SINGLE DOSSIER: WILL NATIONAL EARLY STAGE TRIALS SUFFER OR BENEFIT? A CRO VIEW:

CASE STUDY: A MULTINATIONAL PHASE I/IIA PROOF OF CONCEPT STUDY

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NEW EU REGULATION 536/2014

- Streamlined application procedure via EU portal
- A single set of documents
- Harmonised procedure for the assessment
  - Part I is jointly assessed by all Member States concerned
  - Part II is assessed by each Member State concerned separately
- Strictly defined deadlines
- Simplified reporting procedures
- Increased transparency as regards clinical trials and their outcomes
PHASE I / IIA STUDIES

- ‘Drive’ to have first assessment of efficacy as early as possible
  - Proof of Concept (POC)

- Phase I / Ila study
  - Healthy Volunteer part
  - Patient part

- Patient population sometimes difficult to find in Western Europe
  - HV part in Western Europe
  - Patient part in Eastern Europe
INTRODUCTION

- US biotech company
  - Phase I / IIa study with Hepatitis C compound
    - First in Human part in healthy volunteers
    - Patient arm for early proof of concept
  - Potential issue with non-clinical data

- IND received clinical hold by FDA, due to concern on non-clinical data

- Sponsor looking a rapid solution
AS PERFORMED 1/2

- Assessment of non-clinical issue by internal experts
  - Available non-clinical data deemed acceptable
  - Scientific Advice required

- European scenario proposed
  - Belgium
    - Healthy volunteer part / Patient part
  - Romenia
    - Patient part
  - Poland
    - Patient part

- HV part in Belgium due to short RA timelines
  - HV part almost finished when Romenia / Poland are ready to start patient recruitment
  - Staggered start-up
Type I Scientific Advice in Belgium
- 30 day written response

In Parallel preparation of CTA applications
- Immediate submission if positive scientific advice

CTA submission approved
- Belgium: 15 days
- Romenia: 69 days
- Poland: 94 days

HV part almost completed completed when patient recruitment started
AS IT WILL BE UNDER REGULATION 536/2014

- Scientific Advice
  - 30 day written response

- Constraint
  - Single dossier will lead to single submission
  - No option anymore for staggered start-up

- Two options
  - Submit all countries at once
  - Submit Belgium first for HV part
    - After approval Belgium submit other countries
OPTION 1 – SUBMISSION WITH ALL COUNTRIES

- Single submission
  - Validation:
    - 10 days
  - Assessment (Part I and II)
    - 45 days + 31 days = 76 days

TOTAL: 86 DAYS

- Single submission approval between 60-106 days, average taken
OPTION 2 – STAGGERED SUBMISSION

- Submit application with Belgium only
  - Validation: 10 days
  - Assessment (Part I and II): 45 days + 31 days = 76 days

- Assumption: Belgium
  - Validation: 3 days
  - Assessment: 15 days

- Add Romania and Poland after approval
  - 52 days

TOTAL: 70 DAYS

Additional country: 52 – 83 days, 83 days taken
OVERVIEW

Current CTA pathway
- BEL
- ROM
- POL
  Start Dosing HV

New Regulation: Scenario 1
- All countries
  Start Dosing HV

New Regulation: Scenario 2
- BE
- POL / ROM
  Start Dosing HV
CONCLUSION

- Phase I / IIa proof of concept studies
  - Special case, combining early phase and late phase elements
  - Flexibility and smooth start-up required

- New Regulation offers less flexibility

- Workaround possible

- Goodwill of regulators

- Early phase attractiveness more than timelines alone
THANK YOU FOR YOUR ATTENTION

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QUESTIONS?