Industry Perspective: Incorporation of BE modeling and LAI development challenges

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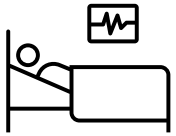
Topics

- Introduction
- Typical considerations for Long-Acting Injectable (LAI) Development
- How PK modeling could assist with
  - Bioequivalence clinical studies
  - Post approval Biostudies
- General scenarios and practical development challenges of adapting a PK model
- Summary of key Topics

Typical Considerations for Long-Acting Injectable Development

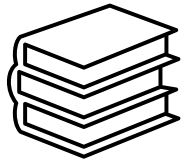
Medicine

- Complex Dosage forms and processing
  - Nanosuspensions
  - Microspheres
  - Polymeric Gels
- Multiphase drug release
- Many interconnecting CQAS, CMAs and CPPs



Patient

- Potent drugs
- Disease area requires patient use in clinical studies
- Maintain Therapy
- Long acting Multidose for steady sate
- Challenging to study variants of formulation, e.g., IVIVC requirements



Study Design

- Higher Patient numbers
- Longer studies

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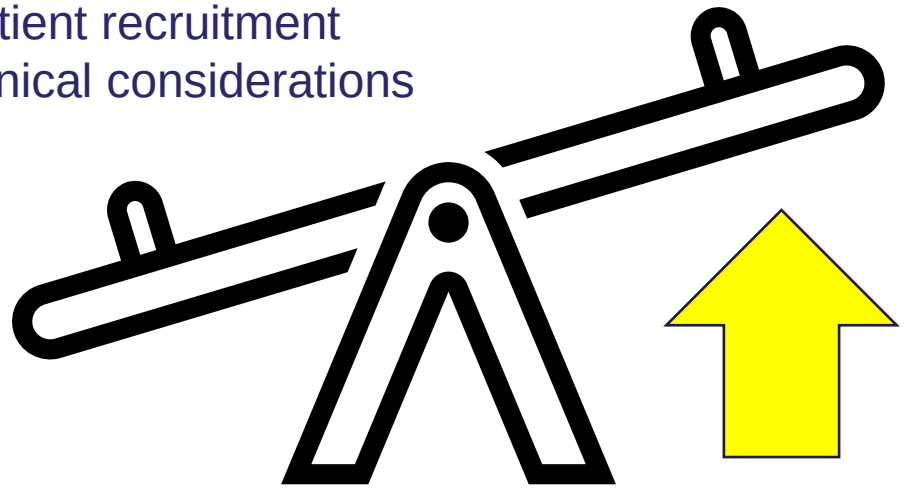
PK model possible benefits for LAI

Conventional study Approach

Higher costs
Longer timeframes
Less access to medicine

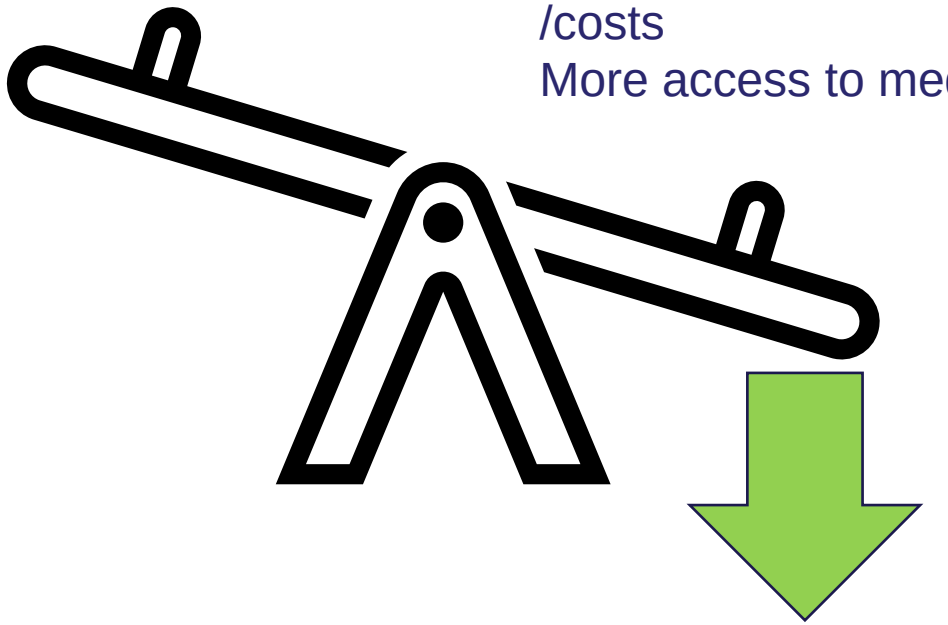
Patient recruitment
Clinical considerations



Potential study Approach

PK modeling
+
Patient recruitment
Clinical considerations

Reduction in timeframes /costs
More access to medicine



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PK models areas of potential benefits

Area	Potential benefit
Development of product	Selection of lead product based on simulated data
Clinical study design	Aid in study design and patient numbers Potential for smaller study size
IVIVC	Overcome clinical challenge of performing studies in Patients
Supporting setting of Specifications (dissolution or other CQAs)	Use PK model simulations to support wider specifications e.g. A dissolution range greater than +/-10% from the mean that achieves simulated BE
Product lifecycle management and post approval changes	Future Changes e.g., CMAs (Critical Material Attributes) with material supplies, processing or specifications

Conventional BE study approaches

(A) Volunteers/single dose

Registration approval

(B) Patients- Clinical considerations/Single dose

Registration approval

(C) Patients- Clinical considerations/Multi dose

Registration approval

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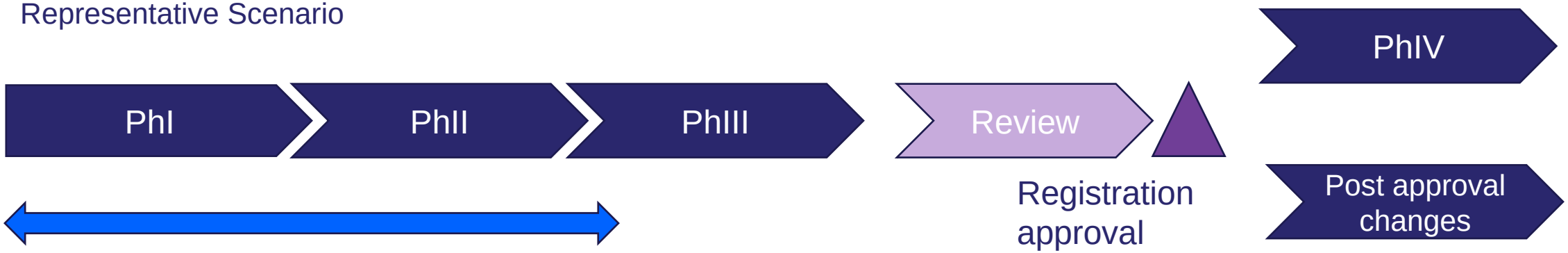
LAI PK model build/validation- Precedent from NDAs

Representative Scenario



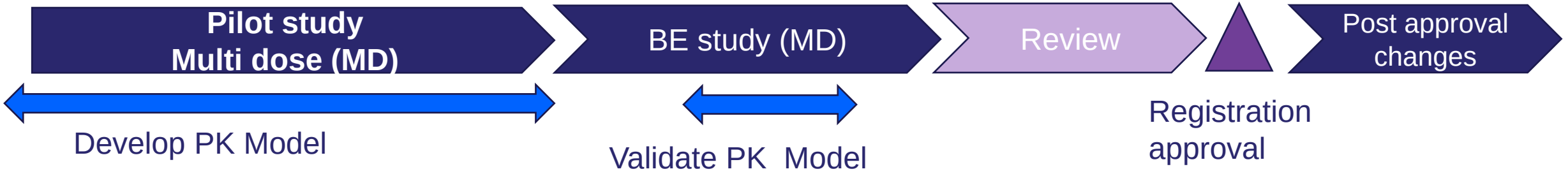
Develop PK Model
- Supports decision making
  - Development
  - Clinical design

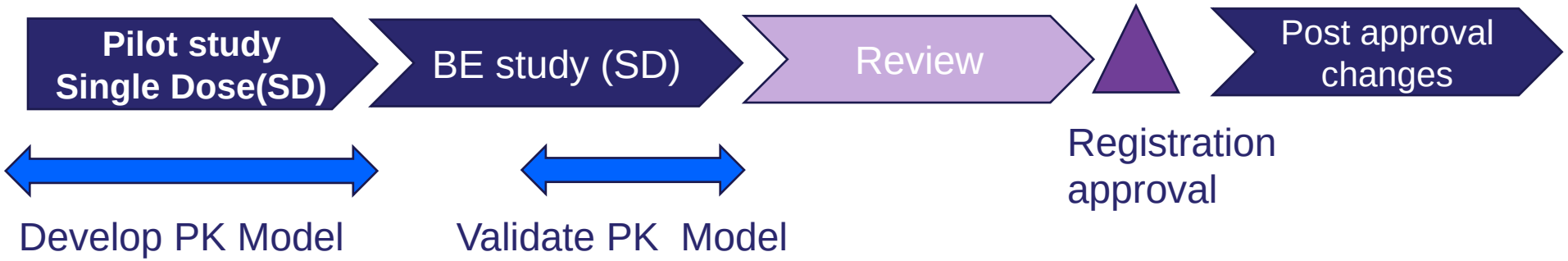
Validate PK Model Supports
- Submission
- Post approval

Potential for use of PK model in supporting Drug Product life cycle management (precedence from oral solids)

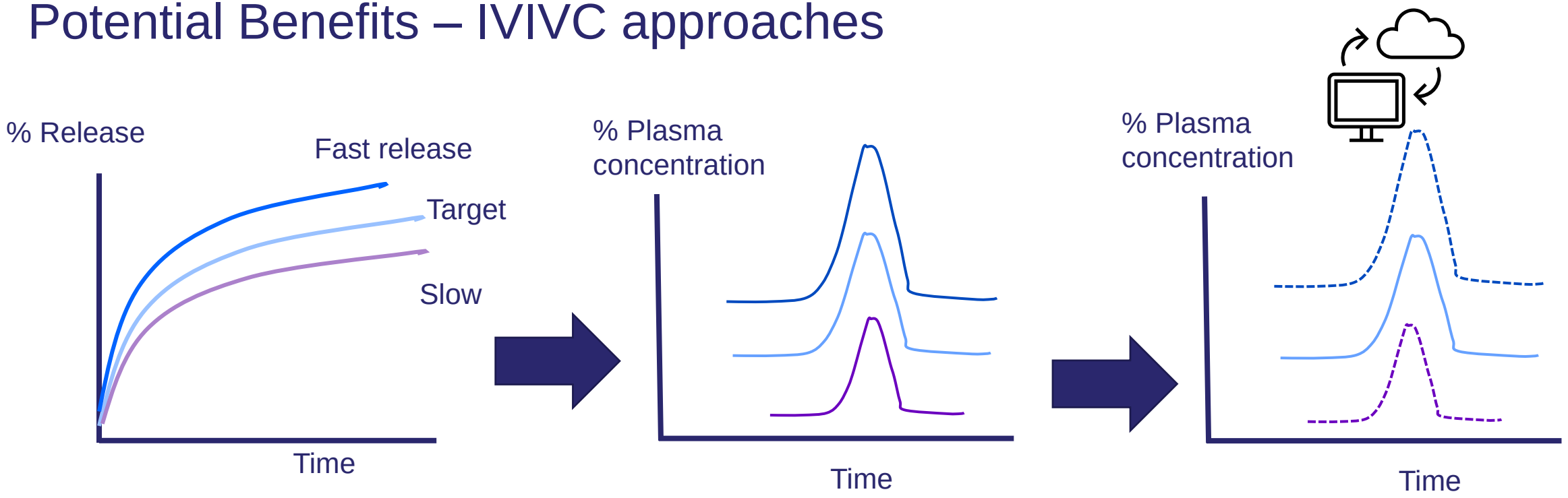
LAI PK model build/validation- Translation to ANDAs

Representative Scenarios





Potential Benefits – IVIVC approaches



Scenario
Potent drug, multi dose
Q1/Q2 matching some Q3 differences
RLD high intra lot Variability
Discriminatory dissolution test
Bio-predictive dissolution test requires IVIVC

Traditional IVIVC using 3 x formulation in a clinical study

Or

(A) Utilise a PK model with clinical data to achieve an IVIVC

(B) Potential to utilise a PK model to simulate faster/slower release and achieve a simulated virtual IVIVC

Key summary points

- PK modeling offers an opportunity to overcome LAI specific development challenges
  - Some of the practical factors and clinical considerations that extend development timelines/costs
  - Support approved Drug Product lifecycle management
- Balancing clinical data requirements to support PK model development and validation
  - Compared to a conventional clinical study design to demonstrate BE
- PK model capability to support lifecycle management e.g.
  - Scenario of fewer clinical studies supported with PK model/ simulations to develop IVIVC approaches
  - Managing any post approval changes to materials, processing and specifications

Thank You

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