Workshop - SME's Perspective on Scientific and Regulatory Advice – European Medicines Agency –

Lene Rose Arfelt MSc, Head of QA and RA Europe

26 May 2011

ThromboGenics
Advancing Science. Enhancing Vision.

SME's Perspective - Agenda

Agenda

General introduction	ThromboGenics
General introduction	Ocriplasmin project
SME perspective on	Scientific advice
	Paediatric applications
	Pre-MAA meetings
Key messages	

General Introduction ThromboGenics Clinical Pipeline

Drug Candidate	Indication	Clinical	Next Milestones
		Phase I / Phase II / Phase III	
Ocriplasmin (microplasmin)	Symptomatic vitreomacular adhesion (sVMA)		Filing H2 2011
	Diabetic retinopathy (DR)		Next study H1 2012
	Age-related macular degeneration (AMD)		Results H2 2012
TB-402 (anti-factor VIII)	Deep vein thrombosis (DVT)		Next Phase Q2 2011
	Atrial fibrillation (AF)		
TB-403 (anti-PIGF)	Cancer		Next Phase H2 2011
Staphylokinase	Acute myocardial infarction (AMI)		Results H2 2011

PIGF indicates placental growth factor.

Ophthalmology Cardiovascular Cancer

ThromboGenics
Advancing Science. Enhancing Vision.

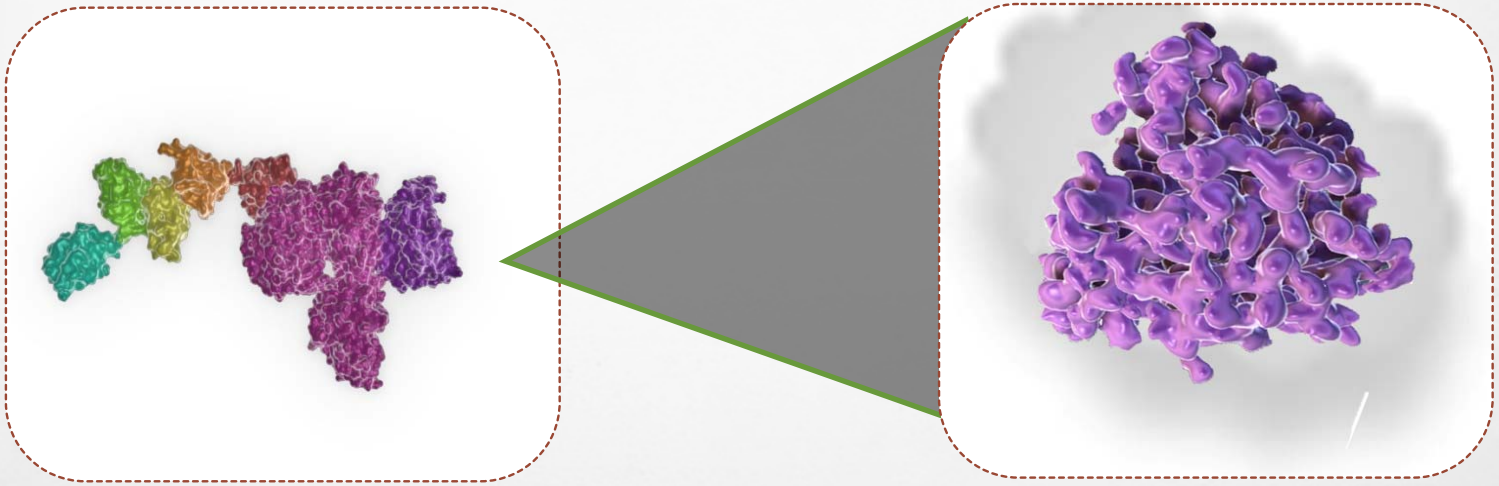
General Introduction – Ocriplasmin Project

Introduction

- Ocriplasmin: a truncated form of plasmin developed as a pharmacologic treatment for symptomatic vitreomacular adhesions (sVMA)
  - sVMA is a result of incomplete separation of the vitreous from the retina[1]
    - Can lead to retinal damage and vitreous inflammation

Plasmin

Ocriplasmin



ThromboGenics
Advancing Science. Enhancing Vision.

1. Gandorfer et al. *Invest Ophthalmol Vis Sci.* 2004;45:641–647. .

General Introduction – European Regulatory Strategy

Introduction

Activity	Timing
SME registration	June 2009 – DONE
Scientific Advice with EMA	November 2009 – DONE
Paediatric Waiver positive opinion	October 2010 – DONE
Letter of intent	October 2010 – DONE
Scientific Advice national authorities	Oct-Nov 2010 – DONE
Rapporteur/Co-Rapporteur appointment	January 2011 - DONE
EMA pre-submission meeting	2011- DONE
Meetings Rapporteur/Co-Rapporteur	2011
Planned submission Centralized Procedure	2011

An example: Pre-activities
Scientific Advice perspective as a SME

Scientific Advice

Activity	Timing
Fee reduction request Scientific Advice (SA) + Letter of intent request for SA	September 2009
SA pre-meeting package	November 2009
SA Pre-submission meeting	November 2009
List of comments from pre-submission meeting + submission of final briefing package	November 2009
Start Scientific Advice Procedure (Day =0)	December 2009
SAWP agreement (Day= 40) – no need for discussion meeting	January 2010
CHMP adoption	January 2010

An Example:
Scientific Advice perspective as a SMEcs

Scientific Advice

Scientific advice learning:

- Take advantage of pre-meetings for scientific advice as they help you as a SME to a more targeted process with SAWP – time invested in pre-meetings can pay off Day 70 vs Day 40 scientific advice procedure

An example: Pre-activities Paediatric Investigational Plan perspective as a SME

PIP

Activity	Timing
Request pre-submission meeting paediatric Letter of intent article 7 (Reg. 1901/2006 as amended)	March 2010
PDCO appointment rapporteur/peer-reviewer	April 2010
PIP pre-submission package draft (app form, part B-F, references, list of issues)	May 2010
PIP pre-submission meeting (2nd pre-PIP)	May 2010

An Example: Paediatric Investigational Plan perspective as a SME

PIP

- **EMA Participants PIP pre-submission meeting:**

  PDCO rapporteur, PDCO Peer reviewer, EMA (Paediatric coordinator, Paediatric Medicines, SME)
  (5 in total)

- **ThromboGenics Participants:**

  Belgium and US (4 in total)

- **Meeting format:** Teleconference for approx 1 hour

An Example:
Paediatric perspective as a SME

PIP

Pre-meeting feed-back on draft PIP application included:

- Agreement on methodology description of prevalence assessment
- More detailed definition of condition
- Clinical feasibility justification should be included and a clinical expert statement from an ophthalmology paediatric expert should be considered
- Comments on paediatric clinical trials in other conditions were addressed
- General comments on level of details in PIP application

An example:
Paediatric Investigational Plan perspective of a SME

PIP

Activity	Timing
Submission of PIP application and request waiver	June 2010
Validation of PIP application (Day=0)	August 2010
First PDCO discussion	Sep 2010
Adoption of PDCO opinion	Oct 2010

An example: Paediatric Investigational Plan perspective of a SME

PIP

Learning:

- Take advantage of pre-meetings for PIP applications as they help you as a SME to a more targeted process with PDCO.
- Time invested in pre-meetings can pay – our perspective Day60 opinion
- Teleconference format for pre-meeting introduces uncertainties in the communication. EMA is recommended to offer also face-to-face pre-meetings for PIP.

An Example:
pre-MAA meeting as a SME

Learnings:

- Pre-submisison meetings for MAA are recommended 6-7 months before start of Centralised Procedure
- Briefing package 2 weeks before pre-MAA meeting
- SME office representative participates in pre-MAA meeting
- SME office helpful in clarifications on administrative matters on letter of intent with Product and Application Business Support (PA-BUS) unit at EMA
- SME clarification on process for translation assistance during the CP under assumption that SME status is still valid at time of submission.

(Example: Applicant has to organise own translations in Norwegian/Icelandic as a minimum)

Key Messages for SME's

Key Messages

- Regulatory strategies including timely and relevant health authority meetings with EMA and national health authorities are a key success factor
- Use all possibilities for pre-submission meetings with EMA whenever possible
- Consider requesting face-to-face pre-meetings and other meetings to avoid uncertainties on teleconferences
- Pre-meetings ensure a more targeted process
- Don't hesitate to contact SME office in case of problems with other sections at EMA