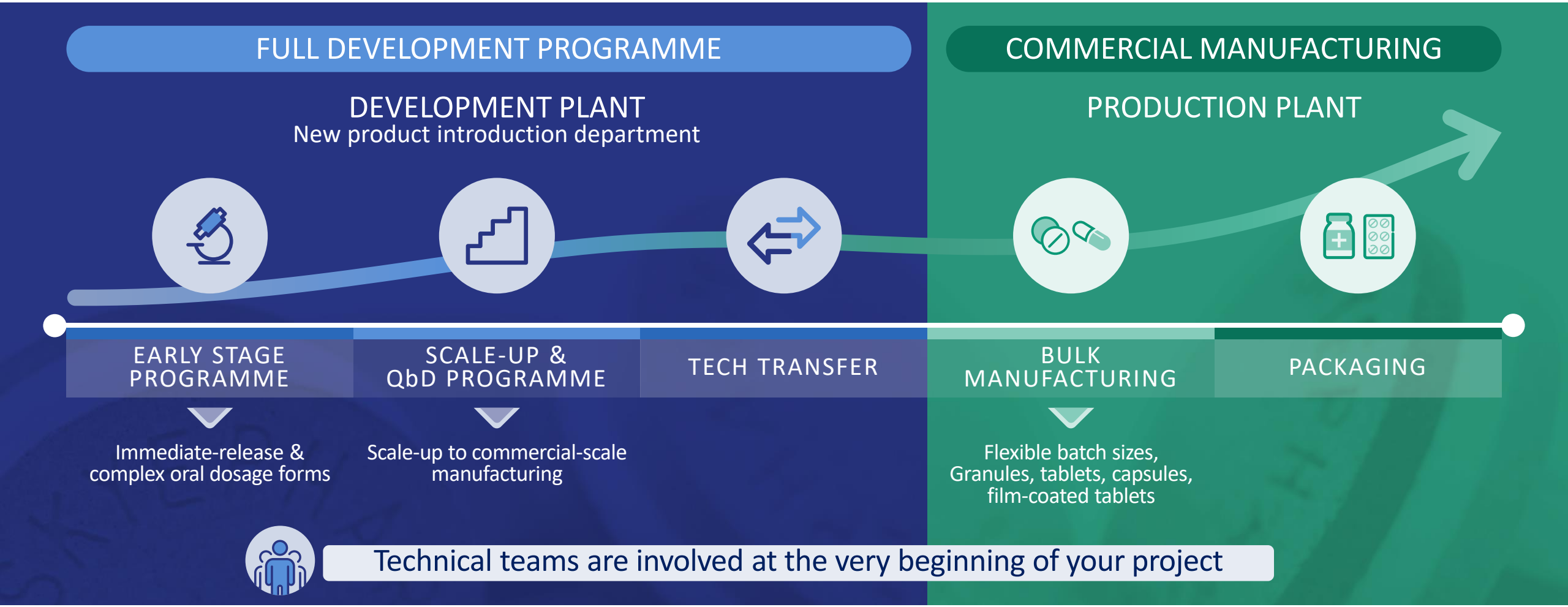
Analytical Development & Technico-Regulatory Expertise

ALL ALONG THE PHARMACEUTICAL DEVELOPMENT & MANUFACTURING PROCESS

Isabelle Bonnaventure PhD

ANALYTICAL DEVELOPMENT MANAGER

DEVELOPMENT & MANUFACTURING PROCESS



QbD = Quality by Design

ANALYTICAL DEVELOPMENT & TECHNICO-REGULATORY EXPERTISE: ALL ALONG THE PHARMACEUTICAL DEVELOPMENT & MANUFACTURING PROCESS

Skyepharma

OUR PARTNERSHIP APPROACH

END-TO-END APPROACH

From development to batch certification and RTM
(Release To Market)

- FLEXIBILITY
- ADAPTABILITY
- AGILITY

"A LA CARTE" APPROACH

Select your need in our offer of services

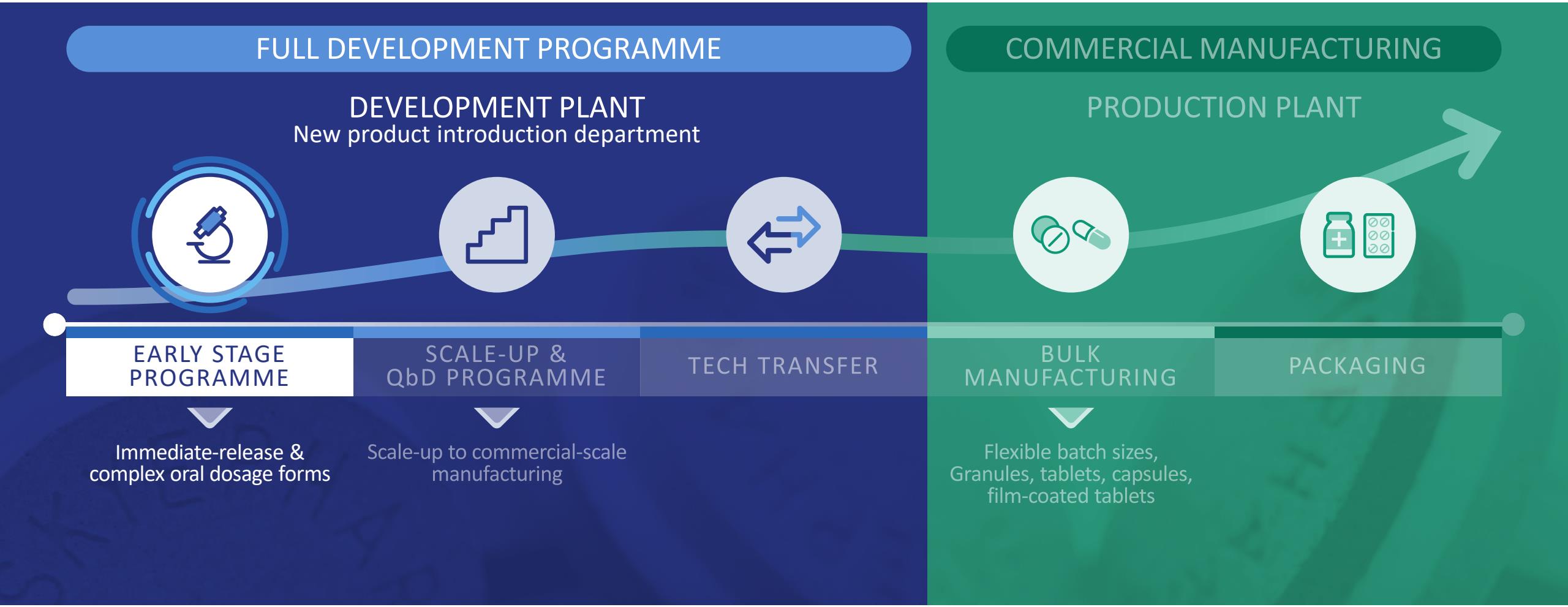
Skyepharma's partnership approach : Right team, right approach from the start

RTM = Release to market

ANALYTICAL DEVELOPMENT & TECHNICO-REGULATORY EXPERTISE: ALL ALONG THE PHARMACEUTICAL DEVELOPMENT & MANUFACTURING PROCESS

Skyepharma

DEVELOPMENT & MANUFACTURING PROCESS



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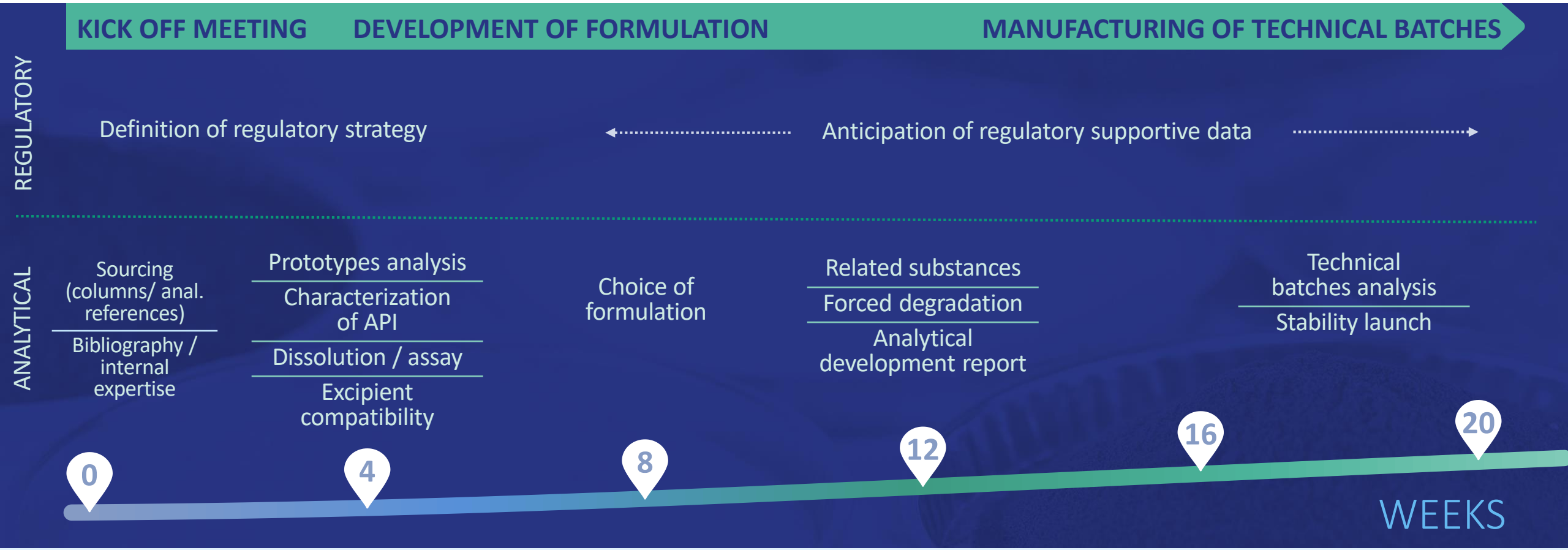
Skyepharma

SKYEPHARMA PARTNERSHIP
IN EARLY-STAGE DEVELOPMENT PROGRAM



Internal meetings with formulation team → Understanding & definition & anticipation of needs

API = Active Pharmaceutical Ingredient

ANALYTICAL DEVELOPMENT & TECHNICO-REGULATORY EXPERTISE: ALL ALONG THE PHARMACEUTICAL DEVELOPMENT & MANUFACTURING PROCESS

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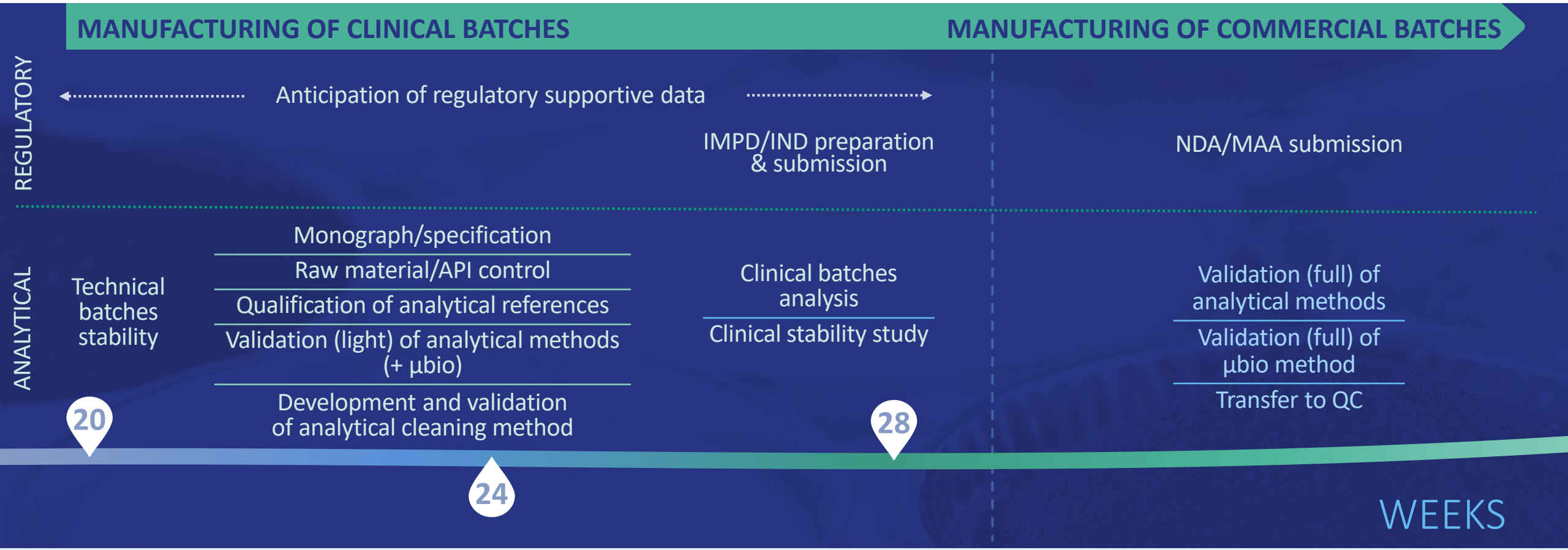

Internal meetings with formulation team → Understanding & definition & anticipation of needs

API = Active Pharmaceutical Ingredient / IMPD = Investigational Medicinal Product Dossier / IND = Investigational New Drug / NDA = New Drug Application / MAA = Marketing Authorization Application

ANALYTICAL DEVELOPMENT & TECHNICO-REGULATORY EXPERTISE: ALL ALONG THE PHARMACEUTICAL DEVELOPMENT & MANUFACTURING PROCESS

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SKYEPHARMA PARTNERSHIP
IN EARLY-STAGE DEVELOPMENT PROGRAM

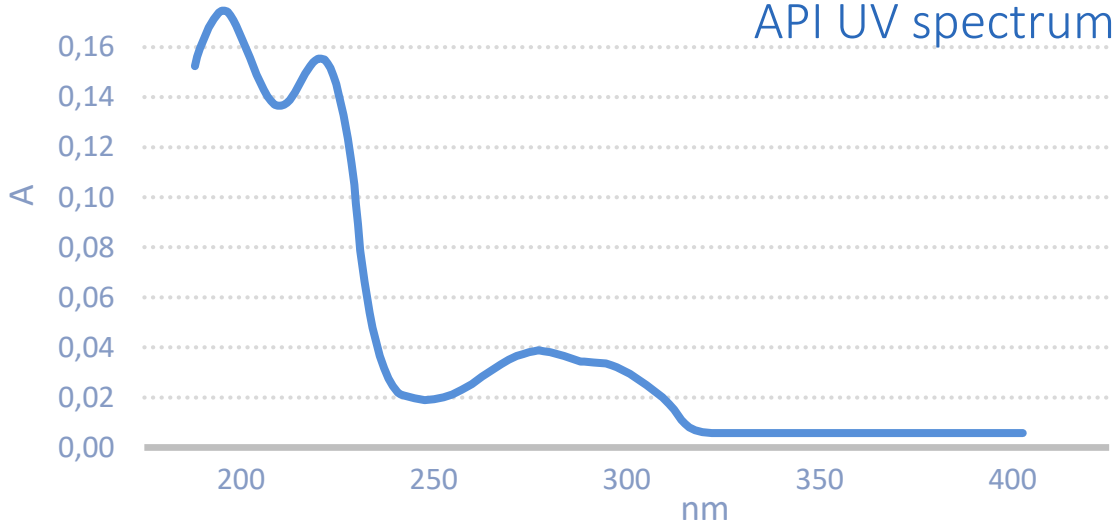
CASE STUDY

OBJECTIVE

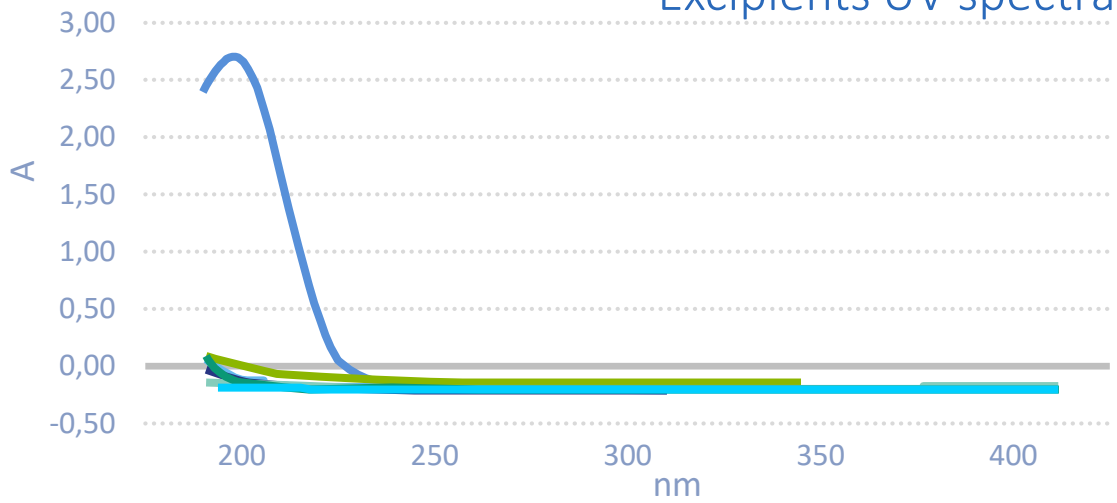
Development of dissolution method during development of a complex formulation

OPTION 1 | ON-LINE DISSOLUTION

API UV spectrum



Excipients UV spectra



RESULT

Option 1 not selected: interference of excipients

API = Active Pharmaceutical Ingredient

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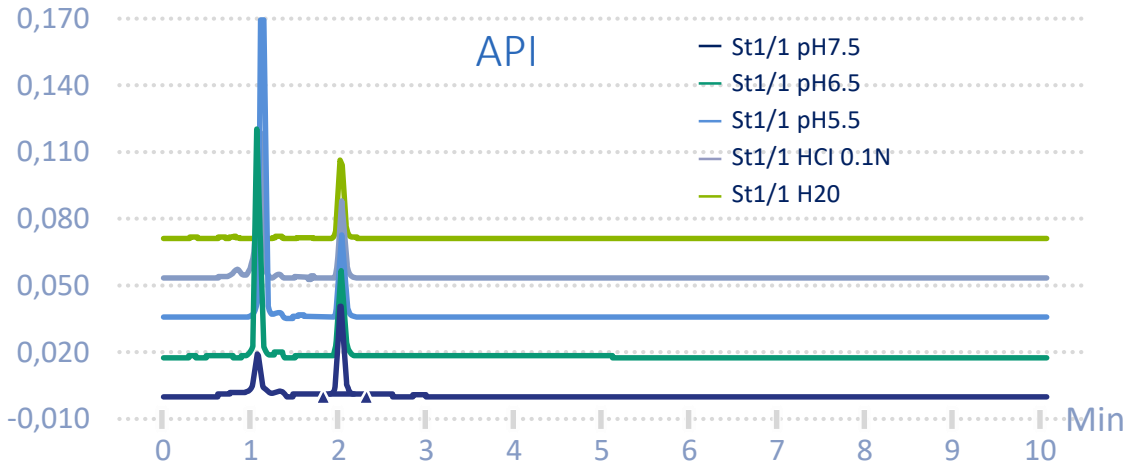
SKYEPHARMA PARTNERSHIP
IN EARLY-STAGE DEVELOPMENT PROGRAM

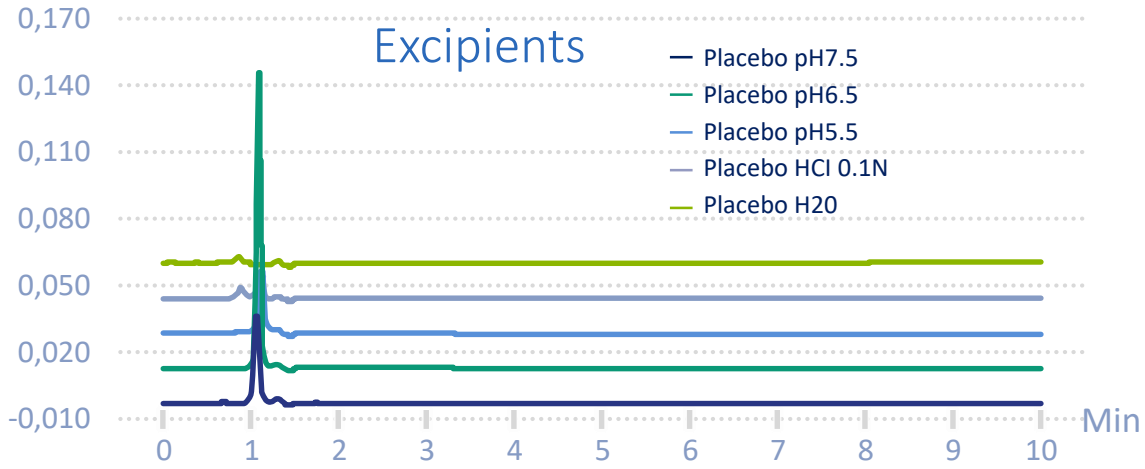
CASE STUDY

OBJECTIVE

Development of dissolution method during development of a complex formulation

OPTION 2 | OFF-LINE DISSOLUTION BY HPLC





RESULT

Option 2 successful : no interference

OUTCOME

Partnership approach at this stage increases efficiency and speed

API = Active Pharmaceutical Ingredient

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DEVELOPMENT OF EXTENDED RELEASE TABLETS

CASE STUDY

OBJECTIVE

Development of dissolution method for extended release formulation with 2 active ingredients

CHALLENGES

- 5 dosage strengths from 2.5/1.25 up to 40/20 mg
- On-line dissolution not possible: both actives have same UV profile

=> development of off-line dissolution by HPLC

RESULT

- 1 single reference solution (at medium dosage strength) instead of 5
- Range: 10% of lowest dosage up to 125% of highest dosage

DATA

	API 1	API 2
LINEARITY RANGE	0,261 to 55,670 µg/mL	0,129 to 27,559 µg/mL
RECOVERY AT 10%	98,0%	98,0%
RECOVERY AT 125%	99,8%	99,8%

OUTCOME

Our expertise in analytical validation allows us to develop an efficient method

API = Active Pharmaceutical Ingredient

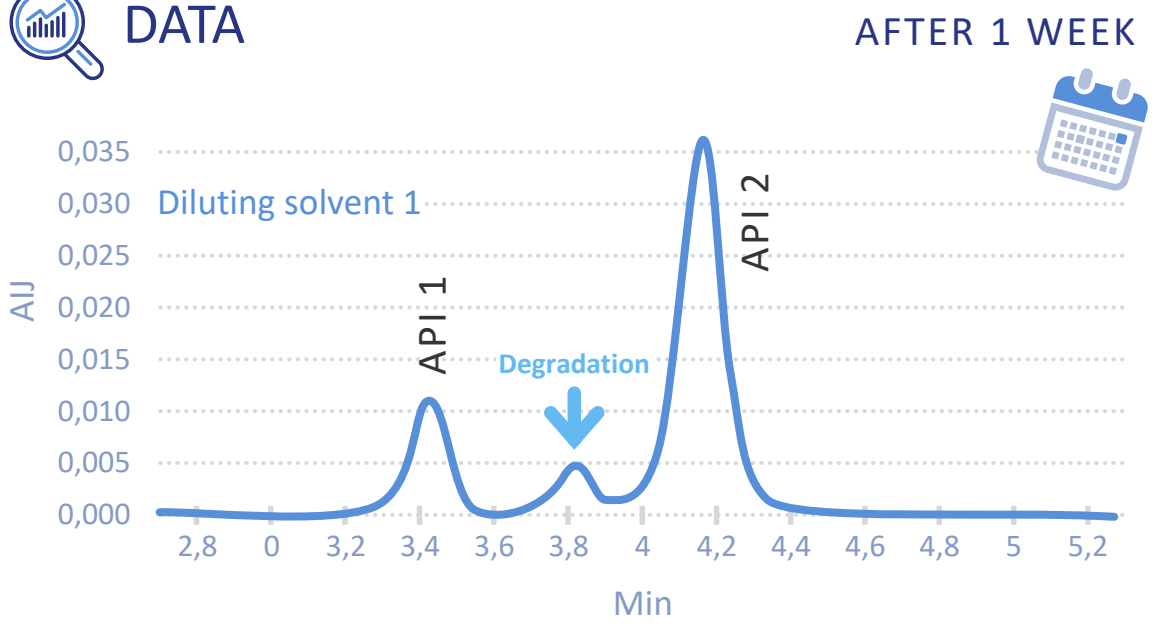
DEVELOPMENT OF EXTENDED RELEASE TABLETS

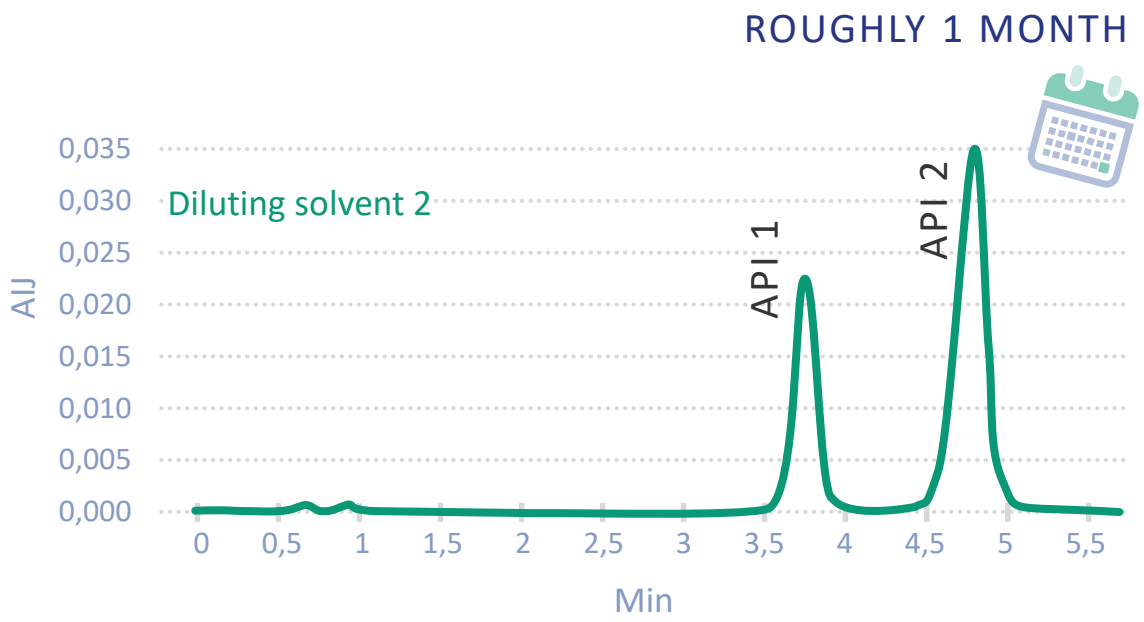
CASE STUDY

RESULT

Stability improvement of reference solution

DATA





OUTCOME

Reduction in process steps | Optimized process | Time & costs savings

API = Active Pharmaceutical Ingredient

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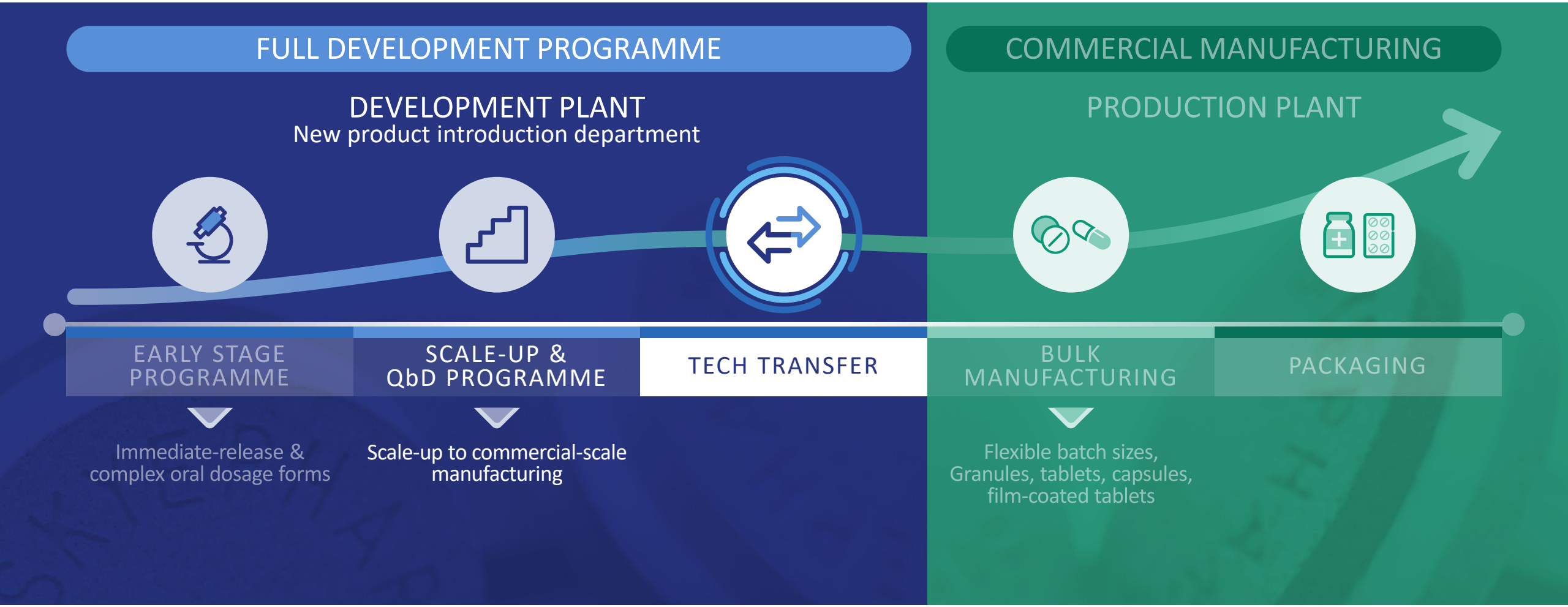
DEVELOPMENT & MANUFACTURING PROCESS



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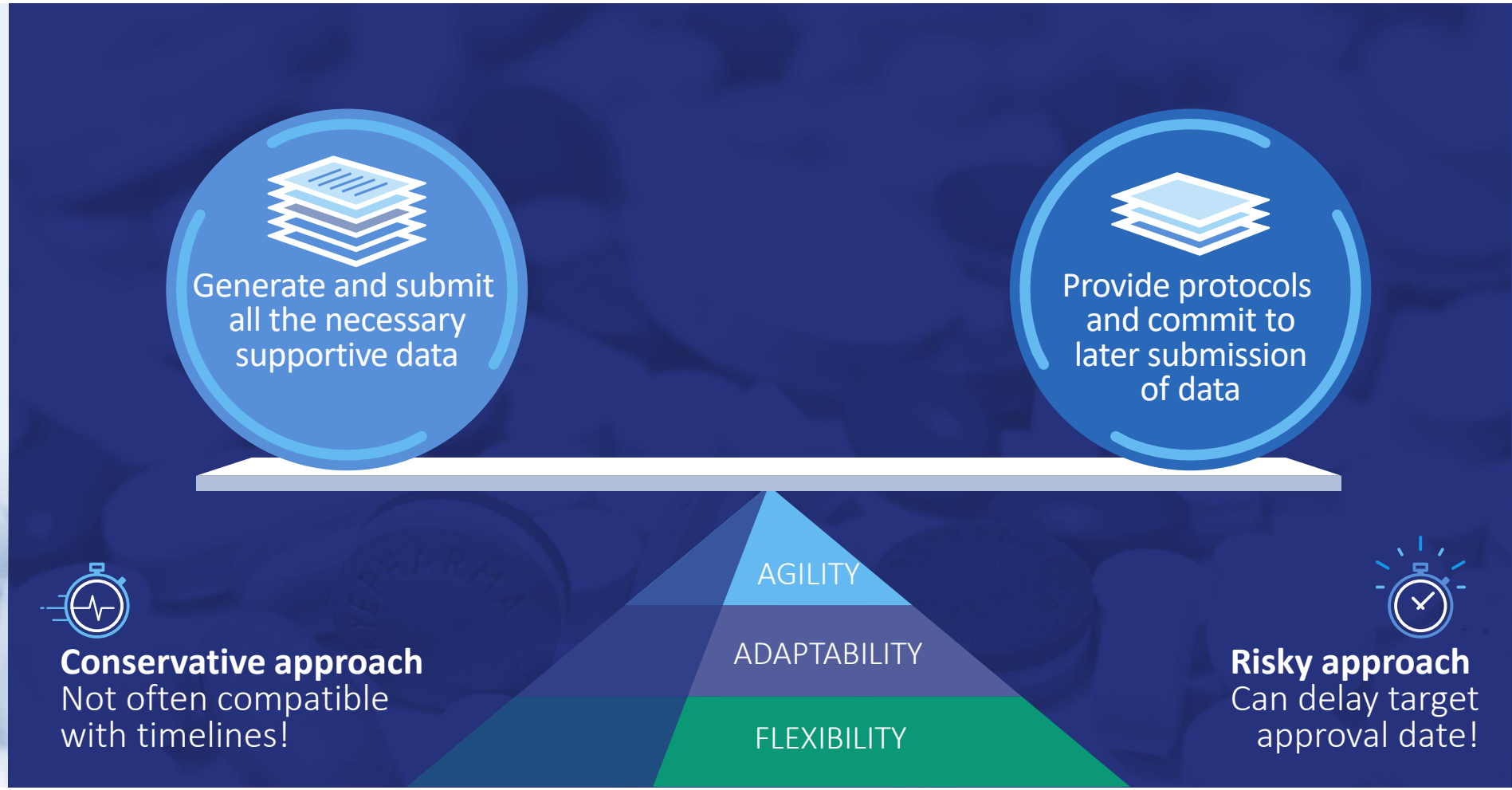
SKYEPHARMA PARTNERSHIP
DURING REGULATORY TECH TRANSFER

Regulatory strategy is defined in early stages of transfer in order to find right approach

Assessment of manufacturing process and analytical method as anticipation key to target the right approach



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SKYEPHARMA PARTNERSHIP
DURING ANALYTICAL TECH TRANSFER

KICK OFF MEETING

Supply of analytical references
Protocol (finished product)
Technical evaluation of methods

Qualification of analytical references
Experimental work (finished product)
Report (finished product)

If necessary: *Development & validation of analytical cleaning method*

If necessary: *Raw material implementation (compendial)*

0 2 8 12

WEEKS

Systematic approach with technical people involved at the beginning: smoother tech transfer process

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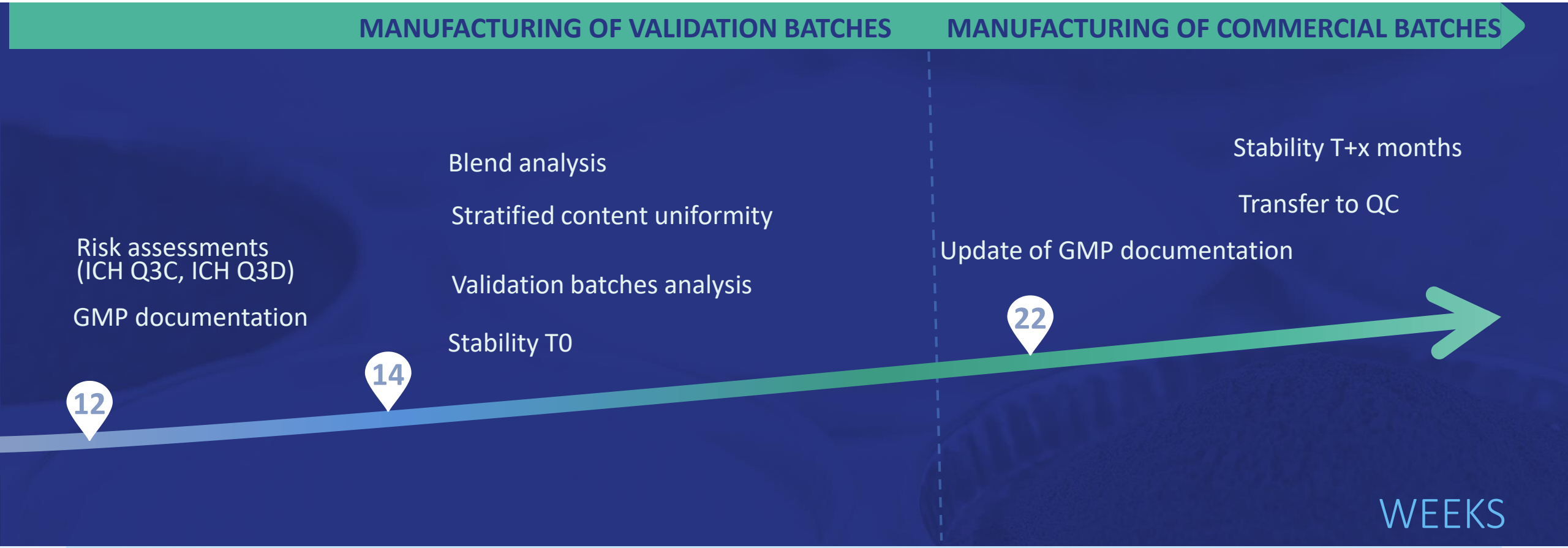
SKYEPHARMA PARTNERSHIP
DURING ANALYTICAL TECH TRANSFER



Systematic approach with technical people involved at the beginning: smoother tech transfer process

Skyepharma

SKYEPHARMA PARTNERSHIP
DURING ANALYTICAL TECH TRANSFER

Skyepharma expertise help you to target the right approach

Transfer waiver (paper-based)
Comparative testing

- Rapid **but** risky
- To be used under limited circumstances
- No knowledge at receiving unit
- Additional costs and materials

Revalidation
Covalidation

- Anticipated approach
- Multi-facility
- Better knowledge at receiving unit
- Covers changes in manufacturing process (anticipation)

AGILITY
ADAPTABILITY
FLEXIBILITY

Skyepharma

SKYEPHARMA PARTNERSHIP
DURING ANALYTICAL TECH TRANSFER

CASE STUDY

OBJECTIVE

Transfer a method of content uniformity
Type of transfer: partial revalidation with accuracy verification and intermediate precision.

DATA

Accuracy verification

	Level 70%	Level 100%	Level 130%
MEAN RECOVERY	105%	103%	102%
ACCEPTANCE CRITERIA		98 – 102%	
STATUS	Failed	Failed	Passed

Failure due to different lab practice in reference solution preparation

MEAN RECOVERY	98%	99%	98%
ACCEPTANCE CRITERIA		98 – 102%	
STATUS	Passed	Passed	Passed

OUTCOME

Skyepharma expertise and agility in investigation (right people, right tools)

SKYEPHARMA PARTNERSHIP
DURING ANALYTICAL TECH TRANSFER

CASE STUDY

OBJECTIVE

Transfer of HPLC for impurity content
Type of transfer: partial revalidation

DATA

Results

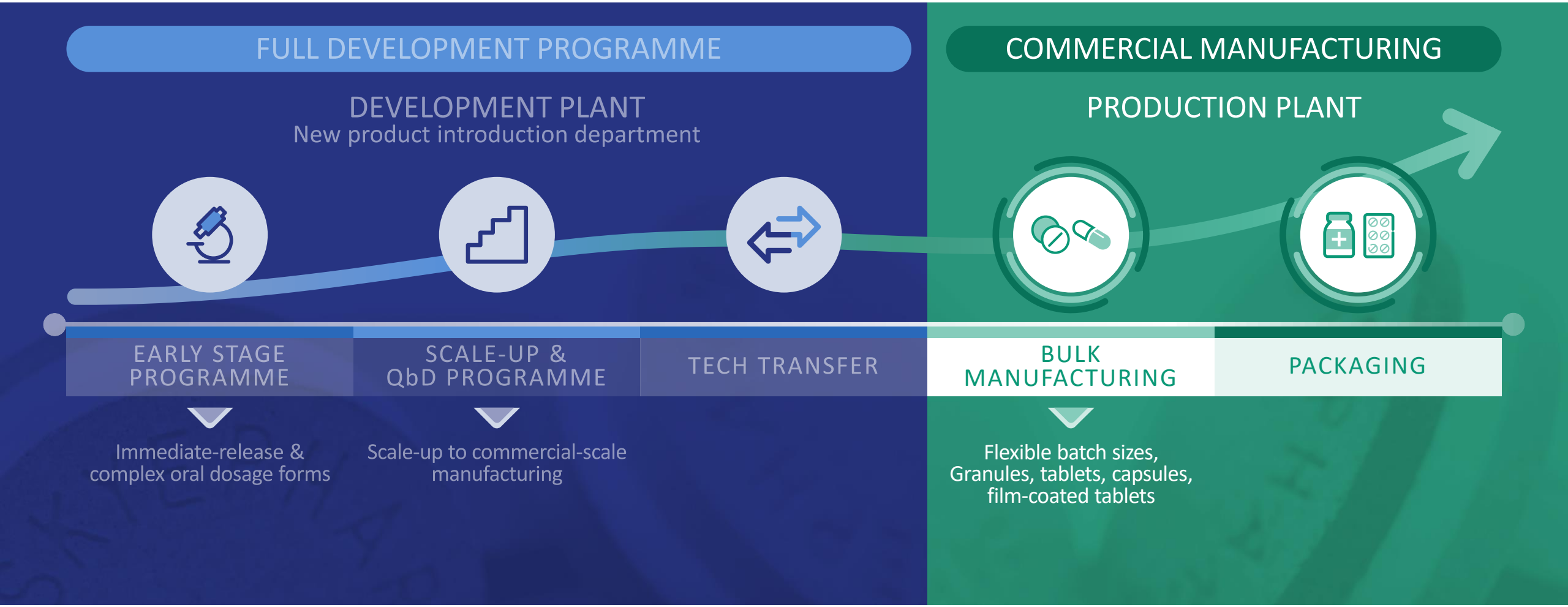
System suitability : Relative standard deviation of areas of 7 injections of reference solution = 8.9% Typical acceptance criteria: ≤ 5.0% → Failed	POTENTIAL IMPACT: underestimation of impurity content on commercialized batches

Solution: Improvement of HPLC operating conditions that allowed for compliant system suitability without modification of regulatory file

OUTCOME

Regulatory and analytical development partnership : right people with right expertise
→ efficiency and rapidity increased on the ground.

DEVELOPMENT & MANUFACTURING PROCESS



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SKYEPHARMA ATTENTION TO QUALITY
DURING MANUFACTURING & PACKAGING PHASES

Right people

Quality team: QA - Reg - Lab

Right processes

- Annual Product Review
- OOS Management
- System Suitability Trend
- Improvement of IPC testing: introduction of PAT

Reduce testing / sampling

Continuous improvement ensures quality every time

OOS = Out Of Specification / IPC = In Process Controls / PAT = Process Analytical Technology

Skyepharma

CONTINUOUS IMPROVEMENT APPROACH DURING MANUFACTURING ROUTINE

CASE STUDY

SITUATION

Assay of API by HPLC

- 30% of non compliant System Suitability in 2018 with impact on batch results
- Analysis of one batch at a time is time consuming

PARTNERSHIP PROCESS

OUTCOME

- Improvement of existing method (addition of internal standard) with very good inter-lab reproducibility (relative standard deviation = 0.3%)
- Reduction of release time of API at Skyepharma
- Secure stability study of the API for supplier / customer

API = Active Pharmaceutical Ingredient

SKYEPHARMA REGULATORY PARTNERSHIP
DURING MANUFACTURING & PACKAGING ROUTINE

CASE STUDY

OBJECTIVE

Progressive transfer of packaging and bulk production from a manufacturing site to Skyepharma

APPROACH

Variation IA Immediate Notification after definition of supply needs

RESULT

- Requirements: need for validation of bulk transportation
- Series of challenges happened during that step
- Our expertise in regulatory affairs allowed us to readjust rapidly the regulatory strategy to approval obtained in expected timelines

OUTCOME

AGILITY AND FLEXIBILITY → ON TIME

ANALYTICAL AND REGULATORY AFFAIRS WORKING IN PARTNERSHIP AS A WARRANTOR FOR ROUTINE PROCESSES

EXPECT THE UNEXPECTED

Skyepharma

Come & meet our team!

7 – 9 November 2019

BOOTH 120F75

CPhI worldwide
where intelligence gathers

Skyepharma

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