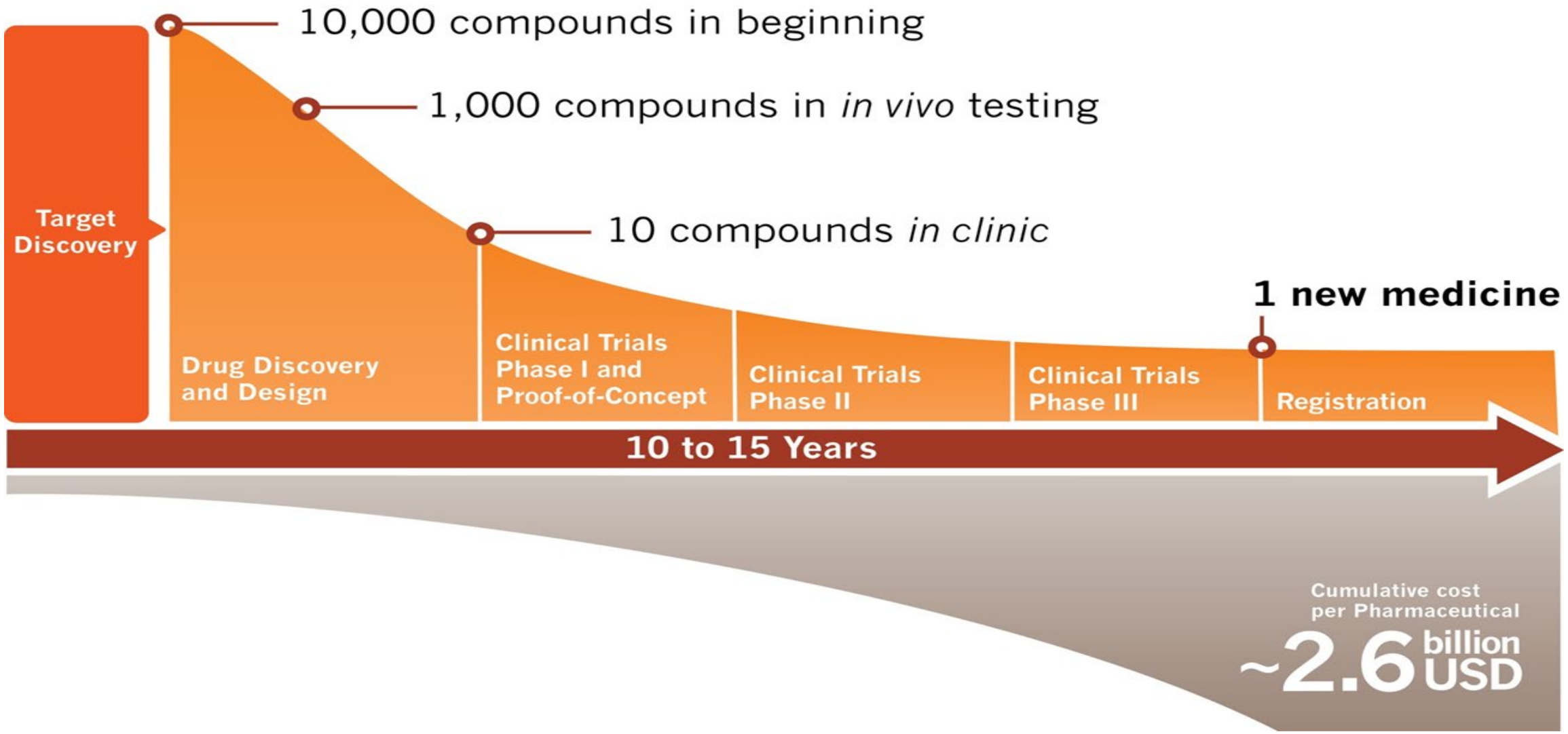
Strategic/Scientific Advisor

- Investment Firms,
- Venture Capital Groups,
- Biotech Startup
- Pharma

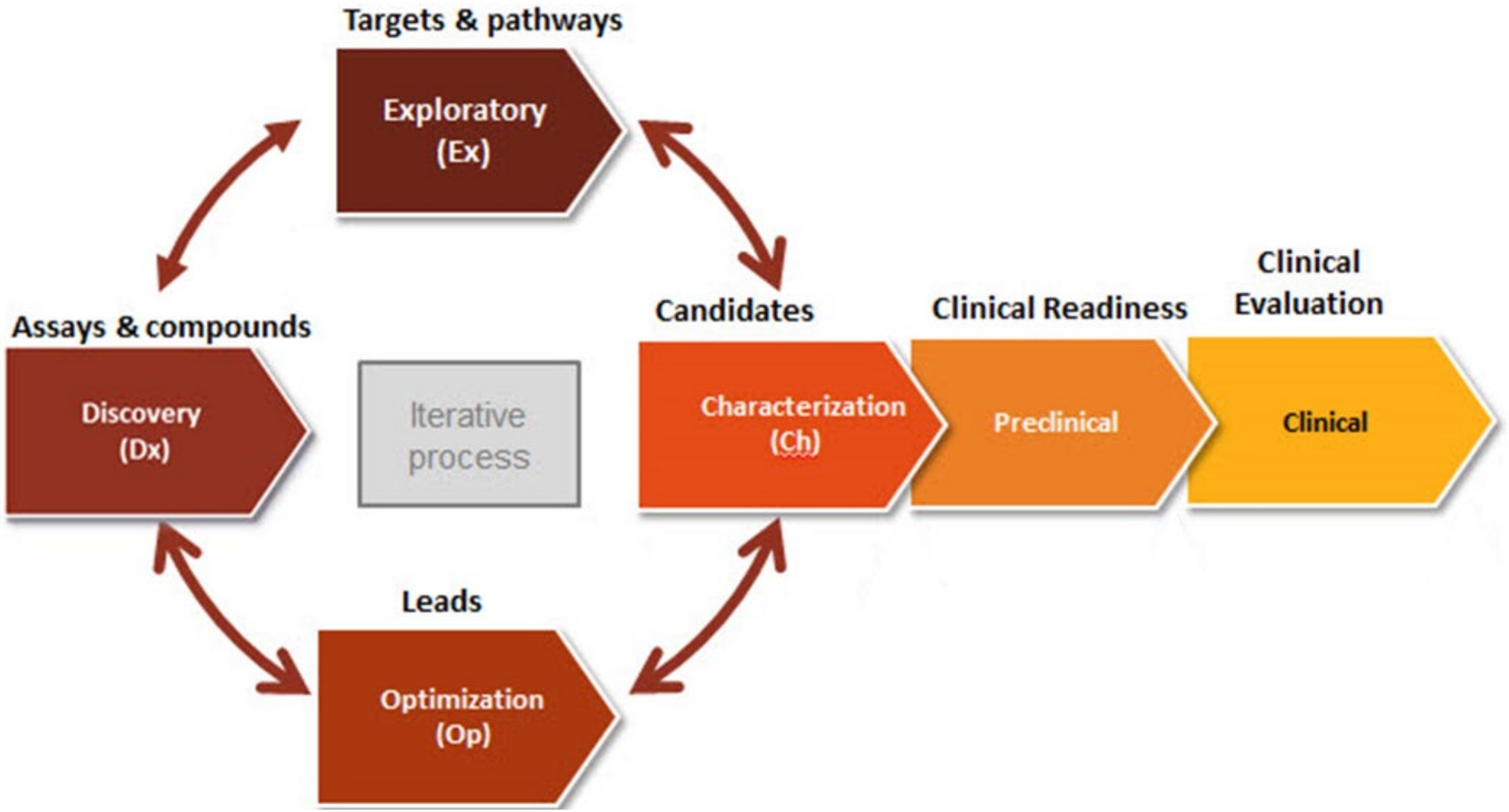
Career has encompassed the research and development of more than seven FDA-approved therapies

“Medicine is not only a science; it is also an art. It does not consist of compounding pills and plasters; it deals with the very processes of life, which must be understood before they may be guided.” - Paracelsus

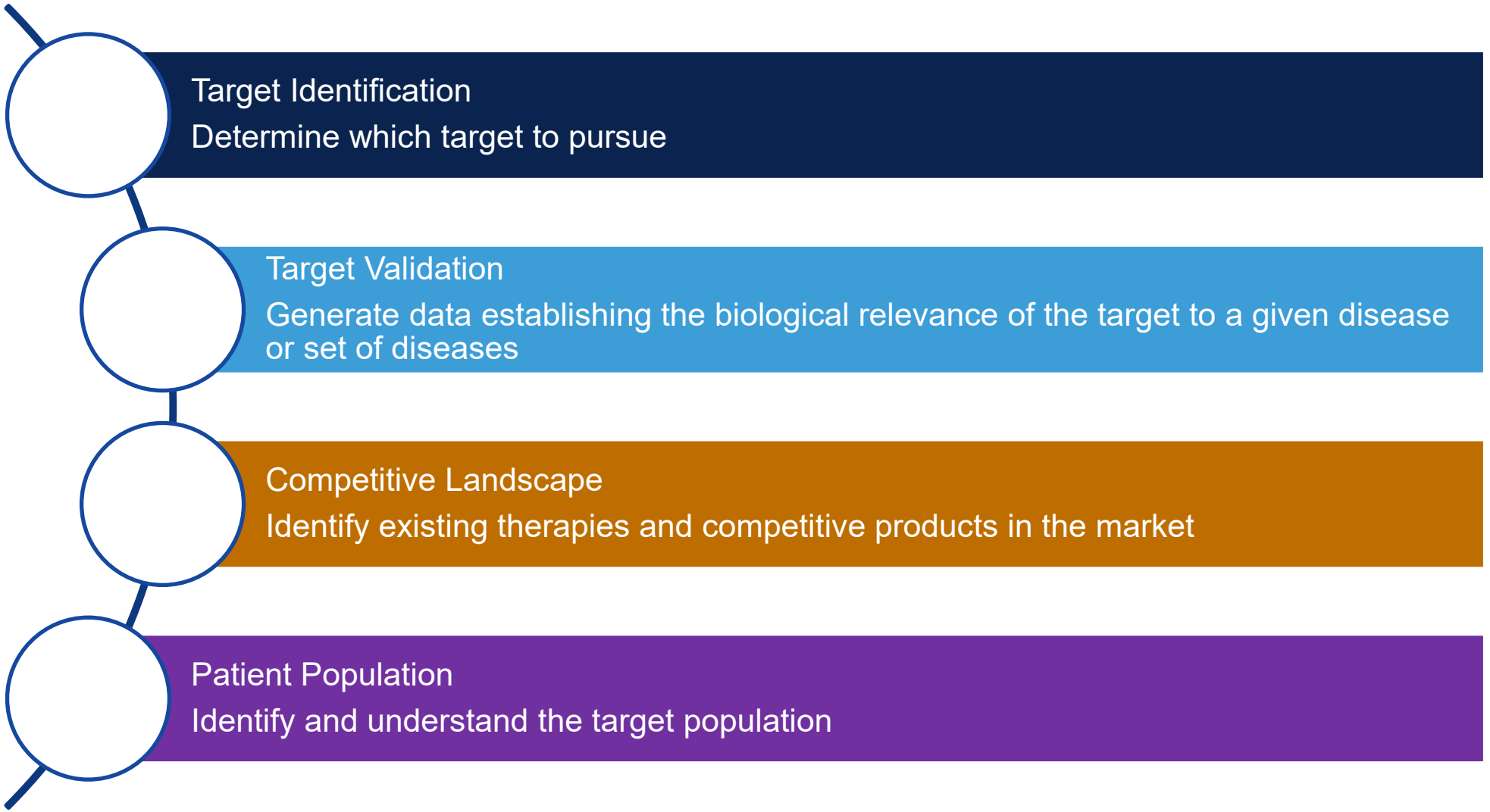
Drug Development is Long, Expensive, and Risky



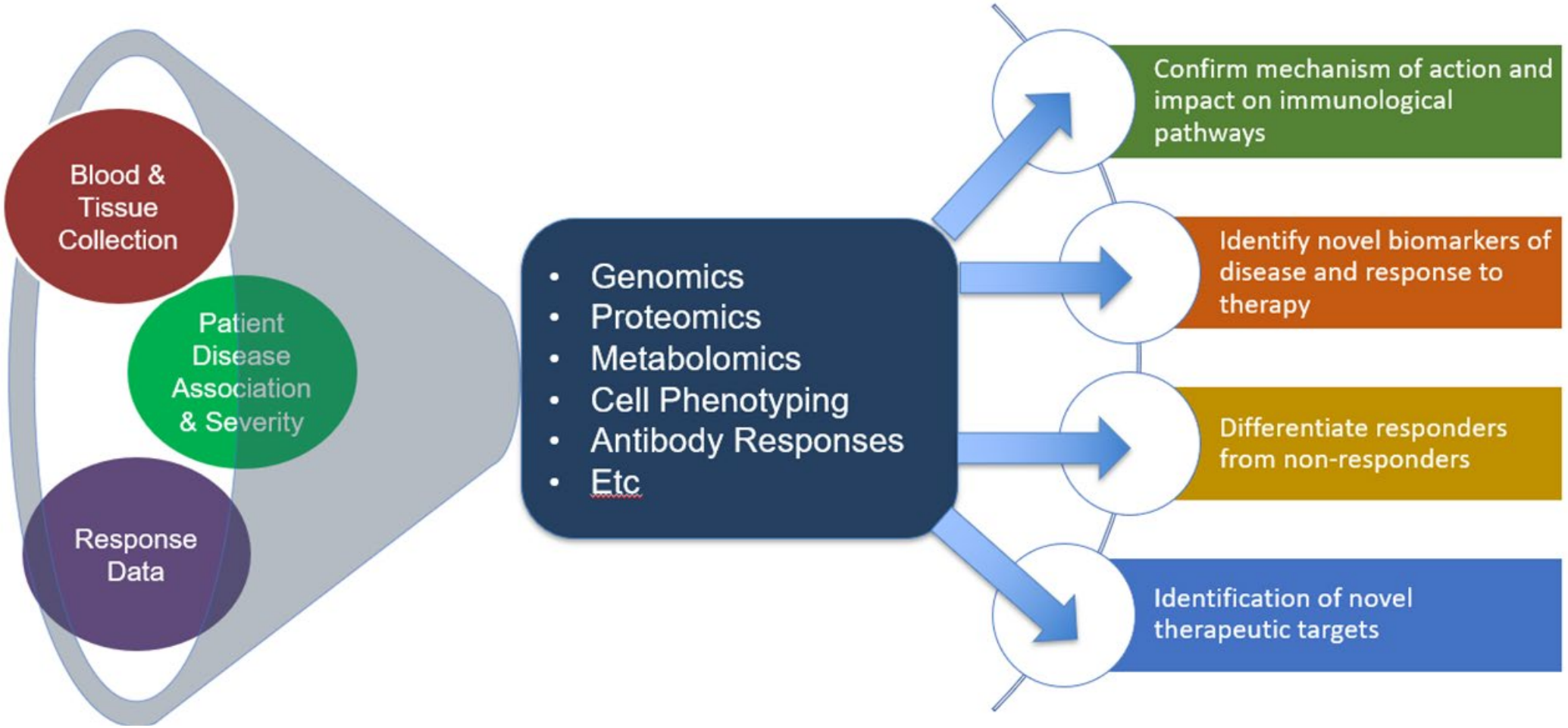
Drug Development is an Iterative Process



Key Questions to Ask/Address During Development



Target Identification and Validation



Derisking Dermatology Development

In Vitro

Cellular activity

3D *in vitro* cultures

Cellular proliferation & function

Off-target safety screening

In Vivo

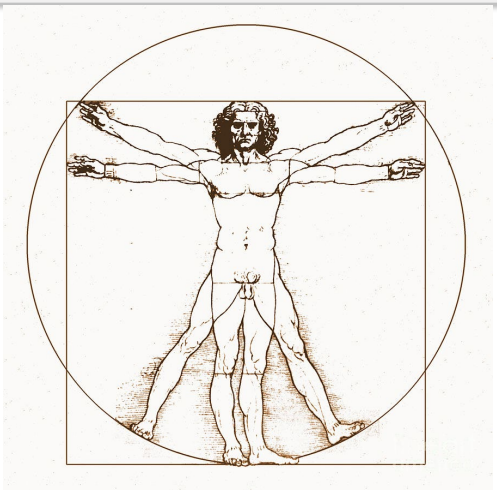
Pharmacokinetics

Pharmacodynamics / target occupancy

Mechanistic models

Disease models

Ex Vivo



Complex 3D *in vitro* co-cultures

Translational Models

Proteomic / genomic profiling

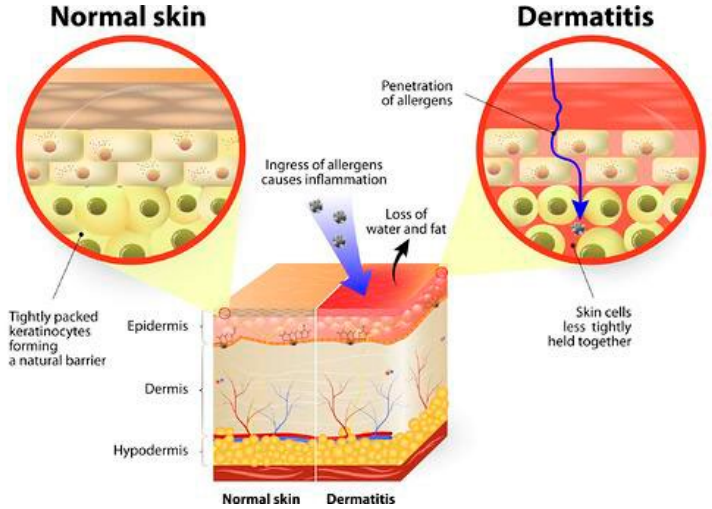
Cytokine / chemokine biomarkers

Integrated In Vitro, In Vivo, and Translational Readouts

Th2

Th2 Stimulated Ex Vivo Skin Explant
- CCL17/TARC (Th2 driven inflammation)
- CCL26/Eotaxin-3 (Eosinophil recruitment)
- Filaggrin (Barrier deficiency)

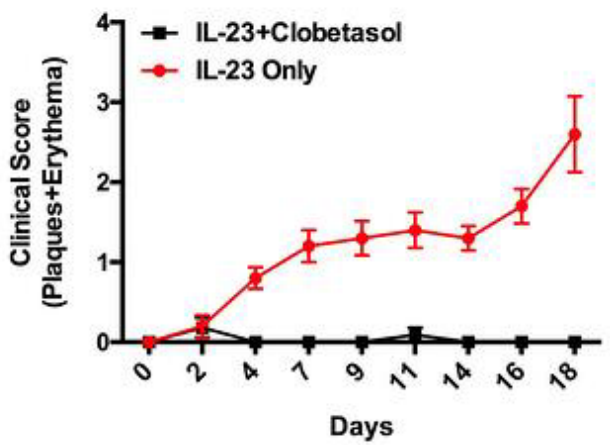
FITC Induced Atopic Dermatitis Murine Model
- Barrier and inflammatory genes
- Eosinophils (CCL26/Eotaxin-3)z

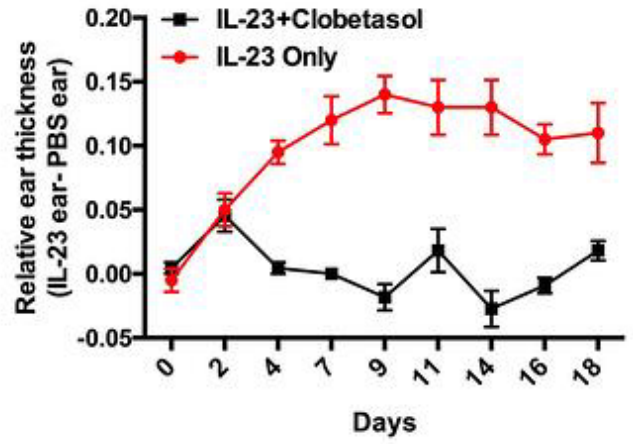


Th17

Th17 Stimulated Ex Vivo Skin Explant
- IL-17A (Disease pathogenesis)
- IL-22 (Acanthosis/epidermal thickening)
- CCL20/MIP3a (Th17 cell recruitment)

IL-23 Induced Psoriasis Murine Model
- Skin severity scores & ear swelling
- Cytokine Expression (IL-17, IL-22)





Additional Studies Needed to Support Drug Development

AMES

- Bacterial reverse mutation test performed with *Salmonella typhimurium*
- Reveals whether the compound is causing direct mutations to the DNA

***In vitro* Micronucleus Test**

- Cell division assay using ChoK1 cell line
- Reveals whether the compound causes abnormalities in chromosome distribution (aneugenity) or even chromosome breaks (clastogenity) during cell division.

Pharmacokinetic

- Define active drug concentration & PK profiles
- Characterize over range of dosages, including expected clinical and toxicology dosages (1x-10x efficacious dosages)
- Single & Repeat-dose PK (3-7 days)

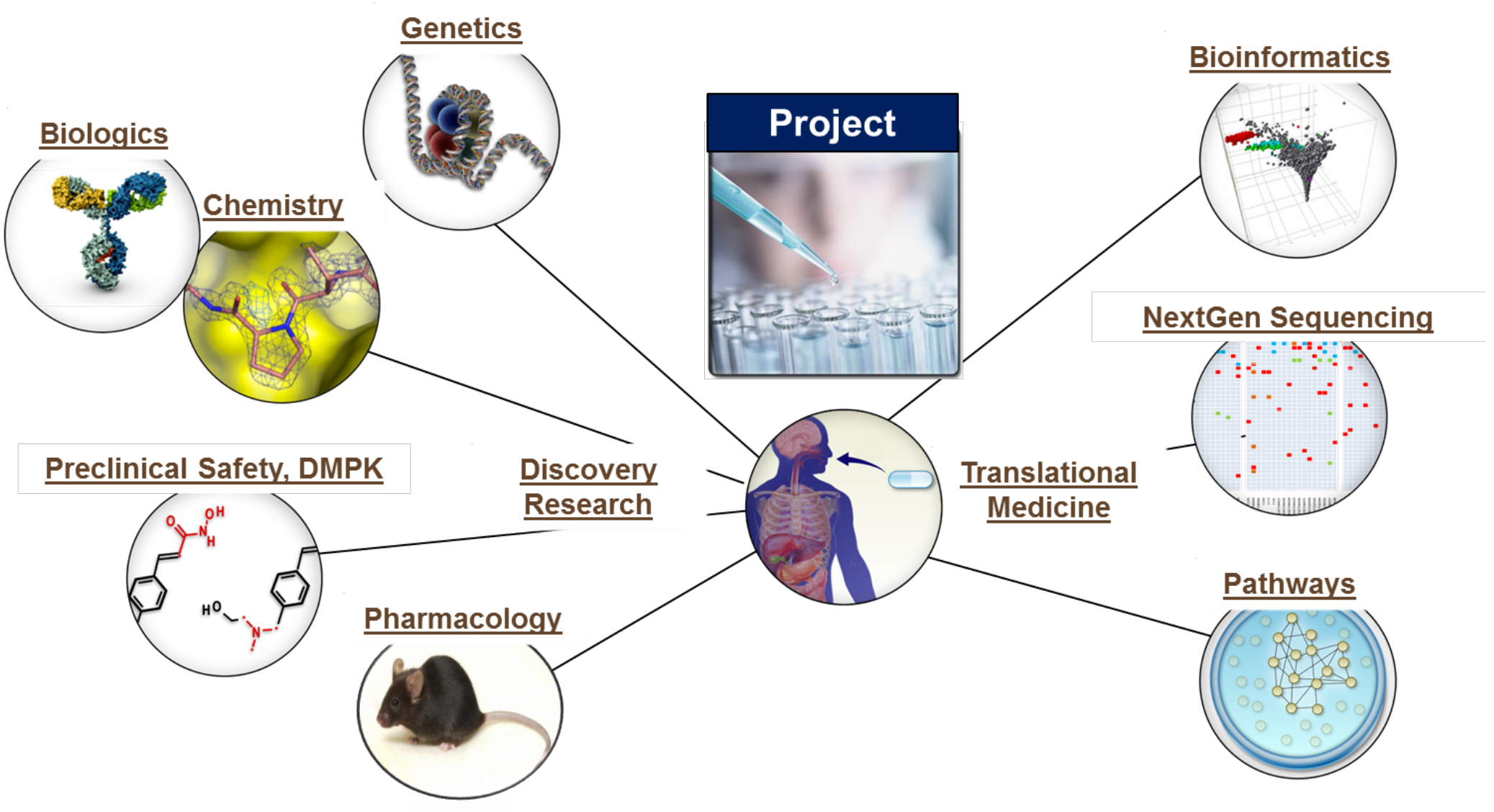
Safety Pharmacology

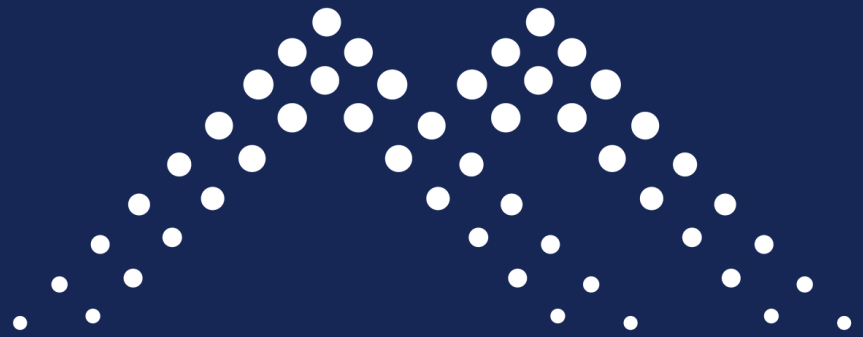
- Detect adverse effects (hazard identification)
- Investigate the mechanism of effect (risk assessment)
- Mitigation strategies (risk management)
- Calculate a projected safety margin

Toxicology

- Maximum tolerated dose
- Repeated dose range finding study
- 14-28 day GLP studies in 2 different species

Drug Development Requires Cross-Functional Collaboration





MOUNTAINEER BIOSCIENCES

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Advancing Innovation in Dermatology®

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Entrepreneur Bootcamp

Unlock the Future of Dermatology Product Development

Vijendra NALAMOTHU, Ph.D.
Founder & CEO
ApoStrata, LLC

Formulation of Dermatological Drugs

- **Topics covered:**
  - **Skin Biology**
  - **Product Development**
  - **Analytical R&D**
  - ***In Vitro* Testing**

- **What you will learn:**
  - Begin with end in mind®
  - Understanding your product
  - Why systematic development matters?
  - Using the skin data properly
  - Pitfalls of analytical data / impurities
  - Other means of verifying product: Skin Biology/IVPT
  - How will you use this data to go to clinic?

Begin with the end in mind®

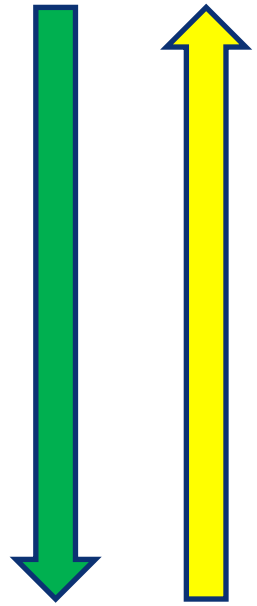
- Next stage gate: tox / clinical / commercial
- Type of dosage form / dossier
- In vitro skin PoC or animal / disease models or straight to FIM / PoC
- Clinical de-risking and reduce CMC surprises
- Irritation / approved ingredients / vehicle effect, permeation, scale-up, QbD, stability, phase-specific validations
- Launch-ready products

® Franklin Covey

Product Development: end-to end approach

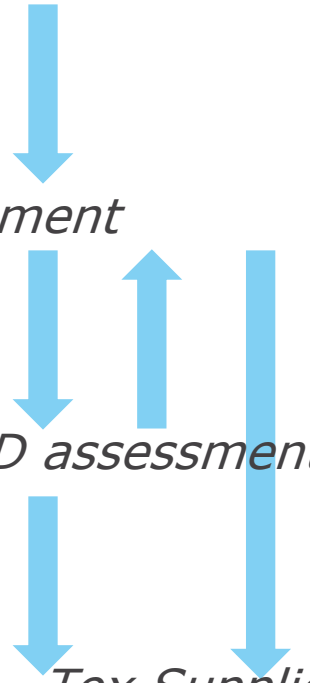
Decide the Commercial Pathway, regulatory strategy and work backwards-

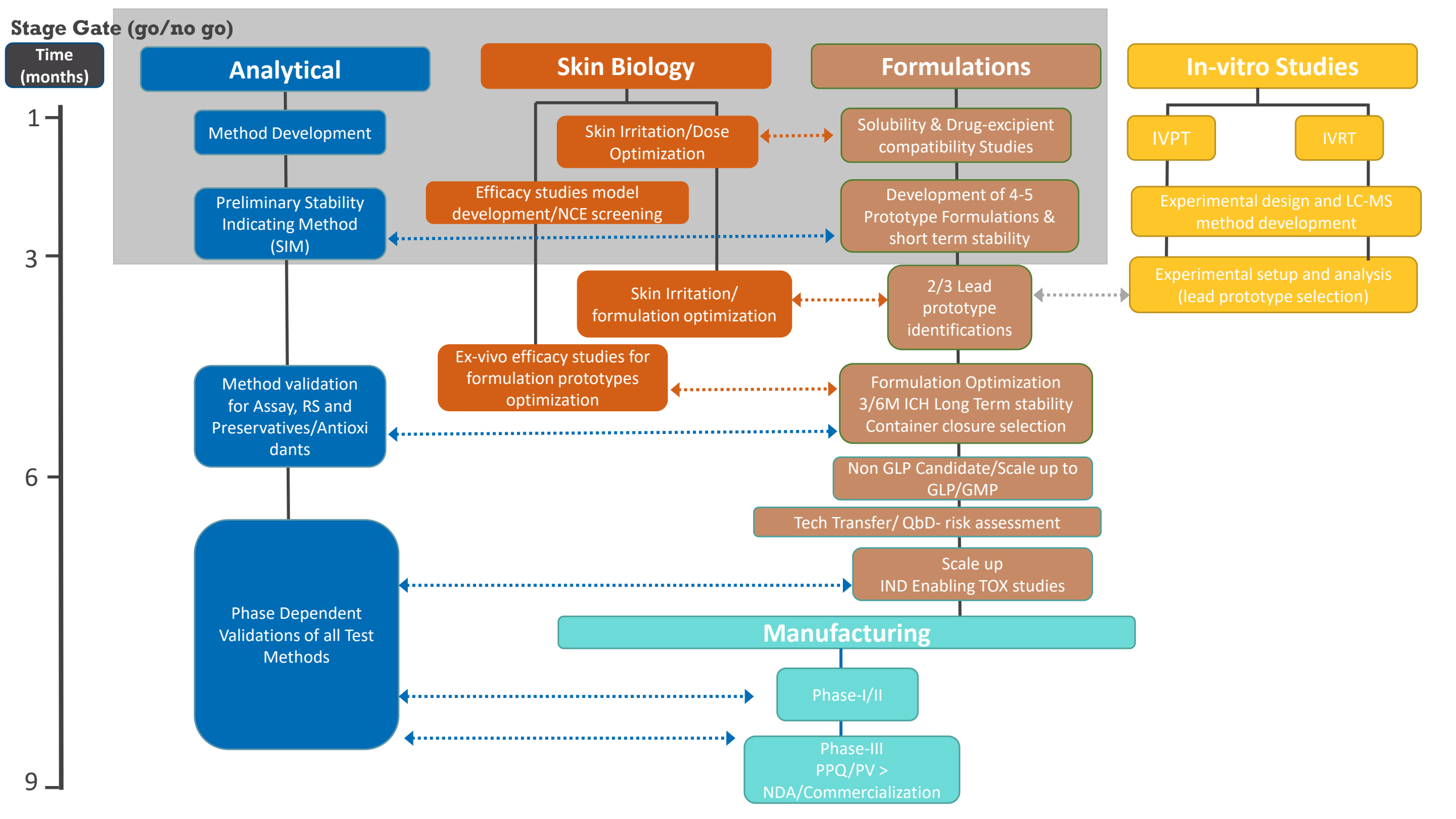
- Launch Plan
- Commercial Manufacturing / Process Validation / Supply Chain activity
- PDUFA / Registration /filing
- Clinical Trial Materials - Phase I/II/III
- Clinical De-Risking / Scale-up / PoC Formulations (FIM)
- R&D Formulations / Tox Safety assessment
- R&D Prototypes / In-Vitro / In-Vivo evaluations
- Idea / Proof-of-Concept / IP



Product Development Snapshot

- Skin Biology
  - *Early Candidate Selection / Molecule Assessment*
- Early Formulation Development
  - *Concurrent Analytical Method Development*
- Skin Permeation (PoC)
  - *Other Proofs-of-Concept such as PK/PD assessment, target engagement*
- Formulation Optimization
  - *Mfg. process Development / Scale Up – Tox Supplies / Clinical Trial Materials*
  - *QbD / Risk Assessment / IVRT*

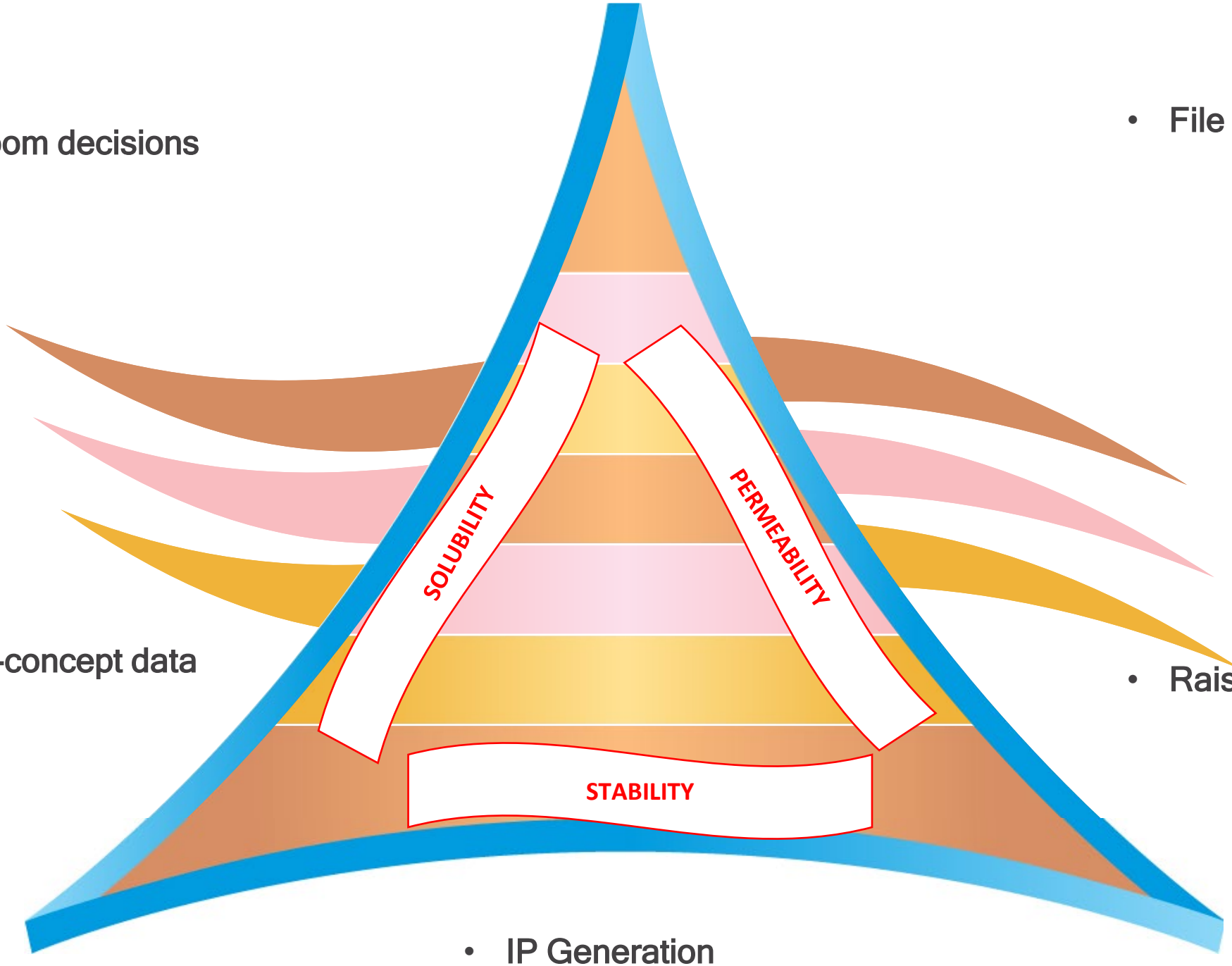



Stage Gate (go/no go)
Time (months)
1
3
6
9
Analytical
Skin Biology
Formulations
In-vitro Studies
Method Development
Skin Irritation/Dose Optimization
Solubility & Drug-excipient compatibility Studies
IVPT
IVRT
Preliminary Stability Indicating Method (SIM)
Efficacy studies model development/NCE screening
Development of 4-5 Prototype Formulations & short term stability
Experimental design and LC-MS method development
Skin Irritation/ formulation optimization
2/3 Lead prototype identifications
Experimental setup and analysis (lead prototype selection)
Ex-vivo efficacy studies for formulation prototypes optimization
Method validation for Assay, RS and Preservatives/Antioxidants
Formulation Optimization 3/6M ICH Long Term stability Container closure selection
Non GLP Candidate/Scale up to GLP/GMP
Tech Transfer/ QbD- risk assessment
Phase Dependent Validations of all Test Methods
Scale up IND Enabling TOX studies
Manufacturing
Phase-I/II
Phase-III PPQ/PV > NDA/Commercialization

Who is your client?

- We all want to win
- Formulate a product for positive pre-clinical and/or clinical outcomes that will:
  - Win Investor's Confidence
  - Win Internal Management's Approval
  - Win Regulatory approval & commercial success
- Design your product development strategy based on the Target Product Profile (TPP)
  - Early Candidates
  - Late-Stage Formulations
  - Me-too brands or differentiated formulations
  - Me-too generics or brand equivalents
- Develop a strategy early on for effective clinical end points and successful manufacturing scale-up

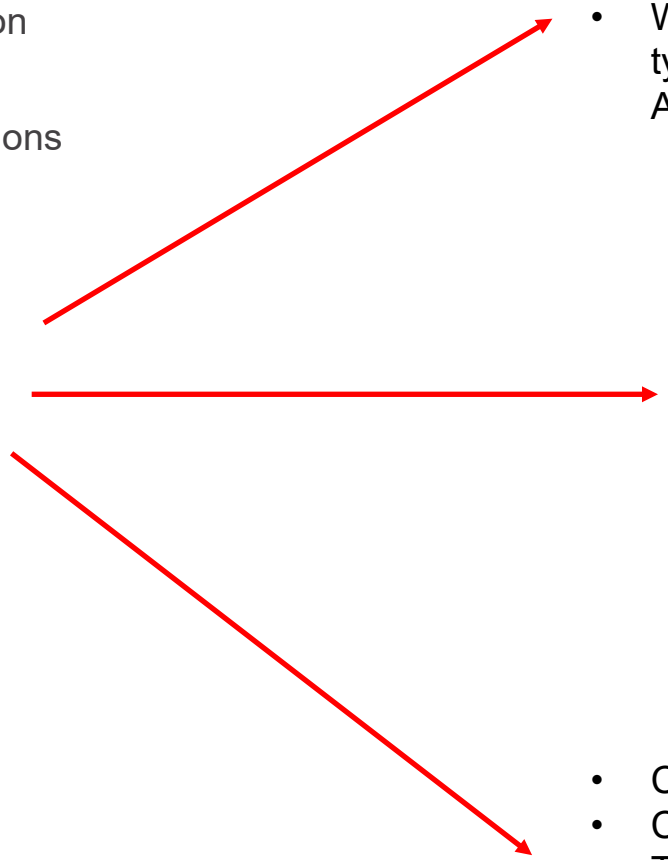
- Board room decisions
- File an IND/CTA



- Proof-of-concept data
- Raise funds
- IP Generation

An Ideal Approach

- **Stages of formulation**
  - Basic (early) Formulation
  - Pre-clinical Formulation
  - Clinical Formulation
  - Commercial Formulations
- **Type of formulation**
  - Disease specific
  - Delivery kinetics
  - Unmet needs
- **Type of Dossier**
  - NDA – 505(b)(1)
  - 505(b)(2)
  - ANDA
    - Q1/Q2/Q3



- Acne formulations are different from Psoriasis
- Anti-fungal delivery is different than Basal Cell Carcinoma
- Wide-surface area coverage of a psoriasis formulation may dictate a type of formulation when compared to a small FTU application of Actinic Keratosis

- Delivery to Stratum Corneum vs. Dermis dictates the selection of right formulation
- Need for a drug to stay in dermis vs. transdermal delivery into systemic circulation drives the choice of excipients
- Targeted delivery for pharmacological action
- Peptide / protein delivery also has its own choice of formulation components

- Clinical Unmet Needs
- Commercial Unmet Needs
- Technical Unmet Needs

Target Product Profile (TPP)

- Talk to your clinical group and/or marketing-sales organization very early on
- Based on early / concept formulations first
- How much levy do you have ‘changing’ the formulation later
    - How much can you change i.e., just preservatives or ..?
    - When or how late can you change i.e., Phase I/II changes?
- Is it a dynamic TPP or etched in stone? Early clinical/late stage/ changing market scenario
- Ask for definitive ‘not acceptables’
- Who drives it? Early feedback vs. Last minute changes
- Setup a minimum acceptable criterion vs. ideal acceptable profile
- Focus on core formulation and achieve it first

Case Studies

- 2 People and a Molecule
- University Tech Transfer
  - Early formulations *vs.* Final Formulations?
  - How much to rely on skin permeation data
  - Formulation stability data: just enough or IND-ready?
- US Development *vs.* Ex-US PoC
- FIM – CTA – IND
  - Is it PoC or powering for future clinical trials
  - Safety / tox formulations?
- Global Large-Pharma Development
  - Dosage form / packaging finalized?
  - Manufacturing process optimized?

Winning Clinical Development Strategy - Where to Start and How to Proceed

Jasmina Jankicevic, MD, MSc, CCRP
Chief Medical & Scientific Officer
Indero Inc.

Innovaderm Research

Speaking from vast experience …

- 20+ years leading global clinical development and medical affairs in dermatology and medical aesthetics for CROs, pharma/biotech, medical device, and cosmetic companies, including Indero (previously) Innovaderm, Premier Research, Allergan, Leo Pharma, and Murad
- Developed drugs and device in 30+ indications (~450 clinical studies)
- Advisor and consultant for multiple companies in the medical and aesthetic dermatology space
- Published author and invited keynote speaker, and lecturer on drug/device clinical development strategy nationally and internationally

Big Picture

Winning Clinical Development Strategy – Where to Start

Breakthrough

Problem Worth Solving

What solutions are most needed?

What are others doing?

What would make your asset a success story?

Conquering Time

Street Smart Clinical Development

What is necessary?

What can save you time & funds?

Who are your champions?

Team with Know-how

Your Clinical Development Village

How to synergize clinical development innovativeness with viable regulatory and savvy operational strategy to get to your next inflection points?

Key Early Steps

Winning Clinical Development Strategy – How to Proceed

Team

- Leadership / BoD / Investors
- Internal & external expertise
- Strategic and operational partnering
- Key input: KOLs, PIs, research staff, patients / caregivers, payers

Starting with the end in mind

- Unmet need – size, growth, competition, market access
- Regulatory environment
- TPP scenarios

FIH & PoC

- SAD & MAD – HV or patients
- Targeted patient population
- CMC / toxicology limits
- Intrapatient vs. interpatient
- Adaptive designs
- Open-label vs. DB
- Dose selection
- Primary objective: safety/tolerability vs. efficacy (power)
- Biomarkers
- Securing high-quality data
- Conclusive study
- Regulatory path negotiations

PoC Study for Success

Winning Clinical Development Strategy – How to Proceed

Key Protocol Considerations
Optimal patient population
Sufficient sample size
Optimal dosing
Sufficient study duration
Endpoints

Key Implementation Considerations
Country selection
Site / PI selection
Training
Data quality: Prevention & mitigation
Participant safety

Winning Clinical Development Strategy - Where to Start and How to Proceed

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Chief Medical & Scientific Officer
Indero Inc.

QUESTIONS TIME:
Discussing & Solving Your Challenges

Innovaderm Research