Experience from an SME in initiating clinical trials

Tom Vanthienen
Senior Director RA & QA

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AGENDA

- Introduction
- PregLem
- Clinical trials at PregLem
- Experience with Phase III trials
- Lessons learned

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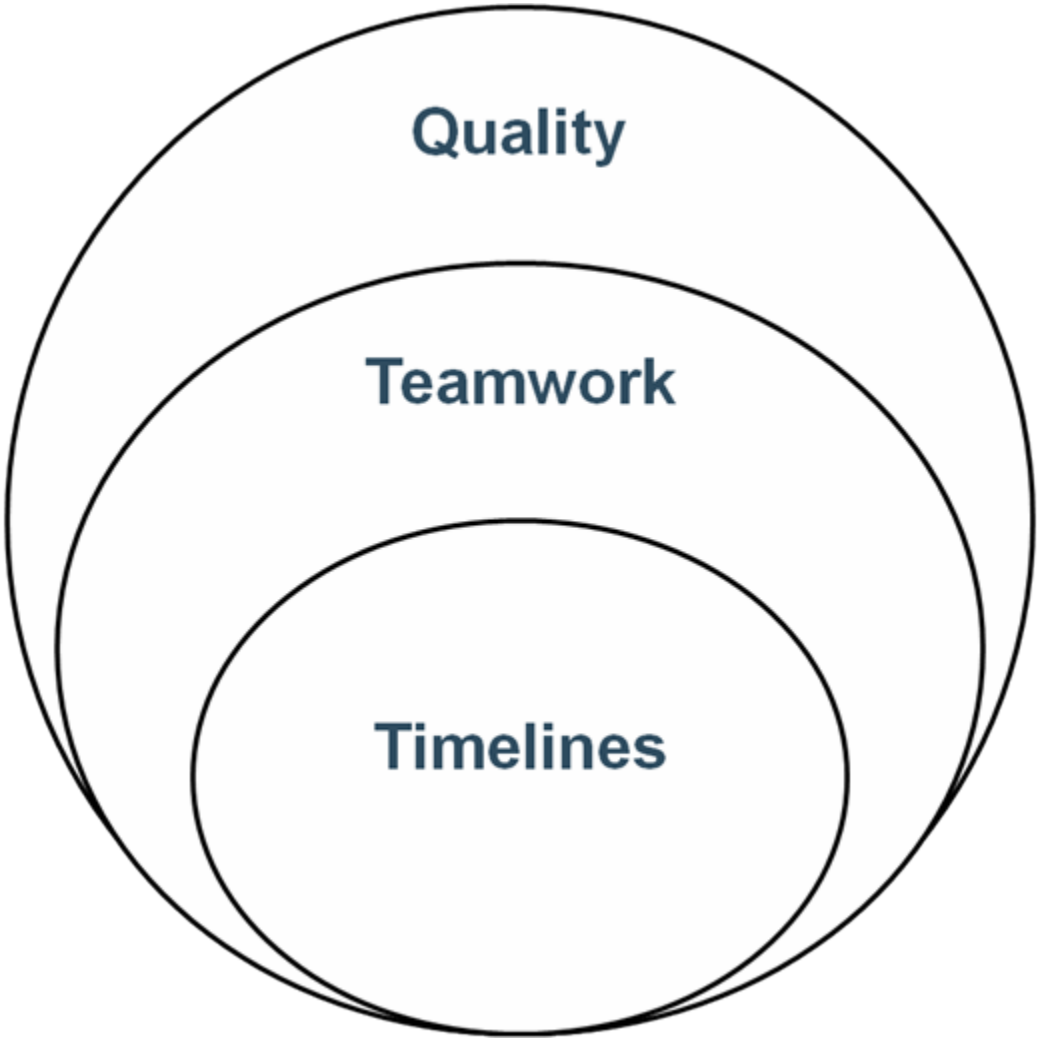
Introduction



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PregLem

- European specialty pharma company founded in Geneva, Switzerland in 2007
- SME status from EMA (PregLem French affiliate)
- Developing drugs addressing significant benign gynecological conditions
- Experienced management team with proven track record in women's reproductive medicine market
- Addressing significant market opportunities
- Advanced pipeline of *first-in-class* products with strong IP protection
- First product launch foreseen in 2011
- Backed by blue chip investors with CHF68.0m in committed capital; CHF15.0m in reserve capital
- www.preglem.com

A fast developing speciality biopharmaceutical company, focused on women's reproductive medicine

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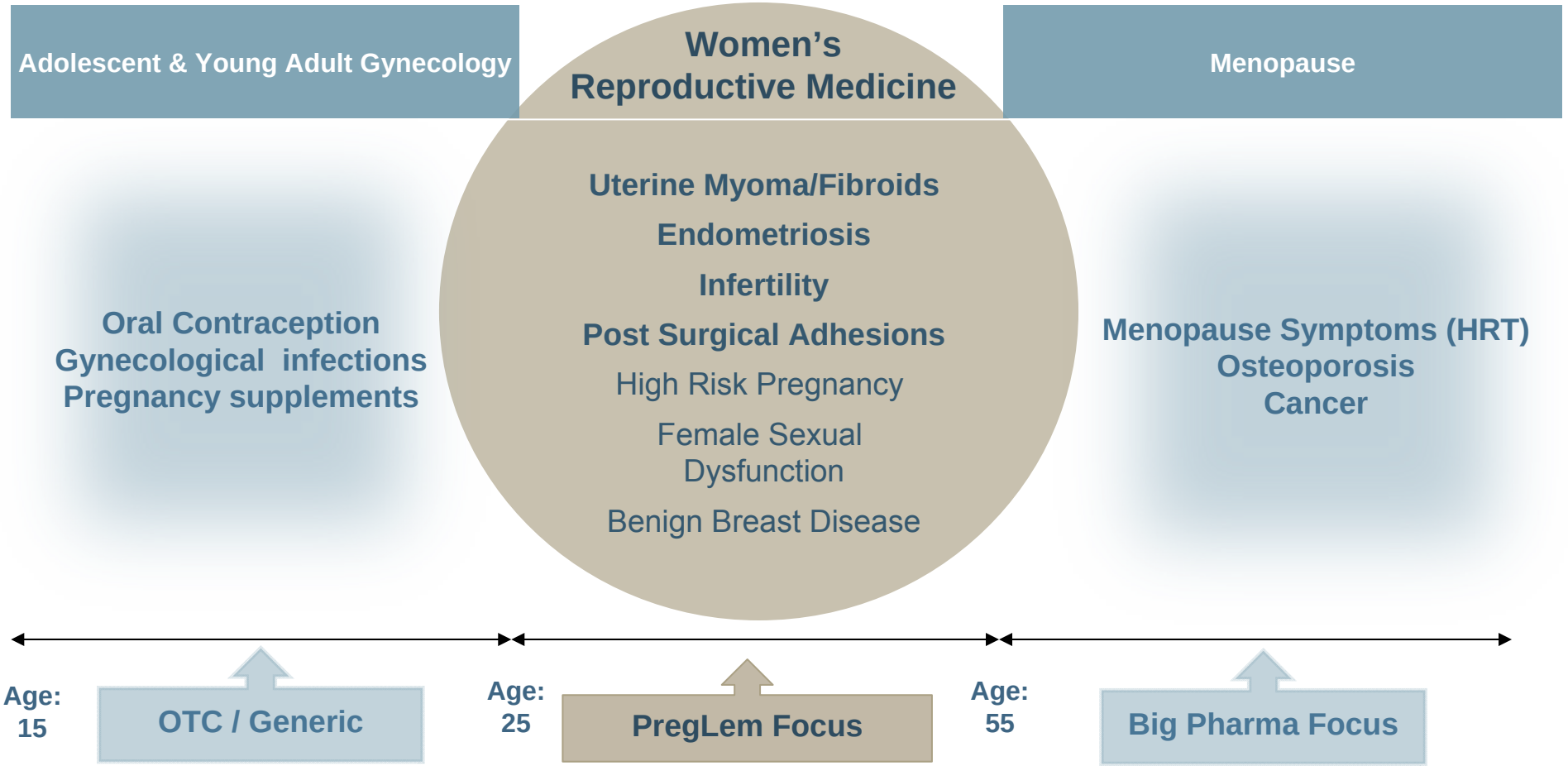
Therapeutic Area Focus

Women's Reproductive Medicine – a €4 Billion Target Market



Source: World Markets Report - CIBC Research 2007, European Equity Research – Bear Stearns 2005, Pipeline Insight: Endometriosis; Datamonitor 2004, Opinions in Uterine Fibroid Management; Datamonitor 2002

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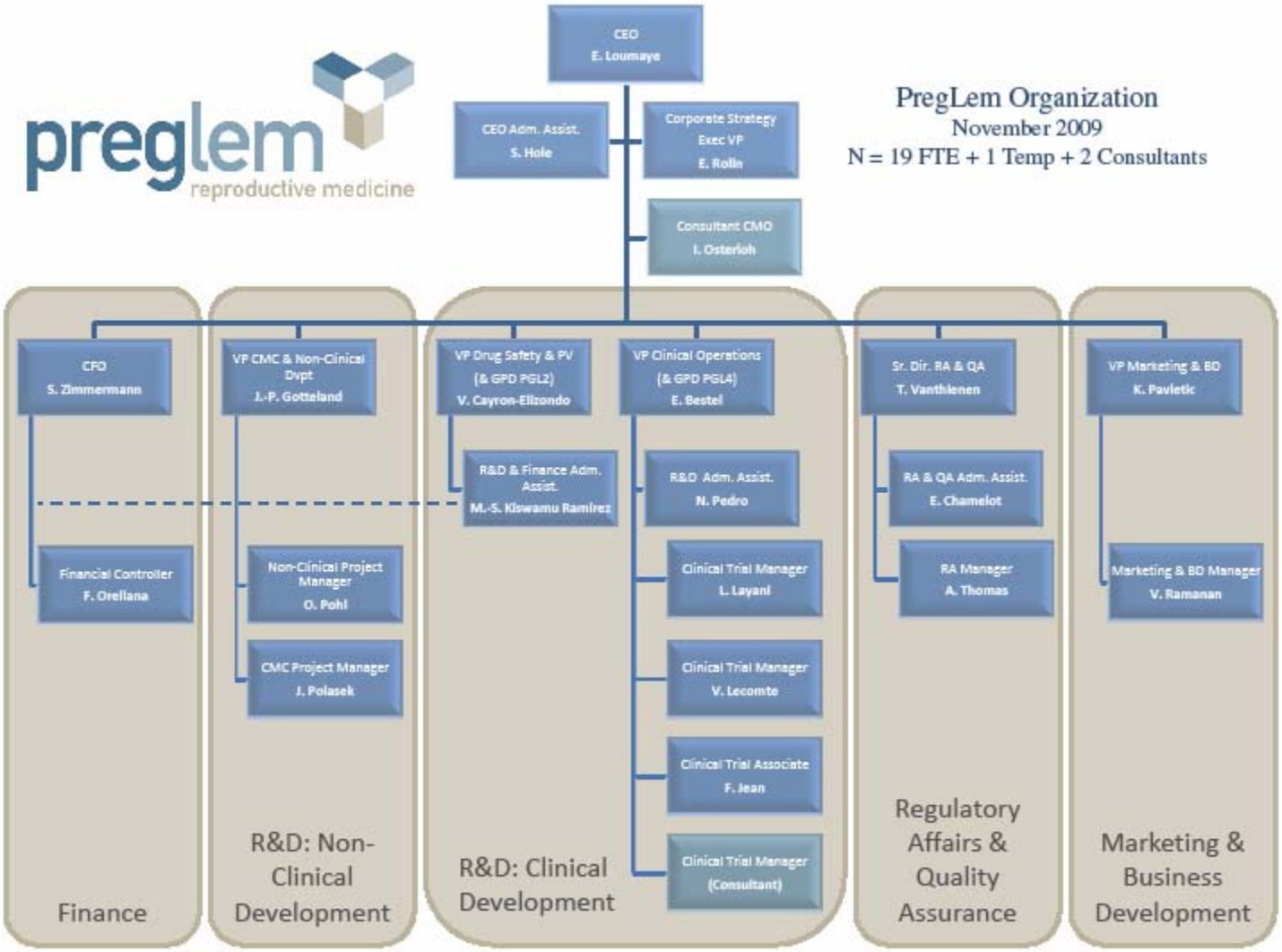

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Clinical trials at PregLem

Product	Indication	Mechanism of Action	Pre Clinical / Phase I / Phase II / Phase III / Marketed	Territory	Comment
PGL4 *Esmya ™* *Ulipristal acetate*	Pre-Operative treatment for Uterus Myoma	SPRM		EU	Marketed in Europe*
	On/Off long term treatment of Uterus Myoma			EU	Pivotal phase III under way
	Pre-Operative treatment for Uterus Myoma (anemia)			US	Pivotal phase III under way
PGL3	Luteal Support in ART	GnRH agonist Ovulation Induction		WW	Supportive product at PGL4 launch
PGL2	Endometriosis Mild to Moderate	(STS-I)		WW	If phase Ib conclusive move to phase II
PGL1	Ovarian Reserve Modulation Age Related Infertility	Somatostatin Antagonist (SST-Antag)		WW	If partnership secured move to phase I
PGLX	Prevention of post surgical adhesions Moderate to severe endometriosis			WW	

*ulipristal acetate already marketed as ellaOne ® in EU

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Experience with Phase III trials
PGL4001 Introduction

- PGL4001 (INN: ulipristal), an NCE, is a Selective Progesterone Receptor Modulator (SPRM)
- Discovered by Research Triangle Institute (RTI, USA)
- Initial development and early clinical studies conducted by National Institute of Child Health and Human Development (NIHCD, USA)
- PregLem in-licensed the molecule from HRA Pharma for the development in significant benign gynaecological conditions, e.g. uterine myoma
- HRA Pharma (France) received EU MAA (15 May 09) for ulipristal acetate in emergency contraception (EllaOne® : 30 mg tablets, single dose)

PEARL I – Randomised, double-blind Phase III trial of ulipristal acetate vs placebo

Pivotal Phase 3 Study Design – PEARL I

PEARL I

Population

Uterine Fibroids
PBAC: > 100
Anaemia: Hb ≤ 10.2 g/dL
& Htc ≤ 30%
Uterus vol: <= 16 weeks
Indication for surgery

Russia, Ukraine, Czech, Hungary, Romania, India
12 weeks

Placebo + iron	n = 48
PGL4: 5 mg + iron	n = 96
PGL4: 10 mg + iron	n = 96

Co- Primary Endpoints

A: % patients with PBAC < 75

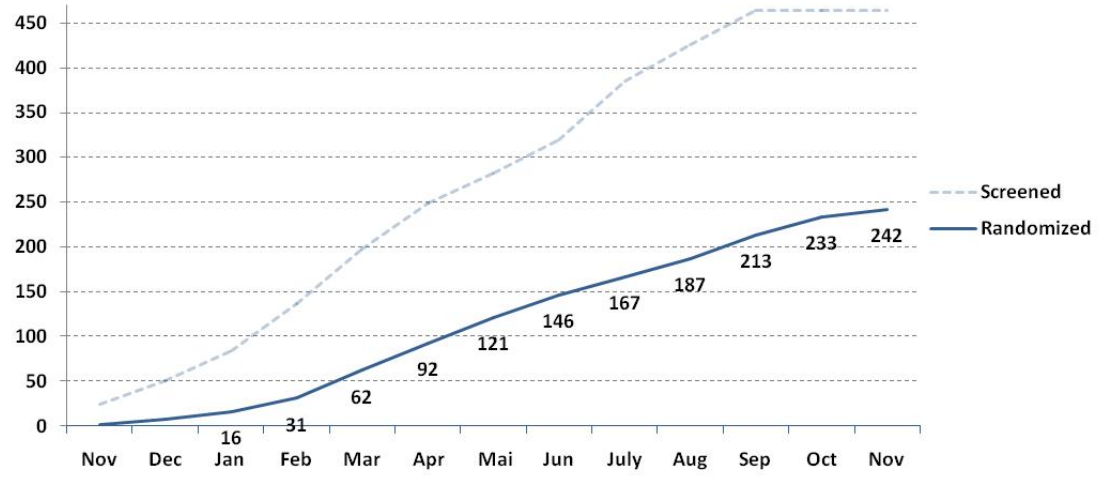
B: change of total myoma volume

Superiority

Power: 90 %
Two comparisons

Primary objective: *Efficacy of ulipristal acetate in reducing excessive bleeding and total fibroid volume compared with placebo*

Recruitment Status: Enrolment Closed, n=240



Last Patient In	Nov 2009
Results	**June 2010**

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PEARL II – Randomised, double-blind Phase III trial of ulipristal acetate vs GnRH agonist

Pivotal Phase 3 Study Design – PEARL II

Belgium, Austria, Spain, Israel, Italy, Poland

12 weeks

PEARL II

Population

- Uterine Fibroids
- PBAC: > 100
- Uterus vol: <= 16 weeks
- Indication for surgery*

GnRH-A (leuprorelin)	**n = 100**
PGL4: 5 mg	**n = 100**
PGL4: 10 mg	**n = 100**

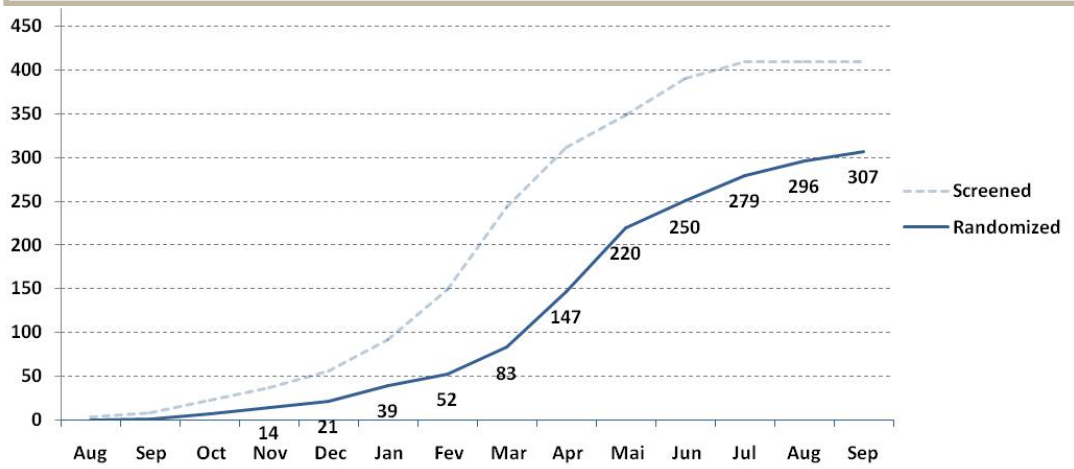
GnRH-A & PGL4: DB & Double Dummy

Primary Endpoints

- **A: % patients with PBAC < 75**
- **A: Mean serum E2 levels**
- **B:% of subjects reporting moderate or severe hot flushes**
- **Non inferiority/Superiority**
- **Power: 90 %**
  Two comparisons

Primary objective: *Efficacy of ulipristal acetate in reducing excessive bleeding compared with GnRH agonist*

Recruitment Status: Enrolment Closed, n=300



Last Patient In	Sep 2009
Results	**May 2010**

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Several steps for PEARL I/II

- Protocol Committee Meeting
- Scientific Advice
- CRO selection + other providers
- Initial submission to EC/CA

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Protocol Committee Meeting

- Sample size
- Drug Safety Monitoring Board
- Dose rational
- Efficacy/safety endpoints
- Choice of comparator
- Risk/benefit

Scientific Advice

- 4 National Health Authorities
- Request and briefing document «in-house»
  - Clinical Aspects (patient exposure, dose selection, control groups, primary/secondary endpoints)
  - Nonclinical Aspects (carcinogenicity study)
  - Quality Aspects (stability data)
- Meetings
  - PregLem team
  - Expert in therapeutic area

CRO selection + other providers

- Bid defense meetings organised by clinical department with CRO
  - To know your counterpart
  - To discuss strategy for country and site selection
  - To discuss timelines for submission to CA/EC
  - To discuss submission package
- Other Service Providers
  - Drug supply
  - Data Management and Statistics
  - Pharmacovigilance
  - Central lab

Initial submission to CA/EC

- Kick-off meeting
- Core documents PregLem
  - IB, IMPD, Protocol, Labelling of IMP
- Core documents CRO
  - Application form CA/EC, Patient Information Sheet/Informed Consent Form, locally required documents
- Review/approval processes
  - Timelines to be agreed
  - Time-consuming but lead to quality

After submission and study approval

- Preparation of responses to CA/EC questions
  - Collaboration with relevant departments
  - Review/approval respecting timelines from CA/EC
- Version control of different documents
- Protocol amendments

QA activities

- Audit of service providers
  - Before signing contract
  - During trial
- Audit of clinical sites

Lessons learned

- Advice from Health Authorities
- Know your service providers and look for the best collaboration
- Keep control internally on your core documents
- Think Quality