

Start-up och biotech företag erbjuds "development-competence" från pharma-industrin

Frukostseminar
Stockholm Science City
12 March 2009



CONTRACT RESEARCH ORGANISATION

A Scandinavian Company with European Coverage

Copenhagen, 2009

KLIFO

KLIFO – a full service CRO offering

- Drug Development Counselling
- Clinical Trial Services
- Clinical Trial Supply

[Alejandra Mørk](#), CEO, 18 years product development experience from Pharma, Nycomed

[Arne Brodin](#), Senior CMC Advisor, +20 years of product development experience from Pharma, AstraZeneca

[Thor-Björn Conradson](#), Senior Medical Advisor, 24 years product development experience from Pharma, AstraZeneca and Nycomed

Drug Development Process



Selection of drug candidate for development

- Assessment of mechanism of action
- Assessment of potency/efficacy potential
- Assessment of toxicity
- Assessment of pharmaceutical/technical properties
- Assessment of possible product profile
 - ? Medical need
 - ? Better than ...
 - ? As good as...

Prepare the first target product profil
(or draft Summary of Product Characteristics)

Drug Development Process



First drug development plan

- Planned "Proof of Concept"

What will be special for this drug ("the concept")?

How can the concept be tested in a clinical context?

- Phase 1 program:

What is mandatory

What would be smart

What to test in healthy volunteers and what to test in patients

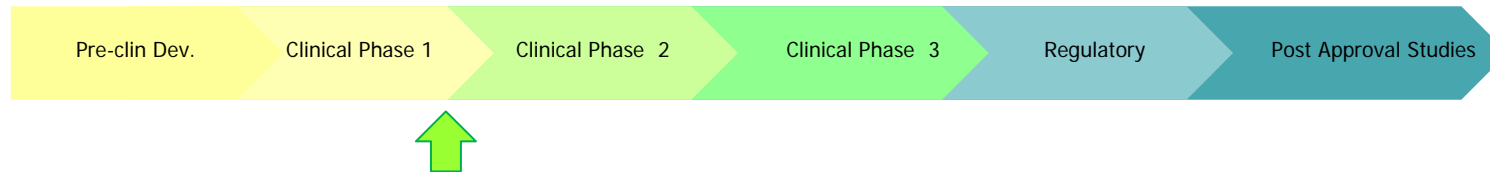
- Phase 2a program:

How to test the concept?

How to design the study?

- Pharmaceutical formulation: What should be ready when

Drug Development Process



Phase 1 program finalised

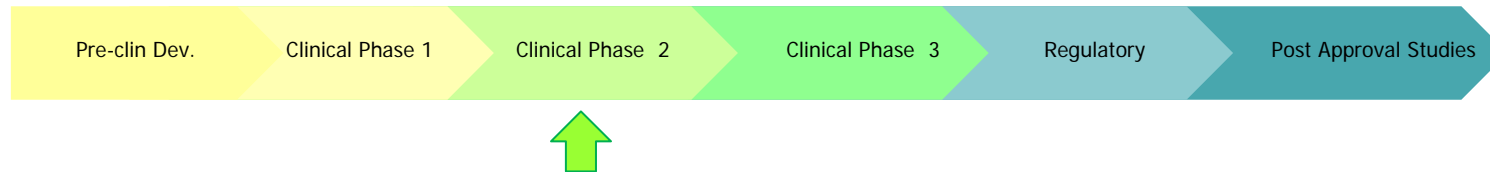
- Assessment of safety of drug
- Confirmation or revision of Target Product Profile
- Decision to continue into phase 2
- Decision to continue independently, to partner or to sell the project

Update and finalise the Phase 2 programme

- Prepare study protocols
- Provide study drugs

Consider a Scientific Advise

Drug Development Process

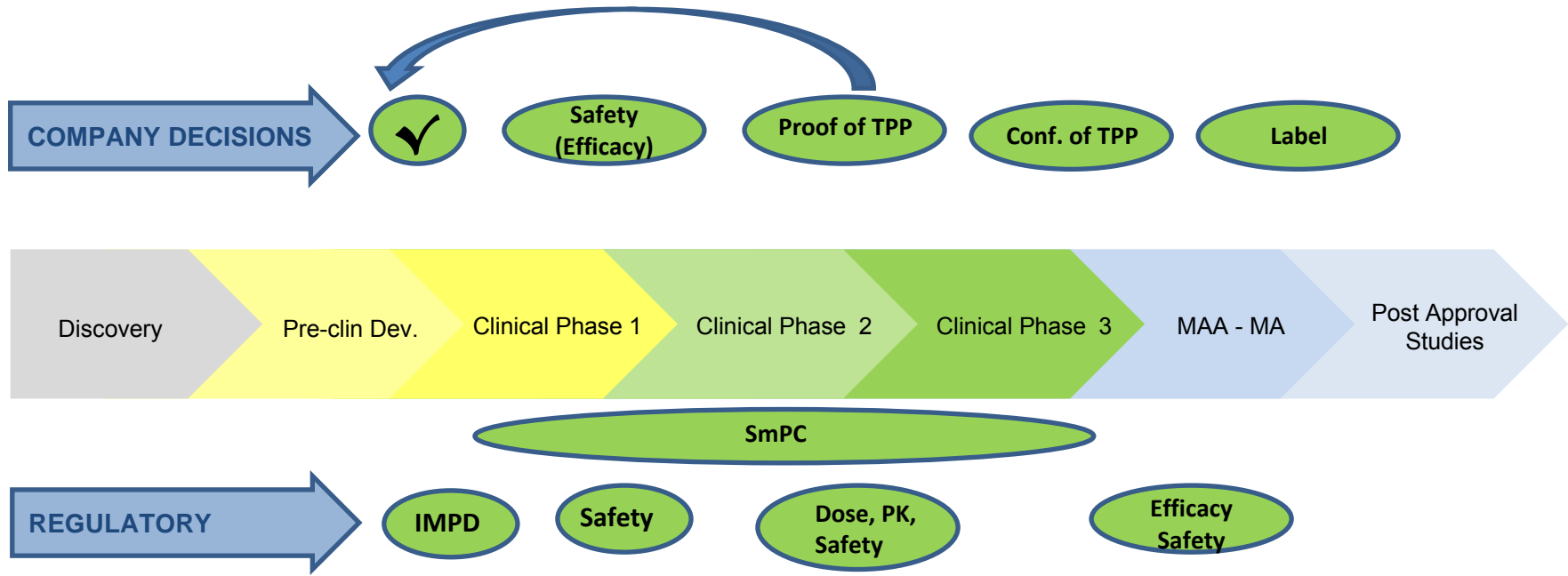


Phase 2a program finalised

- Assessment of "Proof of Concept"
- Confirmation or revision of "Target Product Profile"
- Preparation of registration strategy (e.g. 1st indication, 1st formulation)
- Preparation of development plan until submission of MAA/NDA
- Decision to continue into phase 2b (dose finding)
- Decision to continue independently, to partner or to sell the project

Consider a Scientific Advise

Development Programme



Drug Development Challenges



Technological opportunity



Medical Need

First Target Product Profile

The most important information to get from phase 1 and phase 2

Have a pharmaceutical formulation ready in due time

When to seek scientific advice

Formulation & Product Development

Local delivery

- Challenges
- Local delivery options
- Some scenarios
- Conclusions

Challenges in formulation design

- **The active ingredient – preformulation data**
 - Small molecules / peptides / proteins
 - Physico-chemical properties:
 - Acid/base properties (pK_a)
 - Solubility
 - Hydrophobicity
 - Stability: chemical and physical
 - Vehicle interactions

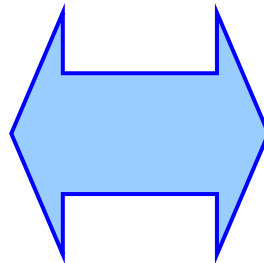
Challenges in formulation design

- **Conditions at the application site**
 - Non-intact area
 - Accessibility
 - Damaging non-involved areas
 - Local irritation

Challenges in formulation design

- **Biopharmaceutical properties**

- The right dose
- At the right time
- To the right place



- **Testing tools**

- In vitro
- In vivo
 - Validated animal models
 - Clinical models

Challenges in formulation design

- **The active ingredient**

- Peptide
- Stability: chemical and physical
- Physico-chemical properties
- Vehicle interactions

- **The candidate drug**

- Limited supply
- Quality not defined?
- Highly limited stability in water
- Can be freeze dried, indicating physical stability
- Antimicrobial properties?

Challenges in formulation design

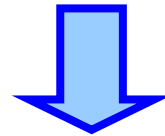
- **Conditions at the application site**
 - Non-intact area
 - Accessibility
 - Damaging non-involved areas
- **Indication not finalised**
 - Local application
 - Topical application
- **Testing models**
 - Cell culture available
 - Validated animal model?
 - Clinical model?

Development scenario

Product concept?



Based on
tradition



Out of box
• Ease of application

Stepwise approach

Vehicle options

Key questions

- **Indication?**
- Dose?
- Duration?
- Ease of application?
- Removal?
- Stability?
- Gel?
- Dry system?
- Patch?
- Wet / dry system?

Vehicle options

Gels / viscous solutions

- Hyaluronic acid
- Chitosans
- Lecithin structures
 - Liposomes
 - Cubic structures
- Non-ionic polymers
 - Cellulose (HPMC, CMC)
 - Poloxamers

All of them aqueous systems!

Vehicle options

Hydrophobic gels / suspensions

- Carbowax (PEG)
 - PEG 300/1500

All of them non-aqueous
systems!

Vehicle options

Patches

- Active ingredient integrated into the molecular structure of a polymer matrix
 - Dissolve and dry

**Non-aqueous, dry
systems!**

Vehicle options

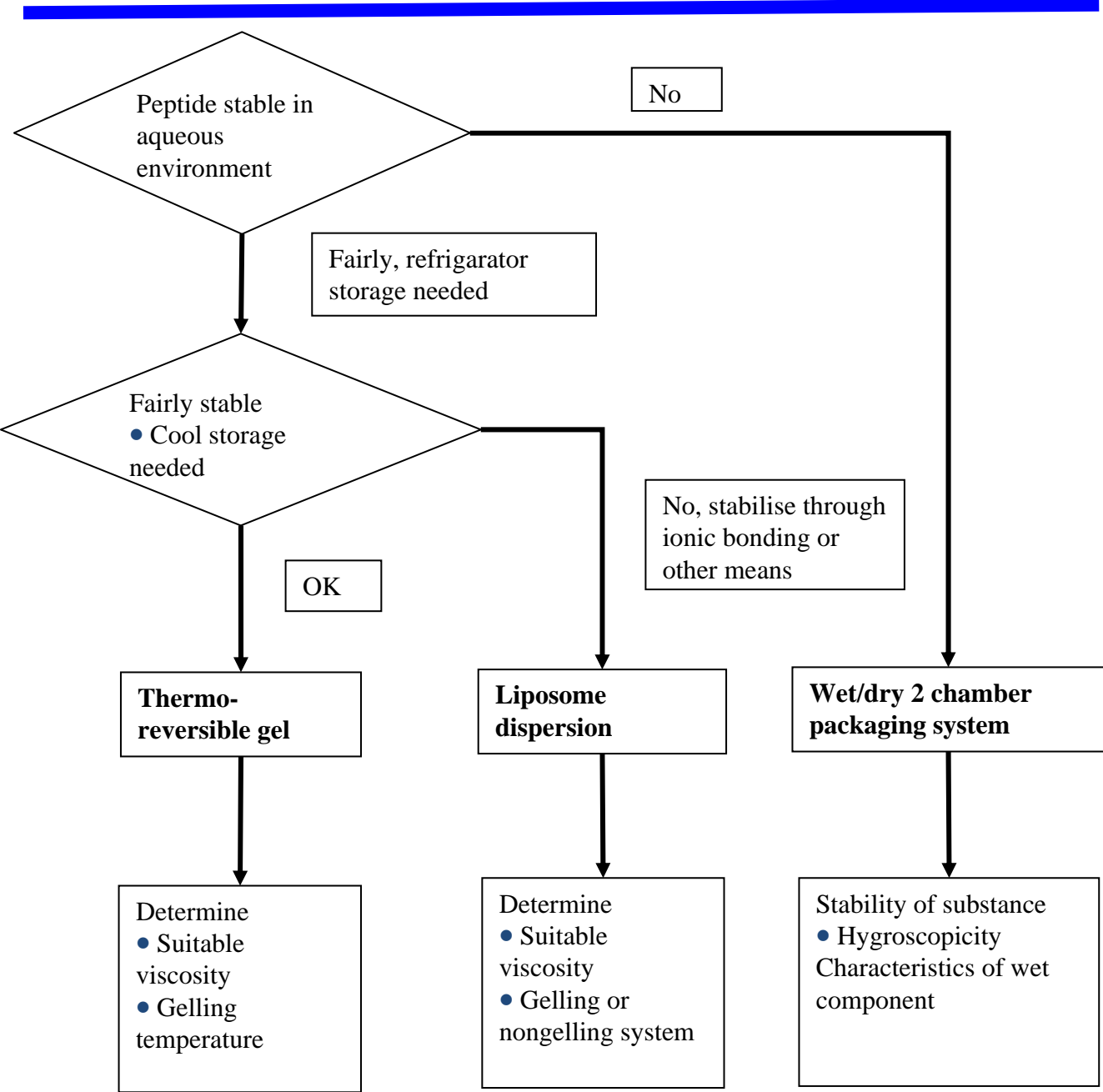
Syringe application

- Two compartment packaging system to be activated
 - Active ingredient in separate dry compartment
 - Vehicle in separate wet compartment

Aqueous and dry systems!

Mix & apply!

Peptide delivery system development



Conclusions

Limited resources

- **Personal**
 - Numbers
 - Know-how
- **Laboratories**
 - Equipment
 - Documentation
 - Quality systems (GXP)
- **Money**
 - Time

Timeline
for
results

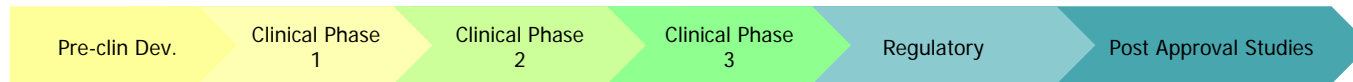
Dependent on CROs and
consultants

Conclusions

- **Define clinical use**
 - List & priorities
- **Consequences**
 - Route of administration
 - Type of formulation
 - Development program

Seek early advice!

DRUG DEVELOPMENT COUNSELLING



- Prepare or review Development Programmes
- Prepare or review Study Outlines (CMC, pre-clinical or clinical programmes)
- Review performed development work
- Scientific support to marketing
- Assessment of in-licensing opportunities (products or portfolios)
- Prepare documentation for out-licensing
- Establish contacts to key opinion leaders

DRUG DEVELOPMENT COUNSELLING

Medical and Clinical Development:

Allan Rosetzsky, MD

Eva Steiness, MD

Jørgen Serup, MD

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Martin Gormsen, MD, MBA

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Peter Damsbo, MD

Thor-Björn Conradson, MD

Previously Sanofi Aventis

Previously Lundbeck, ZEALAND Pharmaceuticals

Previously LEO Pharma

Previously Genmab and Abbott

Previously Janssen Cilag and Lundbeck

Previously Astellas, Novo Nordisk, Nycomed

Previously Pfizer

Previously NovoNordisk and Zealand Pharmaceuticals

Previously AstraZeneca and Nycomed

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Previously NovoNordisk

Previously AstraZeneca

Previously Pharmaxa

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Previously AstraZeneca
Previously AstraZeneca and Nycomed

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IP strategies

Lars Bo Kjerrumgaard, MSc., Eur. Patent Attorney

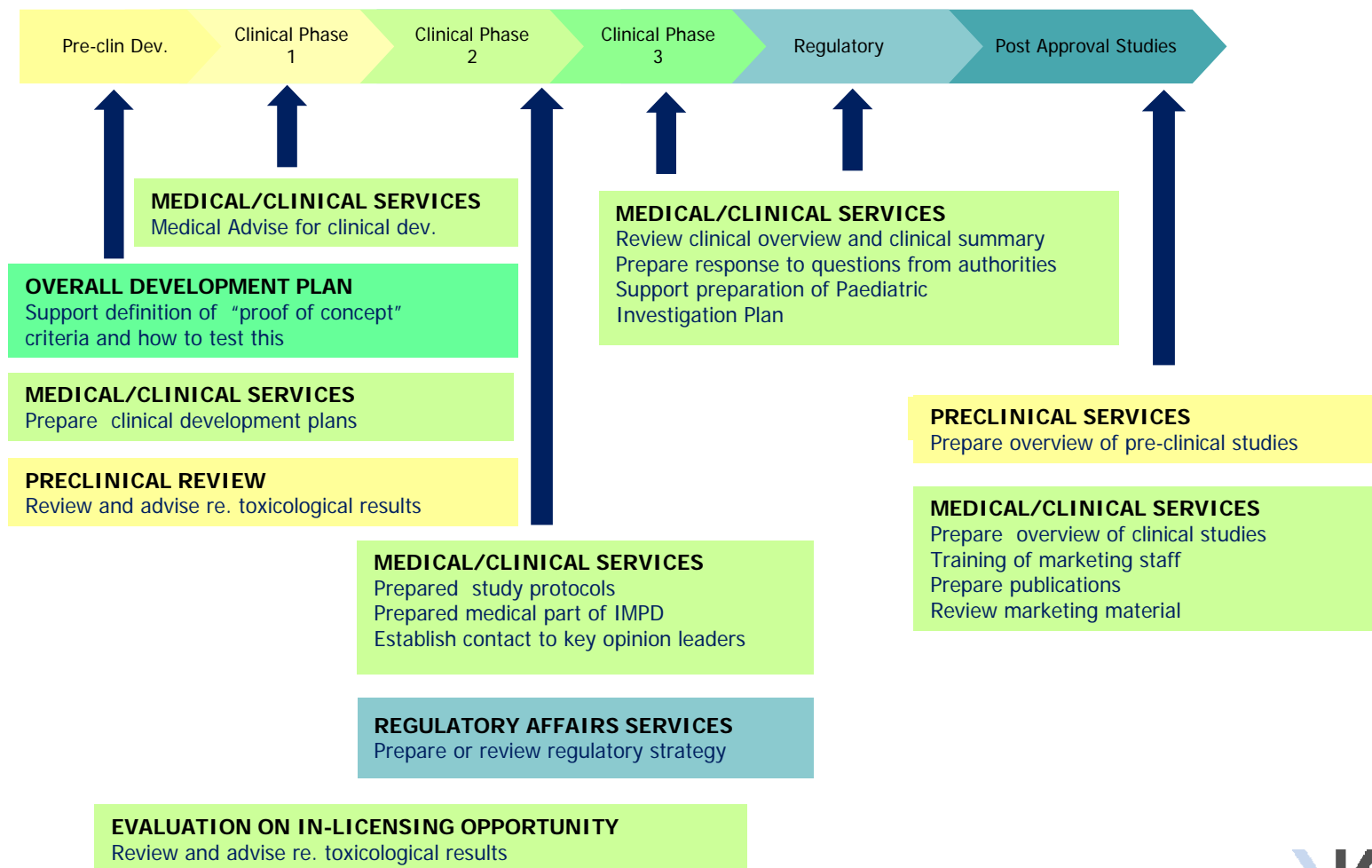
Previously Lundbeck, Maxygen, NovoNordisk

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DAWA consulting, Previously Bayer, Boehringer Ingelheim, LEO Pharma
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