Club Founder
Dr.Mahmoud Bahgat

International
BD
Business Development Club
Sharpen your skills

Co-Founder & Host:
Dr.Mahmoud Ezzat

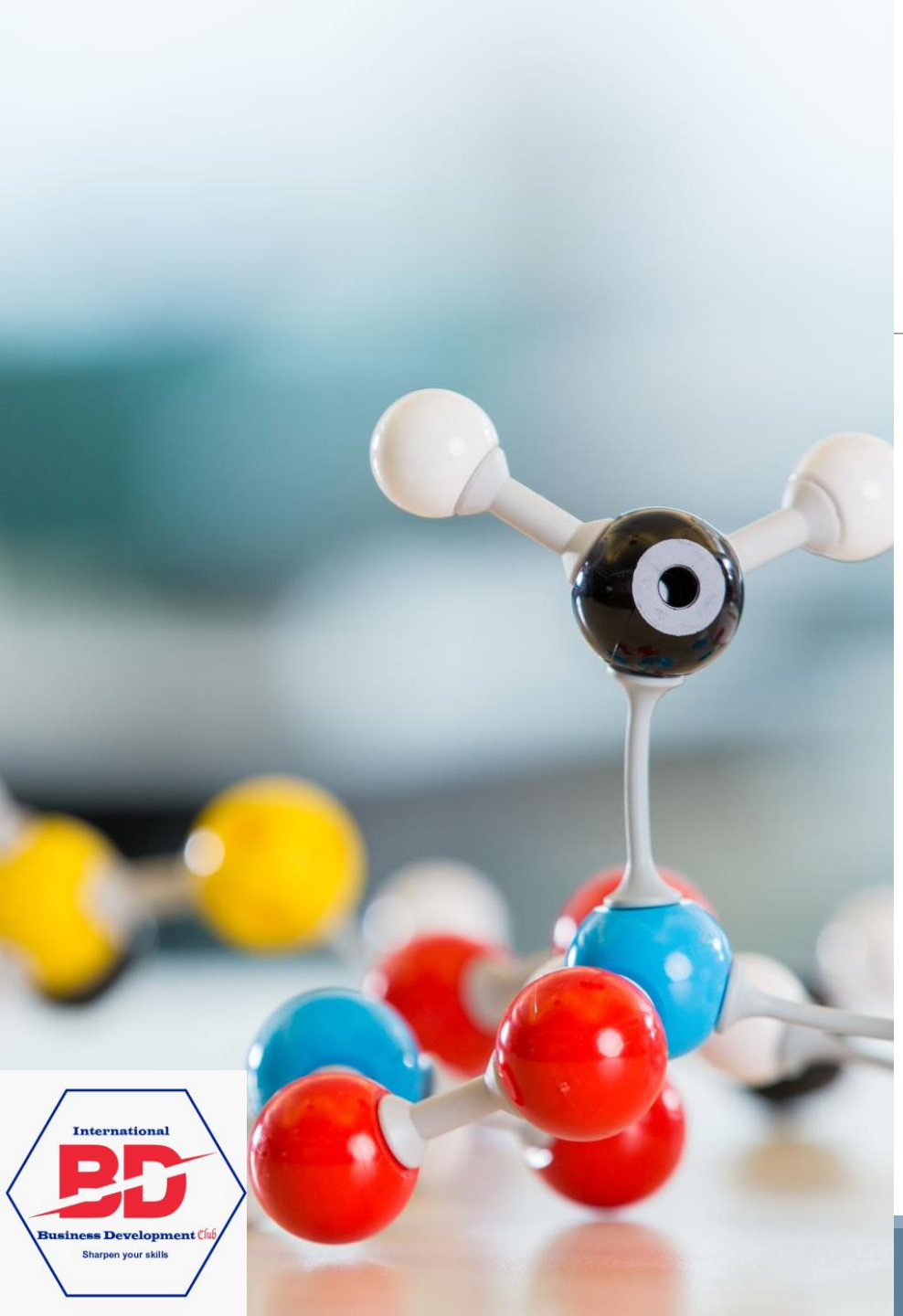
International Business Development Club

Incremental Innovation in Pharma

Online zoom
10pm KSA Egy - 11pm UAE

Dr. Bahaa Rashad
Business Development Director

Wednesday 21st of August



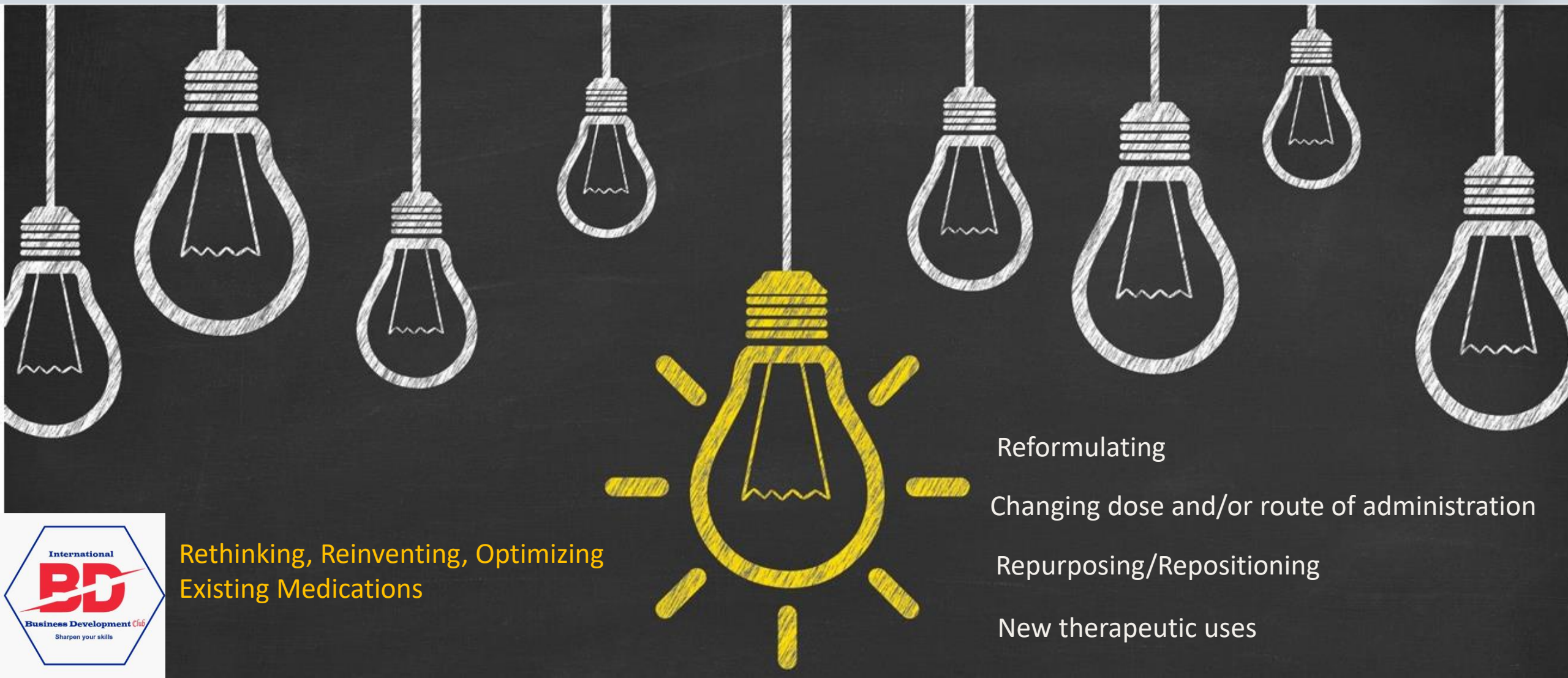
Introduction

- How many of you have been involved in the development, co-development, or licensing of a New Chemical Entity or New Biological Entity?
- How many of you have participated in the development or co-development of generic pharmaceutical products?
- How many of you have contributed to work on any incrementally innovative molecules?

New Drug Development: an Expensive, Slow, and Risky Process

~15 years and ~$1Bn cost on average
~10% of candidates entering clinical development eventually make it to market

What challenges are associated with generic products?



Rethinking, Reinventing, Optimizing Existing Medications

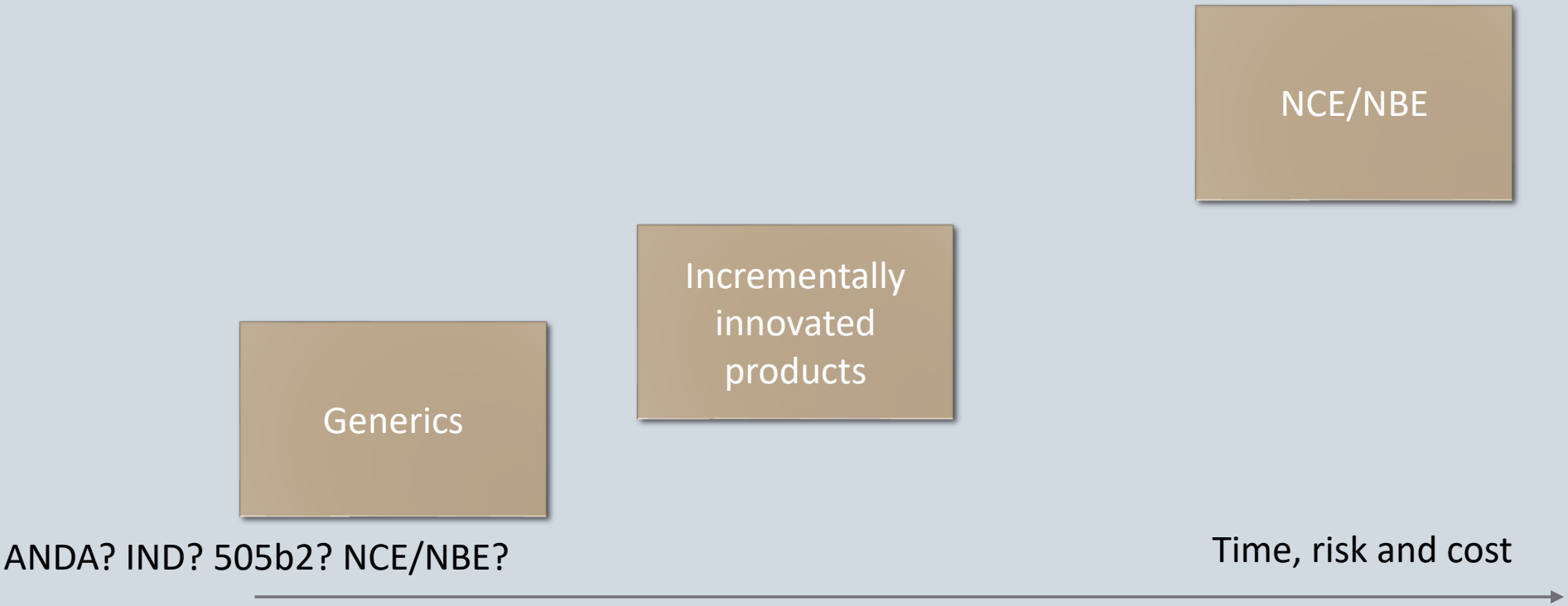
Reformulating

Changing dose and/or route of administration

Repurposing/Repositioning

New therapeutic uses

Development time, risk and cost



Incremental innovations related to pharmaceutical and biopharmaceutical products

1.Drug formulation improvements:

- Enhanced drug delivery systems Extended-release formulations for better pharmacokinetics
- Improved stability or shelf life of biologics
- Better taste or ease of administration for oral medications

2.Manufacturing process enhancements:

- Increased yield or purity in biologic production
- Continuous manufacturing processes for small molecule drugs
- Improved purification techniques for monoclonal antibodies
- Single-use technologies in biopharmaceutical production

3.Dosage optimization:

•Adjustments to dosing regimens for better efficacy or reduced side effects

•Combination therapies that improve overall treatment outcomes

•Development of fixed-dose combinations to improve patient compliance

4.New indications for existing drugs:

- Expanding the use of a drug to treat additional conditions
- Repurposing drugs for rare diseases or unmet medical needs

5.Safety profile enhancements:

- Reducing side effects through targeted drug design
- Improving drug-drug interaction profiles
- Enhancing tolerability for long-term use

6.Improved pharmacokinetics/pharmacodynamics:

- Modifying drug molecules to improve absorption, distribution, metabolism, or excretion
- Enhancing drug-target interactions for improved efficacy

7. Prodrug development:

- Designing inactive precursors that are metabolized into the active drug form in the body, potentially improving bioavailability or reducing side effects

9.Chiral switching:

- Developing single-enantiomer versions of racemic drugs to potentially improve efficacy or reduce side effects

9.Novel salt or crystal forms:

- Creating new salt forms or polymorphs of existing drugs to improve solubility, stability, or bioavailability

Etc.....

Drug formulation improvements - Examples

a) **Enhanced drug delivery systems**: Doxil (liposomal doxorubicin): Encapsulates doxorubicin in liposomes, reducing cardiotoxicity and improving tumor targeting.

b) **Extended-release formulations**: Adderall XR (amphetamine/dextroamphetamine): Once-daily ADHD medication using beaded technology for extended release. Concerta (methylphenidate): Uses osmotic release oral system (OROS) technology for once-daily dosing in ADHD treatment.

c) **Improved stability or shelf l**ife: Gammagard Liquid (immuneoglobulin infusion 10%): Liquid formulation with improved stability compared to lyophilized products.

d) **Better taste or ease of administration**; Zofran ODT (ondansetron): Rapidly dissolving tablet for easier administration of anti-nausea medication.

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Manufacturing process enhancements- Examples

a) **Increased yield or purity**: Example Optimized cell lines for monoclonal antibody production: Humira (adalimumab): Increased yield through cell line optimization and improved fermentation processes.

b) **Continuous manufacturing processes**: Example . Prezista (darunavir): HIV medication produced using continuous manufacturing, reducing production time and enhancing quality consistency.

c) **Single-use technologies**: Examples. Flucelvax (influenza vaccine): Utilizes single-use bioreactors in production, reducing contamination risks.

d) **Process Analytical Technology (PAT):**Real-time monitoring and control of manufacturing processes. Example :Januvia (sitagliptin): Implemented PAT for real-time monitoring of critical quality attributes.

e) **Quality by Design (QbD)**:Systematic approach to pharmaceutical development and manufacturing. Example:Kalydeco (ivacaftor): Developed using QbD principles for enhanced product and process understanding.Sovaldi (sofosbuvir): Implemented QbD for robust manufacturing of this hepatitis C treatment.

Dosage optimization - Examples

a) **Adjustments to dosing regimens**:. Example .Xeljanz XR (tofacitinib): Once-daily extended-release formulation for rheumatoid arthritis, replacing twice-daily dosing.

b) **Combination therapies**: Combining multiple drugs in a single formulation can improve overall treatment outcomes. Example: Triumeq (dolutegravir/abacavir/lamivudine): Single-tablet regimen for HIV, combining three antiretrovirals.

c) **Fixed-dose combinations**. Example. Vytorin (ezetimibe/simvastatin): Cholesterol-lowering medication combining two different mechanisms of action.

d) **Chronotherapy-based dosing**: Timing drug administration based on the body's circadian rhythms. Example : Lodotra/Rayos (prednisone delayed-release): Timed-release formulation for rheumatoid arthritis, synchronizing with circadian cortisol rhythms.

New indications for existing drugs- Examples

a) **Expanded use within the same therapeutic area**: Rituxan (rituximab): Original indication: Non-Hodgkin's lymphoma New indications: Rheumatoid arthritis, granulomatosis with polyangiitis, pemphigus vulgaris

b) **Repurposing for entirely different therapeutic areas**: Metformin: Original indication: Type 2 diabetes. Potential new uses: Polycystic ovary syndrome, cancer prevention, anti-aging studies.

c**) Repurposing based on new understanding of disease mechanisms**: Applying drugs to conditions newly recognized to share similar pathways or mechanisms. Examples :Rapamycin (sirolimus): Original indication: Preventing organ rejection. New potential uses: Various cancers, neurodegenerative diseases based on mTOR pathway involvement

d) **Repurposing for global health challenges**: Doxycycline: Original indication: Bacterial infections. New use: Malaria prophylaxis

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Safety profile enhancements - Examples

Reducing side effects:. Examples: Neupogen (filgrastim) vs. Neulasta (pegfilgrastim) for neutropenia. Neulasta requires less frequent dosing and reduces injection-related side effects compared to Neupogen.

Reducing immunogenicity: Modifications to decrease the potential for immune responses to biologics. Examples: Plegridy (peginterferon beta-1a) vs. Avonex (interferon beta-1a) for multiple sclerosis:The pegylated formulation of Plegridy has reduced immunogenicity compared to the standard interferon beta-1a.

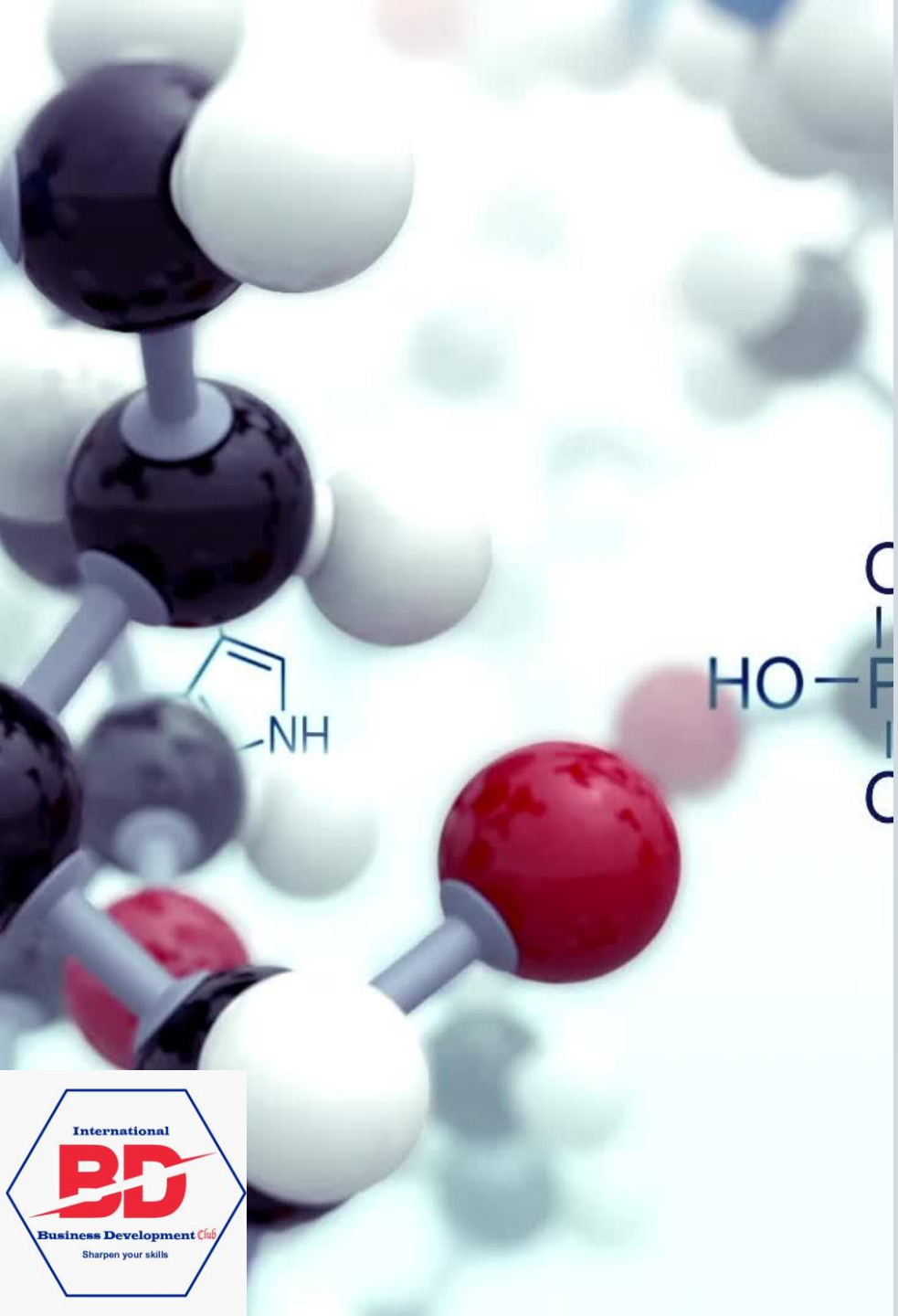
Improved pharmacokinetics/pharmacodynamics: Examples

a) **Enhanced absorption**: Sporanox (itraconazole) for fungal infections: Employs a cyclodextrin-based formulation to improve oral absorption.

b) **Improved distribution** : Onivyde (irinotecan liposome injection) for pancreatic cancer. Liposomal formulation enhances tumor targeting and drug accumulation.

c) **Enhanced metabolism**: Examples: Prezista (darunavir) for HIV: Structural modifications improve metabolic stability and reduce interactions with CYP3A enzymes.

d) **Improved delivery systems** : Butrans (buprenorphine transdermal system) for chronic pain:• Transdermal patch delivery system for improved drug absorption and steady-state levels.



Prodrug development : Examples

a) **Improved bioavailability**: a prodrug of ampicillin that has higher absorption from the gastrointestinal tract.

b) **Reduced first-pass metabolism**: Oseltamivir (Tamiflu): a prodrug of the active metabolite oseltamivir carboxylate, which has improved oral bioavailability compared to the parent compound.

c) **Improved tissue targeting** : Example: Sulfasalazine : a prodrug that is cleaved by bacterial enzymes in the colon, allowing targeted delivery of the active 5-aminosalicylic acid for ulcerative colitis.

d) **Reduced side effects**: Examples: Lisdexamfetamine (Vyvanse): a prodrug of dextroamphetamine, which has a lower abuse potential and reduced cardiovascular side effects compared to the parent stimulant.

The key stakeholders that benefit from incremental innovations in the biopharmaceutical industry include:

- **Patients:**
- Improved efficacy, safety, and tolerability of existing drugs
- Enhanced convenience and adherence through better formulations or dosing regimens
- Expanded treatment options for unmet medical needs
- Potential for lower cost of goods and affordability.
- Etc

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The key stakeholders that benefit from incremental innovations in the biopharmaceutical industry include:

2. **Healthcare Providers**:

- Access to more effective and optimized treatment options
- Improved ability to manage patient conditions and achieve better outcomes
- Simplified administration and monitoring of medications
- Increased confidence in the safety and quality of established drugs

The key stakeholders that benefit from incremental innovations in the biopharmaceutical industry include:

3. **Payers** (e.g., insurance providers, government healthcare systems):

- Potential cost savings from less expensive, incremental innovations compared to new drug development
- Improved treatment outcomes leading to reduced long-term healthcare costs
- Expanded access to enhanced versions of existing, proven medications

The key stakeholders that benefit from incremental innovations in the biopharmaceutical industry include:

Regulators

Incremental innovations often require less extensive clinical testing, streamlining the review and approval process

Improvements to existing drugs can provide additional safety and efficacy data to inform regulatory decisions

Expanded treatment options and enhanced medications benefit public health

Pharmaceutical companies benefit significantly from incremental innovations in several ways:

1. Lifecycle management:
2. Competitive advantage:
3. Reduced development costs and risks:
4. Diversification and portfolio expansion:
5. Improved manufacturing and supply chain:
6. Enhanced patient and provider relationships:
7. Etc:

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As a business development manager in the pharmaceutical industry, there are several key ways you can leverage and capitalize on incremental innovations to drive strategic growth and value for your company:

- Identify and prioritize opportunity areas:
- Engage in collaborations and partnerships:
- Facilitate internal innovation:
- Optimize product lifecycle management:
- Enhance commercial strategies:
- Leverage regulatory and intellectual property expertise:

Business cases

1, Pregabalin Extended release

2. Abiraterone acetate new formulation.

3. once yearly therapy

4. biyearly sinus treatment

ABIRATERONE ACETATE

Products profile

	New Formulation	Zytiga® 250mg	Zytiga® 500mg	Yonsa® 125mg
Dose reduction vs RLD, potentially reducing adverse effects	Yes, 200-250mg	N/A	N/A	Yes, 500mg
Number of Tablets				
Size of Tablets	Normal	Normal	Very large	Normal
Food Restrictions	No	Yes	Yes	No
Patient compliance	• Reduced pill burden • Easy to take tablets • No food restrictions	• Significant pill burden • Food restriction	• Fewer tablets • Large tablet size • Food restrictions	• Pill burden • No food restrictions

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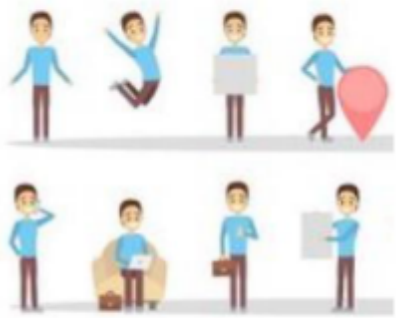
D Technology Enables Once Yearly Therapies

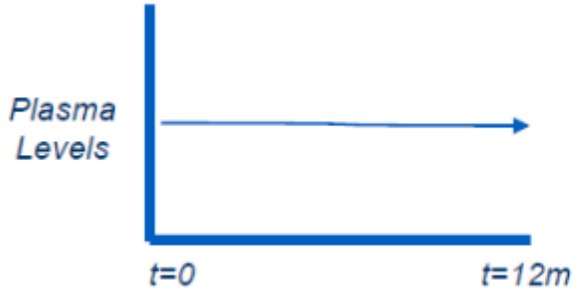
Product Requirements for Once-yearly Therapy

- **Reversible**
  - Must deliver daily dose for 365 days and be reversible at any time
  - Reversible in case treatment interruption is required (washout in 24hrs)

- **Comfortable and Convenient**
  - Unnoticeable by the patient during daily activities



- **Steady Release**
  - Flat PK for 1 year without decline
  - Does not drift below the therapeutic threshold



RHINITIS & SINUSITIS

Current therapeutic strategy

Rhinitis

Sinusitis

1 ST LINE

Antihistamines, intranasal steroids

- > 30% failure
- 50% compliance

2ND LINE

1st line +/- systemic steroids, decongestant, bronchodilator, Leukotriene receptor antagonist

Steroids

- Systemic absorption

Decongestant

- Only for nasal obstruction

LTRA

- Patients with intolerance to anti-H1 and CS +/- with asthma or nasal polyps

Broncholiator (Ipratropium)

- Only treats hypersecretions

3RD LINE

Immunotherapy, Monoclonal antibodies, In-office medical devices

Immunotherapy

- Systemic anaph. reactions
- Cumbersome process
- Upfront cost

MABs

- Cost +++ (only for the most severe patients)

Energy (rhinitis)

- Tissue burns, epistaxis

Balloon sinuplasty (sinusitis)

- Only treats symptoms

4TH LINE

Surgery

> 80% of patients eligible for surgery decline it ("watchful waiters")

- Irreversible removal of bone and tissue
- Painful
- Extended leave from job

New biyearly treatment

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Need to know more, I will be happy to discuss with you

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