UNIVERSITY OF MARYLAND
UM VENTURES
MPOWERING THE STATE

EXPLORING FDA'S REGULATORY PATHWAYS

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REGULATORY PATHWAYS

- OVERVIEW OF "IDEA TO EVALUATION"
- DATA NEEDED TO SUPPORT A CLINICAL STUDY
- DRUG DEVELOPMENT AND REGULATORY STRATEGY

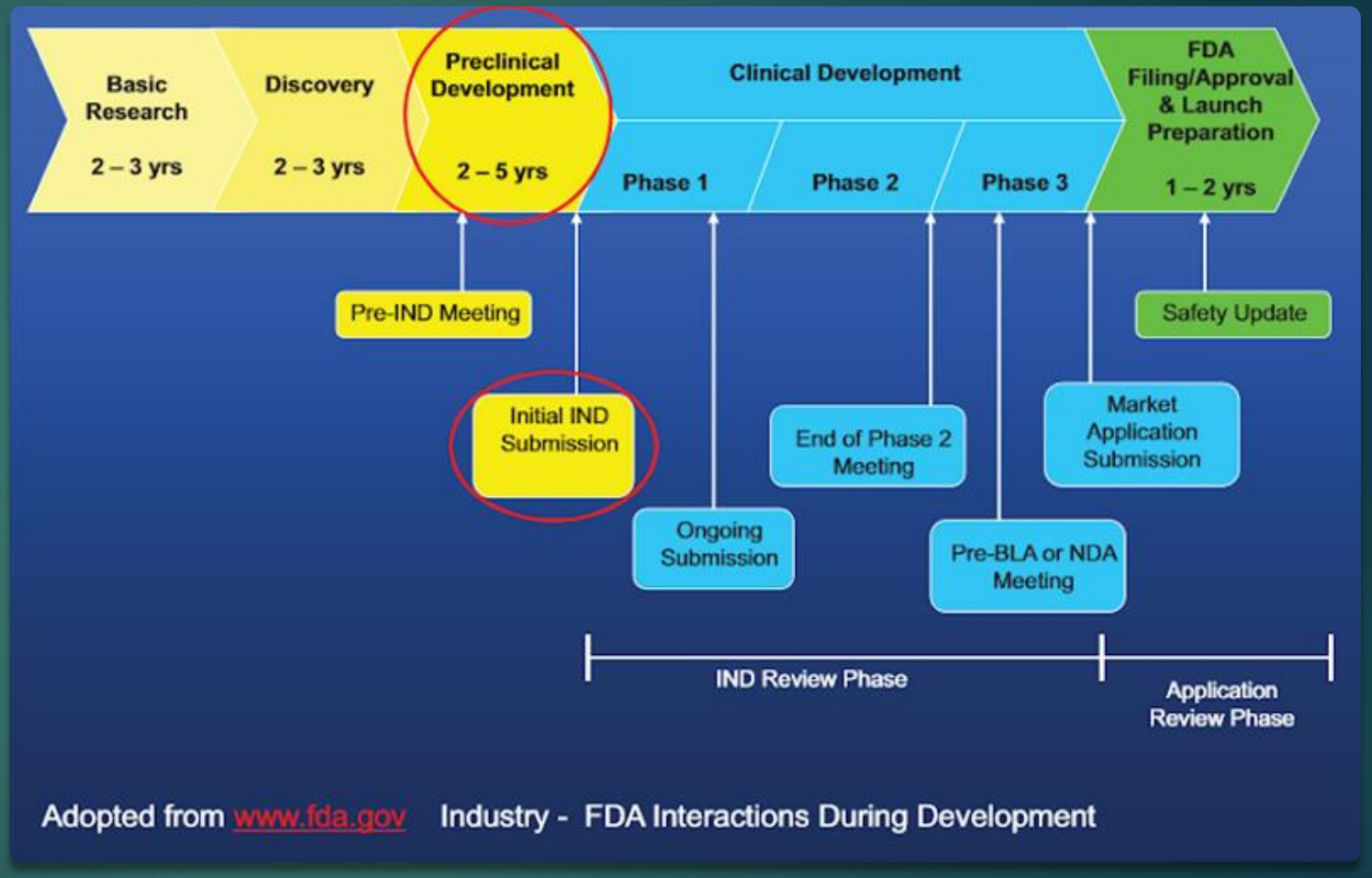
ULTIMATE GOALS

Make patients:

- Live longer
- Feel better
- Do things they were previously unable to do (or do these better)

FROM IDEA TO CLINICAL TESTING

- You have a target and a compound/drug (small molecule or biologic)
- You have data showing your drug has a physiological effect at the target
- You have *in vitro* and/or animal data showing your drug has a therapeutic effect on a model of a disease
  - Now what?



REGULATORY PATHWAYS

When is IND required?

A. Before animal tox

B. Before first in humans

C. Not required for academia

D. After first in humans

REGULATORY PATHWAYS

Primary evaluation focus?

A. Product quality, Animal tox

B. Product quality, Animal tox, Pharmacology

C. Animal tox

D. Pharmacology

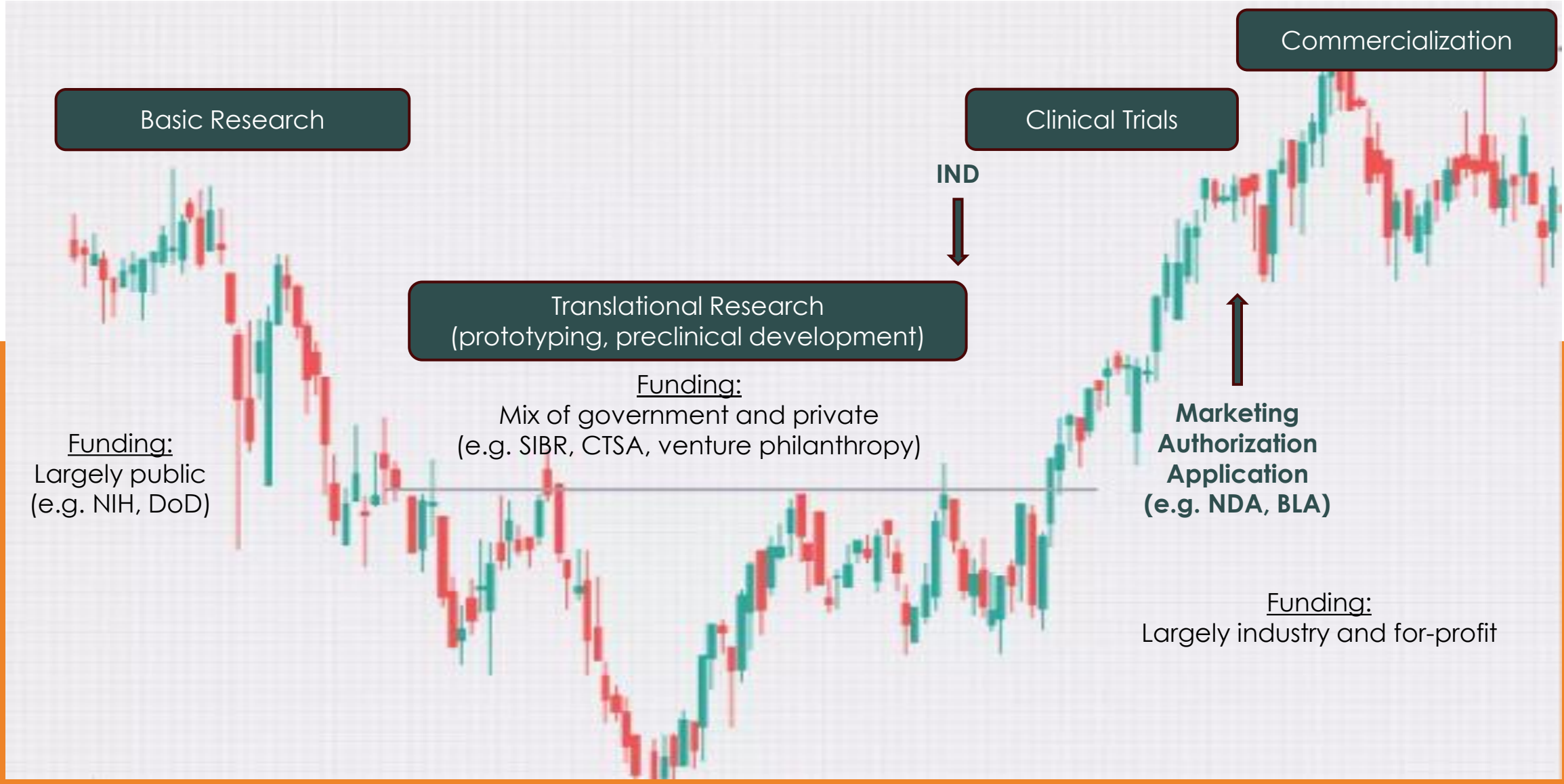
FROM IDEA TO CLINICAL TESTING

- **Investigational New Drug Application (IND):** living document repository submitted to FDA that allows clinical testing, for commercial or research purposes
  - Known as Clinical Trial Applications (CTAs) to Health Authorities (HA) in other countries
  - Data is reviewed in the context of a clinical protocol, the dose used, the duration of treatment
    - First-in-human (FIH) study may be in healthy volunteers or in patients

FROM IDEA TO CLINICAL TESTING

- Data on the Quality of the Drug (Chemistry and Manufacturing Controls (CMC))
- Comprehensive Preclinical *In Vivo* Studies to Assess Safety
  - Some with Good Laboratory Practices (GLP) requirements
- Clinical protocol
- $$$$$ and requires substantial project management
- Often performed by Contract Research Organizations (CRO)

R&D costs per new drug ranges from $1-2 billion (Congressional Budget Office, 2021)



Adapted from Parkinson's Action Network

REGULATORY PATHWAYS

What does IB stand for?

A. Investment Banking

B. Investigational Board

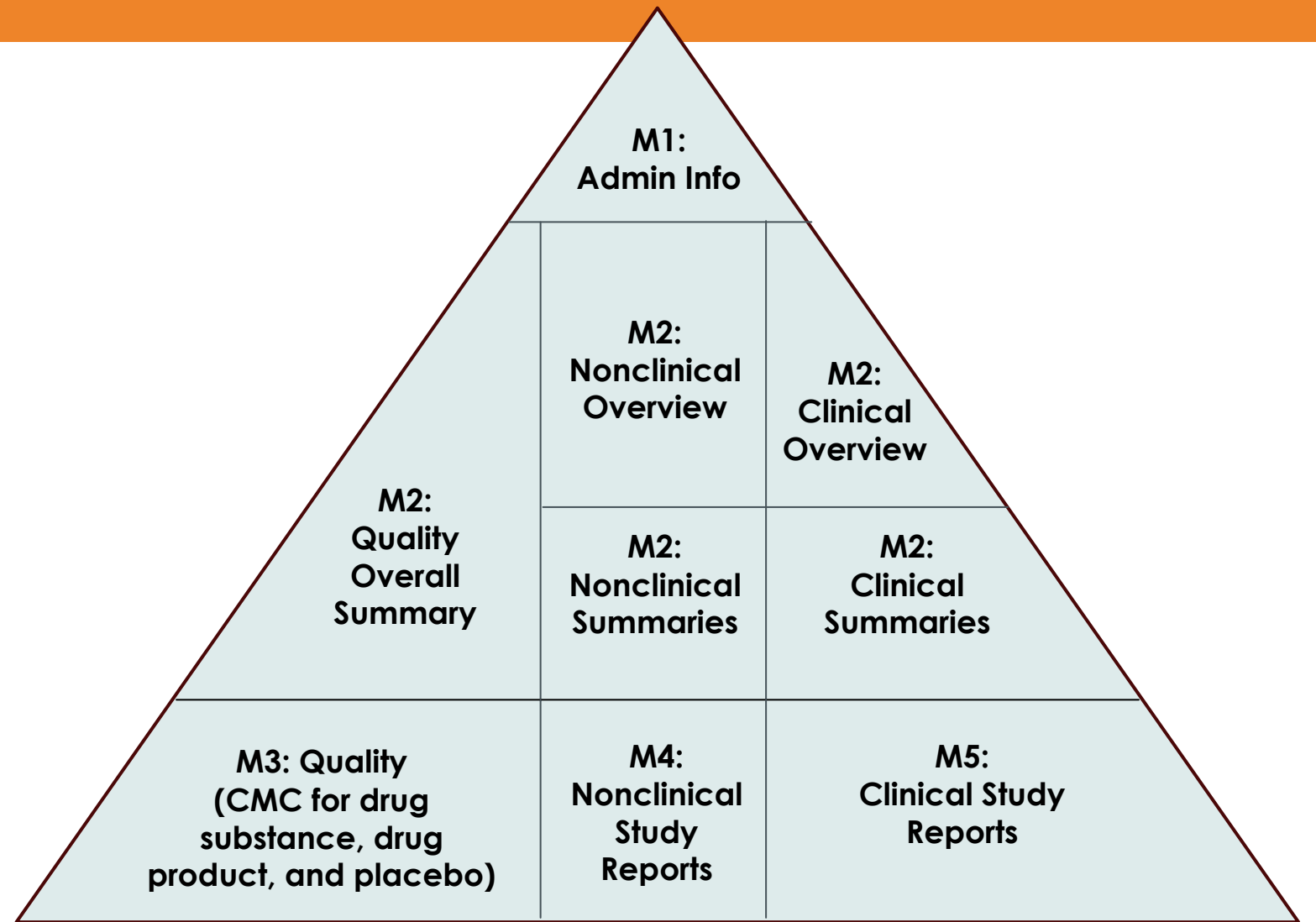
C. Investigator's Brochure

D. Investigator's Book

INVESTIGATIONAL NEW DRUG APPLICATION (IND): LIVING DOCUMENT

- Comprised of Administrative, Chemistry, Nonclinical and Clinical documents
- Clinical study protocol with at least one identified PI
- General Investigational Plan
- Investigator's Brochure
- Investigational label
- Comprehensive nonclinical safety data, chemistry and manufacturing data for the drug substance/drug product you are administering to participants

IND: LIVING DOCUMENT



IND
MODULE 3: CMC

For drug substance, drug product, and placebo to be used in a given clinical trial:

- Structure and general properties
- Manufacturing descriptions (non-GMP OK for Ph1 studies)
- Analytical procedures used
- Certificates of analyses
- Stability

IND MODULE 4: NONCLINICAL

- Pharmacology
  - Primary and secondary
- Safety
  - CNS, cardiovascular and respiratory
- Pharmacodynamic interactions
- PK: Absorption, Distribution, Metabolism, Excretion (ADME)
- Toxicology (at least 2 species)
- Genotoxicity
- Immunotoxicity

IND: ICH RECOMMENDED PRECLINICAL STUDIES ENABLING FIRST IN HUMAN (FIH) TRIALS

(adapted from Clin Transl Sci. 2019 Jan; 12(1): 6–19.)

Study Type *(italics denotes GLP study(ies) required)*		
Pharmacodynamics • In vitro (MOA) • In vivo (MOA and therapeutic effect)	***Safety pharmacology (ICH S7A & S7B)*** • In vitro (concentration-effect relationship) • In vivo (dose-response for CNS, CV, respiratory effects)	**Genotoxicity battery (ICH S2(R1)7)** • In vitro Ames test • In vitro and/or in vivo mammalian cell chromosomal damage evaluation
Pharmacokinetics (ICH M3(R2)) • In vitro metabolism (across species microsomal metabolism) • In vitro plasma protein binding • *Toxicokinetics from repeat dose GLP toxicity studies (ICH S3A)* • ADME	***Single-dose / dose range finding**** • Rodent single-dose • Nonrodent single-dose ***Repeat dose toxicity (ICH M3(R2)6)**** • Rodent multidose • Nonrodent multidose	**Other studies** • Immunotoxicity (ICH S8) • Photosafety (ICH S10) • Abuse liability

ADME: Absorption, distribution, metabolism, and excretion; CNS, central nervous system; CV, cardiovascular; ICH, International Conference on Harmonization; MOA, mechanism of action

Species selection dependent on similarity in metabolism to humans.

*If single-dose study is pivotal (i.e., used to support a single-dose FIH trial), it should be GLP

**Duration and dosing route dependent on clinical trial design

IND MODULE 5: CLINICAL

- Bioavailability, analytical methods, drug-drug interactions, PK/PD, safety and efficacy reports
- For initial IND, the only Module 5 documents you need are the protocol for your intended study and information of at least 1 investigator
- Study cannot start until you have IRB approval

FROM IDEA TO CLINICAL TESTING

- **FDA Resources**
  - **Small Business Assistance**
    - Technical assistance to small companies
    - Hold exchange meetings to hear the views and perspectives of small businesses
    - Conduct educational workshops, develop informational materials, and provide an accessible, efficient channel through which small businesses can acquire information from the FDA.
  - Division of Industry and Consumer Education (Devices and Radiological Health), Small Business and Industry Assistance (Drugs), Assistance Programs in the five FDA regional offices, small business assistance offices in each of the Centers
  - **Pre-IND meetings with specific FDA division and scientific staff**

FROM IDEA TO CLINICAL TESTING

- **Pre-IND Meeting**
  - Opportunity to ask FDA specific questions around your data and the design of the proposed studies to support opening an IND
  - Should ask FDA about the design of your proposed clinical study

RESOURCES

$$$$$ and requires substantial project management, strategic decision-making

- Office of Technology Transfer!
  - Securing intellectual rights
  - Licensing, spin-off company, partnerships
  - & more!

- CROs and consulting firms to guide the process:
  - Help w/ design of IND-enabling studies
  - Perform the studies and provide audited study reports
  - Provide manufacturing and formulation support
  - Serve as project managers
  - Author, compile, and submit regulatory documents
  - Strategy and execution of meetings with health authorities
  - Large one-stop shops or ‘boutique’ firms

ENTREPRENEURSHIP

ENTREPRENEURSHIP

01 **Pre-Commercialization**
Assessment | Market Research | IP Protection | Business Plan | Funding

02 **Execution**
Licensing or Spin-Off | Regulatory | Marketing and Branding | Sales and Distribution | Partnerships

03 **Growth**
Scale-up | Continuous Improvement

ENTREPRENEURSHIP

Question here

A Answer

B Answer

C Answer

D Answer

ENTREPRENEURSHIP

What is a key aspect of technology assessment in the commercialization process?

A. Identifying potential competitors

B. Developing a marketing strategy

C. Securing IP

D. Scaling up production operations

ENTREPRENEURSHIP

Primary objective of intellectual property protection in the commercialization of university inventions?

A Scaling up production operations

B Building brand awareness

C Identifying potential competitors

D Safeguarding against unauthorized use

ENTREPRENEURSHIP

Fundamental goal of market research during the commercialization of an invention?

A. Obtaining regulatory approvals

B. Building a strong brand identity

C. Identifying potential customers and market trends

D. Developing a working prototype

ENTREPRENEURSHIP

Key component of a business plan in the commercialization of an invention?

A Securing intellectual property rights

B Building a working prototype

C Identifying potential competitors

D Outlining the commercialization strategy, financial projections, and go-to-market plan

ENTREPRENEURSHIP

What strategic decision involves deciding whether to collaborate with an existing company or create a new startup?

A. Market segmentation

B. Licensing or spin-off decision

C. Regulatory compliance

D. Prototype development

ENTREPRENEURSHIP

Strategies	Licensing	Spin-off
Control, Autonomy	○ Allows the university to retain control over the invention while granting rights to a third party	○ Provides greater autonomy as the researcher establishes its own company to commercialize the invention
Expertise, Resources	○ Relies on the expertise and resources of the licensee for development, manufacturing, and distribution	○ Requires the university to build its own team and secure resources for the entire commercialization process
Financial Needs	○ Involves licensing fees, royalties, or other financial arrangements negotiated with the licensee.	○ Requires initial funding for the startup but provides the potential for greater long-term returns
Risk & Responsibility	○ Transfers some of the commercialization risks to the licensee	○ Places the responsibility and risks of the entire commercialization process on the university.
Technology Stage	○ Suitable for mature technologies ready for commercialization	○ Well-suited for early-stage technologies that require further developmen

ENTREPRENEURSHIP

The most important consideration for funding acquisition for a spin-off, especially when commercializing a university invention, is often:

Alignment with long-term vision:

- Ensuring that the chosen funding source aligns with the long-term goals and vision of the spin-off company. This includes assessing whether the investor or funding partner shares the same strategic objectives, understands the technology, and supports the company's growth trajectory.

While factors like the amount of funding, equity terms, and investor reputation are crucial, alignment in vision and strategic direction is often the key determinant of a successful partnership in the context of spin-offs from university inventions. This alignment helps to secure not just immediate financial support but also ongoing support and collaboration as the spin-off develops and scales its operations.

ENTREPRENEURSHIP

01 Investor Expectations

- Investors, including venture capitalists, angel investors, and others, expect a clear exit strategy, crucial for securing initial funding

02 Strategic Decision-Making

- The chosen exit strategy guides strategic decisions throughout the spin-off's lifecycle, influencing choices in growth, partnerships, and market positioning

03 Risk Mitigation

- A well-defined exit strategy mitigates risks amid business uncertainties, offering a roadmap to address challenges and navigate market changes

04 Investor Confidence

- A clear exit strategy boosts investor confidence, showcasing the spin-off team's thoughtful and realistic plan for creating value and delivering returns on investment

05 Valuation Considerations

- The chosen exit strategy influences the spin-off's valuation, impacting negotiations with investors and potential acquirers through different valuation models

04 Timing Considerations

- The timing of the exit is crucial, allowing the spin-off team and investors to capitalize on favorable market conditions and align the exit with the overall strategic goals of the company

07 Alignment with Stakeholder Interests

- A well-planned exit strategy aligns stakeholder expectations—founders, employees, and early investors—ensuring all interests are considered

08 Funding Continuity

- Planning an exit strategy involves ensuring adequate financial resources for the spin-off's chosen strategy until the exit event, considering additional funding rounds or sources

09 Competitive Positioning

- The chosen exit strategy, be it acquisition, IPO, or other means, directly influences how the spin-off is perceived in the market and positioned among competitors

ENTREPRENEURSHIP

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ENTREPRENEURSHIP

Question here

A Answer

B Answer

C Answer

D Answer

ENTREPRENEURSHIP

Most Relevant Market Research Tool

A. CSF

B. PESTEL

C. SWOT

D. None

ENTREPRENEURSHIP

For Spin-off, what is the most important?

A. Marketing Strategy

B. Exit Strategy

C. Funding Strategy

D. Partnership Strategy