ORPHANDEV, ACCELERATOR PLATFORM FOR THE DEVELOPMENT OF ORPHAN DRUGS

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INTRODUCTION

The European Union (EU) introduced a new legislation in 2000 in order to stimulate the research and development of orphan drugs. This regulation establishes a centralised procedure for the designation of orphan medicinal products and puts in place incentives for the research, development and marketing of orphan medicinal products (Regulation (EC) No 141/2000) [1]. 15 years after, this disposal is a success, with 1406 designated orphan medicinal products (January 1st 2015). However, this regulation remains poorly known by the academic sector while it is often at the origin of the proof-of-concept and the creation of start-ups.

15 YEARS OF ORPHAN DESIGNATION IN EUROPE

The procedure:

- Pre-submission meeting with EMA: Optional but strongly recommended
- Submission of the application: According to the EMA deadlines
- Validation by EMA: (day 1)
- Evaluation by the COMP (Committee for Orphan Medicinal Products): positive or negative opinion (60 to 90 days)
- Evaluation by the European commission (EC): final decision (30 days)

The incentives:

- Fee reductions in the regulatory procedures at the EMA (ex: Protocol assistance, Marketing Authorisation Application (MAA))
- A 10 years commercial exclusivity after MAA in Europe and 7 years in the US
- Visibility and recognition of the project and its sponsor
- Eligibility for European calls for projects

Eligibility criteria:

- prevalence (< 1/2000, to be proven)
- medical plausibility (proof-of-concept)
- significant benefit (vs standard care)
- Life-threatening or debilitating condition

Protocol assistance:

Aims to support sponsors to provide adequate data for benefit-risk assessment at the time of MAA:

- Reduction in major objections
- Higher MAA success rate
- Shorter MAA procedure

25% of the applications failed (negative COMP opinion or withdrawal during assessment) ➔ need to evaluate the admissibility of the application before submitting

ORPHANDEV: A SUPPORT FOR ORPHAN DESIGNATIONS

Mean time of the procedure

<table>
<thead>
<tr>
<th>Activity</th>
<th>Months</th>
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<tbody>
<tr>
<td>Preparation of the application (until validation by EMA)</td>
<td>6,7</td>
</tr>
<tr>
<td>Evaluation by EMA (COMP) and EC</td>
<td>3</td>
</tr>
<tr>
<td>Negative COMP opinions</td>
<td>3</td>
</tr>
<tr>
<td>Withdrawals during assessment</td>
<td>11</td>
</tr>
<tr>
<td>EC designations</td>
<td>12</td>
</tr>
<tr>
<td>Positive COMP opinions</td>
<td>15</td>
</tr>
<tr>
<td>Applications submitted</td>
<td>15</td>
</tr>
</tbody>
</table>

Fig 3: Number of orphan applications submitted with OrphanDev support (2013-2015)

OrphanDev information tools:

A pedagogical sheet:
OrphanDoc « The orphan designation »

A clinical research professionals' training:
Eudipharm’s « Orphan Drug & Rare Disease Seminar »
labeled IMI Pharmatrain

OrphanDev support reduces the risk of failure:

- 4 applications not submitted after the feasibility study
- only 3 applications were withdrawal during assessment

OrphanDev offers:

- Support for establishing a work calendar
- Support for drafting the scientific document
- Support for compiling the administrative dossier
- A specific expertise for a feasibility study before the submission assistance in the meetings with the agencies
- Submission and follow-up of the application

REASONS FOR WITHDRAWAL OR NON-SUBMISSION

<table>
<thead>
<tr>
<th>Prevalence</th>
<th>Medical plausibility</th>
<th>other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feasibility study</td>
<td>Pre-submission meeting</td>
<td>Withdrawal during assessment</td>
</tr>
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Figures 1 & 2: Evolution and total number of orphan applications [2]

REFERENCES