Date: 19. December 2019
Topic: Regulatory Scientific Advice
Presentation for: Biopeople - Denmark's Life Science Cluster
Presentation by: Nicklas Lindland Roest

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Outline

1. Scientific Advice – essential aspects for consideration
2. Timelines and activities
3. Activities related documentation
   - Request
   - Pre-meeting
   - The meeting
   - Post-meeting
4. Case example – Scandion Oncology

Professional details

Lindland Roest
Pharmaceutical Development Consulting

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Nicklas Lindland Roest

Owner & Senior Consultant at Lindland Roest

Copenhagen, Capital Region, Denmark · See 500+ connections · See contact info

Lindland Roest

Faculty of Pharmaceutical Sciences, University of Copenhagen

Faculty of Pharmaceutical Sciences, University of Copenhagen
M. Sc. Pharm. 2011

Experience

Owner & Senior Consultant
Lindland Roest
Dec 2016 – Present · 3 yrs 1 mo
Copenhagen Area, Denmark

Lindland Roest ApS is a professional pharmaceutical consulting business offering services to biotech and pharmaceutical companies. With a strong background in Regulatory Affairs and CMC development I consult and provide hands-on expertise within the following areas:

- Project Management, pharmaceutical & biotech development projects
- CMC writing (IMPD) and consulting
- Regulatory Affairs: Clinical trial support
- Regulatory Affairs: Strategic development support

Welcome to Lindland Roest ApS

Director Regulatory Affairs
Scandion Oncology
Apr 2019 – Present · 9 mos

Director Regulatory Affairs
WntResearch AB
Apr 2018 – Jan 2019 · 10 mos
Malmo, Sweden

Regulatory Affairs Specialist
IWA Consulting
Nov 2011 – Dec 2016 · 5 yrs 2 mos

Consultant within regulatory and medical affairs, incl. develoment projects and product lifecycle management .

Scientific Advice

- Essential aspects to consider: Purpose

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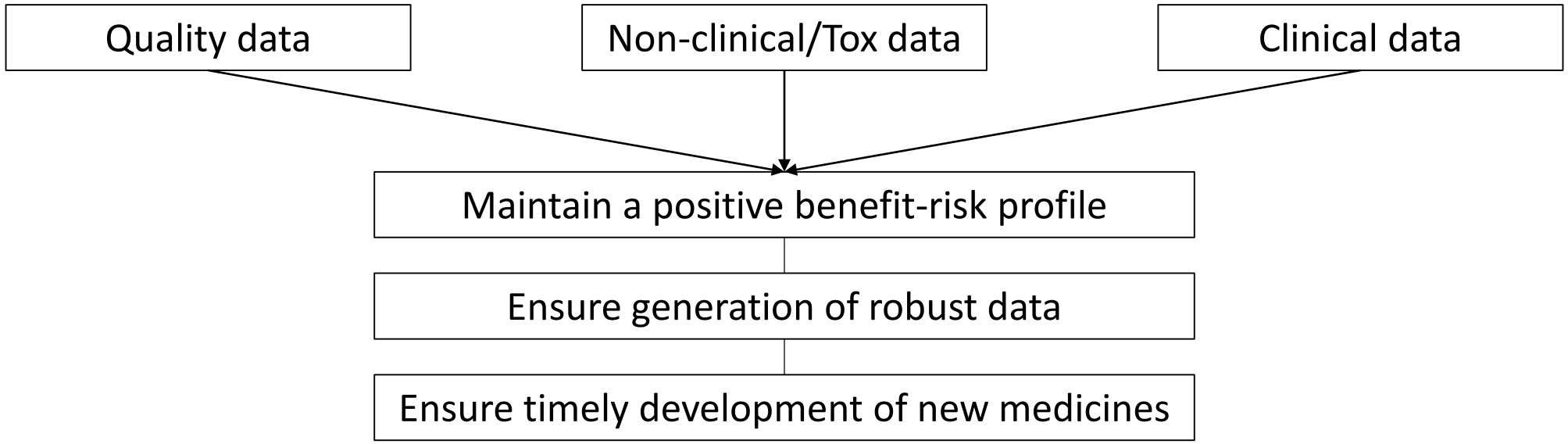
Purpose of Scientific Advice:

Risk mitigation

*-to make sure that the data (to be) generated is fit for the **intended purpose**-*



Scientific Advice

- Essential aspects to consider: Project planning

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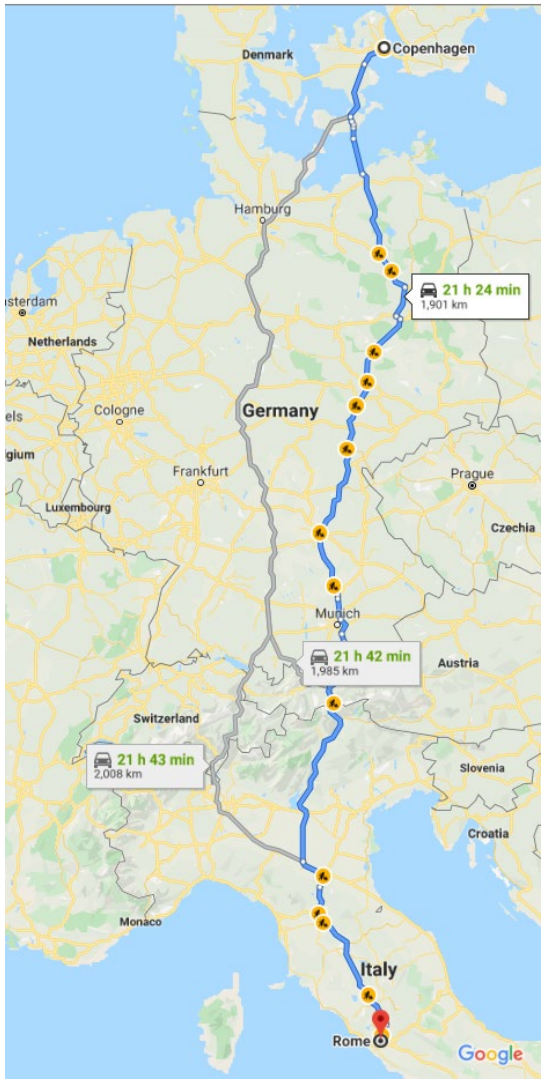

<u>Plan your project:</u>

- Make sure you know where you are going
  - Establish a target product profile
- Make sure the authorities know where you are going
  - Establish a plan for authority interactions
    - National or central advice?
    - When to interact

Difficult for authorities to give you **the right advice to your questions** if they do not know where you plan to go and how you plan to get there

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Scientific Advice
- Activities and timelines

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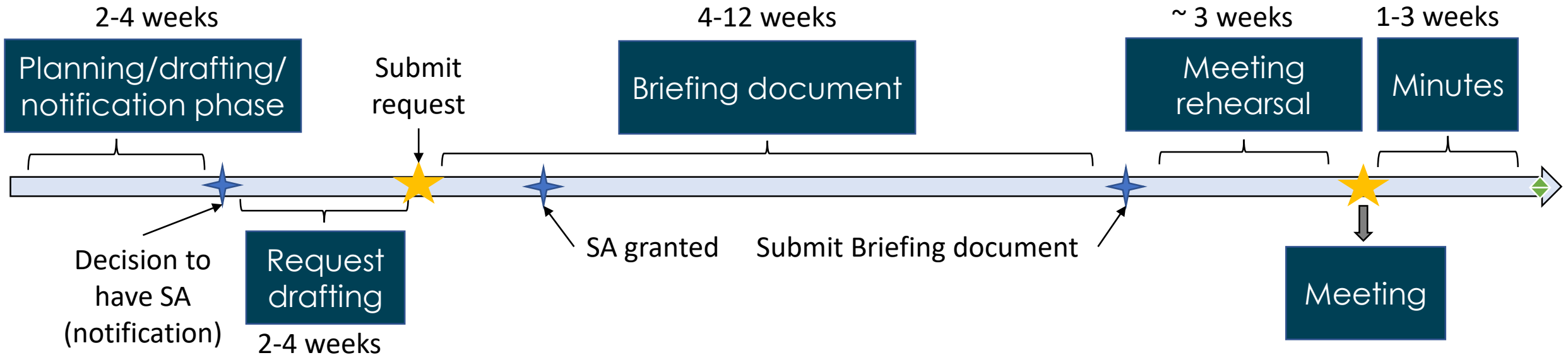
General timeline and activities

(may vary considerably…)



Total 3-6 months

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Scientific Advice
- Planning phase

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Process may vary depending on type of meeting (planned or needed) and the authority (notification of intent)

(Activities as required per company policy and/or need)

Scientific Advice
- Request drafting

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Meeting request for Scientific Advice are for authorities to assess meeting necessity and usually includes:

- **Background**
  - Disease to be treated (unmet need)
  - Summary of relevant quality, non-clinical and clinical data
  - Rationale for seeking advice
- **Draft questions**
  - Questions may be revised in final briefing document
- **Requests for meeting dates**

National Advice and don´t have a template?

Use EMA Briefing document template

Regarding questions: Excerpt from EMA briefing document template

"It is recommended that questions are phrased in a way to allow for an unambiguous understanding of the question. The scope should be carefully considered in order to avoid too broad or too narrow questions."

Scientific Advice
- Briefing document

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Briefing Document consist of three overall parts:

- Summary/introduction
- Questions and company position
- Background/Annexes

Before you start including all the details, remember

Authority experts are not:	superhuman beings capable of digesting 150 pages of scientific information on a new product in 10-15 hours
Authority experts are:	Regular professionals with **limited knowledge on your specific product** and development strategy and limited time for review of your submission

Keep it lean, clean and to the point
Briefing document should not exceed more than approx. 40 pages (summary, Questions & Company position and background)
Storyline (thread of consistency) and terminology – consider one person with overall responsibility (FDA for guidance on terminology)

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Scientific Advice
- Briefing document

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Summary/introduction

- Essentially similar to summary submitted with the request
- May be updated with additional information if appropriate compared to request
- Focus on describing unmet medical need (nudging…)

Should leave the reader with a solid understanding of where you are going, what you have done to this point, how you plan to move forward and why you need scientific advice at this point in time.

Consider: To include the target product profile either as part of the summary/introduction or as annex (FDA recommendation)

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Questions and company position

Questions should not be regular “open questions”, but “requests for confirmation” that the direction the company has chosen is acceptable considering the data presented and company´s development strategy, e.g.:

“should we go left or right?” vs. “Does the agency agree that going right…”

Company position should outline the companys *scientific reasoning* for choice of direction (compared to alternative options, if relevant).
- Can include relevant data supporting the position to limited extent. Additional data referenced to background/annexes.
- Length of company position: 1-3 pages

Proceed (word questions) with caution…

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Background & Annexes

Background

- Relevant tables, figures or other data supported by summary text
- Background information should match and support summary, questions and company positions (storyline…)
- Background is included as part of the primary briefing document (maximum approx. 40 pages) – annexes are not

Annexes

- Relevant additional data for in depth review
- May include relevant reports, minutes from previous meetings with (other) authorities, other relevant documentation
- Consider using the CTD-format to structure annexes

Scientific Advice
- Meeting rehearsal

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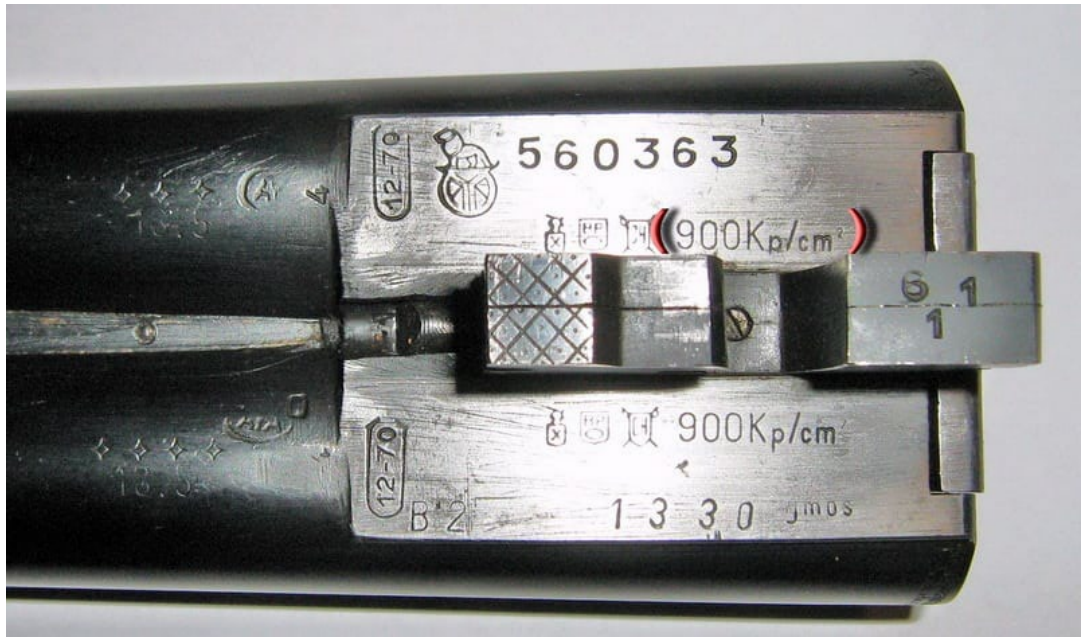
Don't go to war with an unproven gun

Preparations

- Outline the meeting strategy
- Prepare a presentation to match the strategy
- Discuss and outline possible fallback positions depending on (negative) advice outcome
- Assign participant roles and responsibilities
- Prepare, rehearse, adjust, repeat
    - It is not possible to be too prepared



Consider: A Q&A session where peers can ask any possible questions that may come up at the meeting to prepare participants answers

Scientific Advice
- The meeting

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This is YOUR meeting

- Prepare a presentation with essential figures, graphs etc. to help navigate the discussions
- Manage the time – and keep introductions short!
- Discuss critical questions first
- Maintain focus

Three rules to a good Scientific Advice meeting:

1. Don´t flood the meeting:
Number of company participants should be limited to key people only
2. Don´t speak unless you have to:
You are there to receive their advice and provide clarifying arguments
3. Stick to your agenda:
Discussions sometimes drift off course – make sure you control the meeting

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Scientific Advice
- The meeting

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Key participants:

- **Moderator**

Responsible for time keeping and ensuring meeting strategy is adhered to

- **Minutesman**

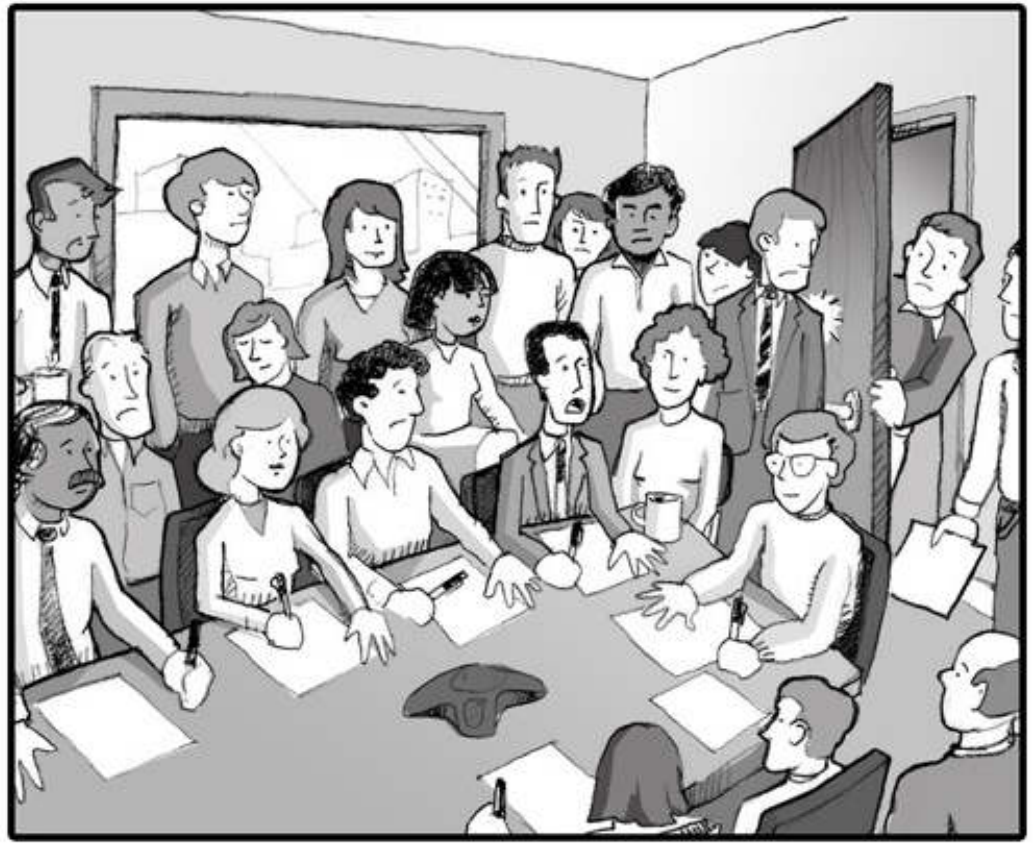
Responsible for writing comprehensive minutes

- **Relevant scientific experts**

Depending on scope of meeting.

- **Project owner/CEO (small biotech) (key stakeholder)**

The person responsible for communicating outcome to decision makers



"We're still waiting for a couple of folks if you can all squeeze together a bit..."

Scientific Advice
- Minutes

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If it´s not documented, it´s not done

[Quote: your QA department]

Comprehensive minutes are essential for a good Scientific Advice

Thoroughly and clearly document the outcome of the meeting – must be clear for anyone not present at the meeting

- Debrief ASAP after the meeting
- Gather notes from everyone
- Draft minutes the same day or the day after
- Be thorough during drafting – more is less (personal opinion…)! Easier to delete than to add
- Be thorough during review

Consider: Include minutes in the briefing document below company position to have a stand-alone document that includes: 1. the question 2. the company position and 3. the outcome of the discussions

Final comments

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Never be afraid to interact with authorities – embrace the possibility

Involve authorities early in possible “out-of-guideline” questions

Guidelines do not (always) trump sound scientific arguments backed by data

Value of the outcome of a Scientific Advice meeting is directly proportional to work invested

Try not to overanalyze wordings/questions – often, the initial wording is just as good as the final

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CASE STUDY: Scandion Oncology

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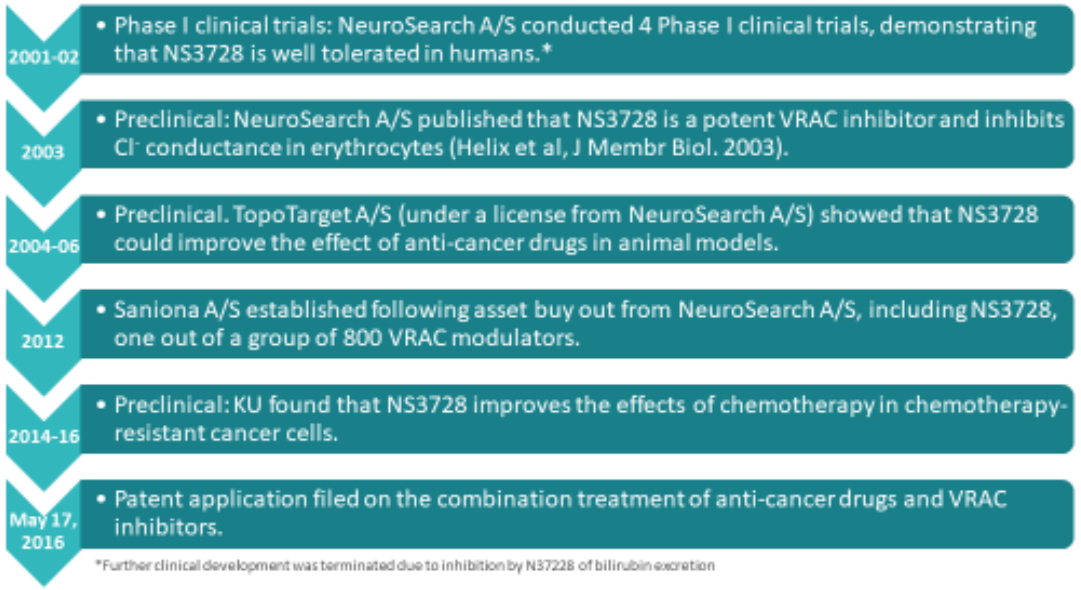
SCANDION ONCOLOGY

IMP: SCO-101 (NS3728)
Indication: Combination with chemotherapy for treatment of chemotherapy resistant cancer
Administration: Oral tablets
Study: Phase I/II study with dose escalation (stage I, safety) and efficacy part (stage 2) + possible extension



Cancer cells develop resistance to chemotherapy

One mechanism is upregulation of cellular efflux pumps where chemotherapy is substrate

SCO-101 initially developed for sickle cell aneamia, but since then shown to re-sensitise resistant cancer cells to chemotherapy through interaction with efflux pump

Potential to increase intracellular concentrations of chemotherapy and re-sensitise cancer cells

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CASE STUDY: Scandion Oncology

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Purpose of meeting:

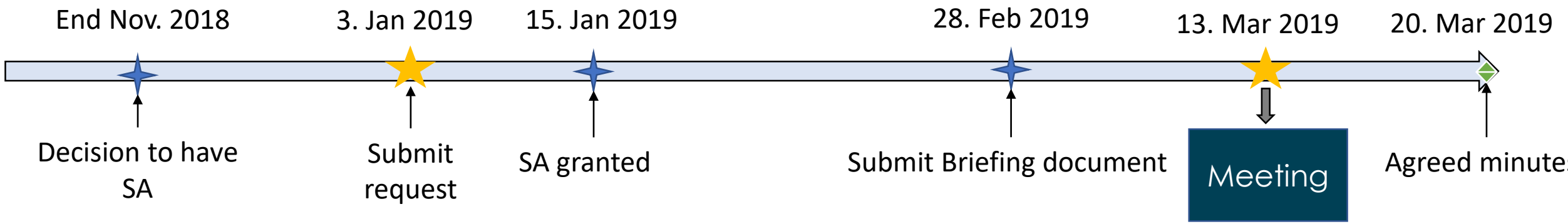
Primary:

- Confirm that non-clinical and clinical data generated was considered acceptable for intended purpose
- Confirm that clinical trial design and safety measurements were considered appropriate
- Confirm that study objectives and endpoints were considered appropriate

Secondary:

Familiarize DMA with SCO-101 to smooth review during CTA process

Timeline
~ 3.5 months total



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3. Confirm that study objectives and endpoints were considered appropriate

Secondary:

Familiarize DMA with SCO-101 to smooth review during CTA process

Outcome of meeting:

Primary:

1. DMA confirmed that data presented was considered acceptable to support proposed study (duration, dose levels and dosing scheme) and highlighted aspect that required specific attention in the CTA
2. DMA found dose escalation too aggressive – discussions led to agreement on acceptable escalation scheme
   - Fallback position was planned (identical to DMA suggestion)
3. Primary study objectives/end-points were acceptable, but discussions led to modifications based on DMA recommendations.

Secondary:

CTA submitted 01. Oct 2019 and approved 28 Nov. 2019.
Minimum of comments, primarily to patient information

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CASE STUDY: Scandion Oncology

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- Timelines could be kept
- No need for additional (non-planned) funding
- Investors were comfortable
- Authorities were comfortable when CTA submitted

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Q&A

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Questions?

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