R&D – The key engine for profitable growth

Christer Nordstedt
SVP, Research & Development

Disclaimer

This presentation contains forward-looking statements which involve risks and uncertainty factors. These statements are not based on historical facts but relate to the Company's future activities and performance. They include statements about future strategies and anticipated benefits of these strategies.

These statements are subject to risks and uncertainties. Actual results may differ substantially from those stated in any forward-looking statement. This is due to a number of factors, including the possibility that Orion may decide not to implement these strategies and the possibility that the anticipated benefits of implemented strategies are not achieved. Orion assumes no obligation to update or revise any information included in this presentation.

Strategic goals

Deliver late-stage portfolio

Build early portfolio

Maximize value of assets

Innovation system

Competence base

Therapy area work

Achieving more in R&D

Research			Early development		Late stage development	
Target identification and validation 8–24 mo.	Hit to Lead generation 12–24 mo.	Lead optimisation 18–36 mo.	Candidate selection, preclinical development 12–24 mo.	**Phase I** 12–14 mo.	**Phase II** 12–36 mo.	**Phase III** 18–48 mo.

Collaboration with partners

WISCONSIN UNIVERSITY OF WISCONSIN–MADISON

DZNE Deutsches Zentrum für Neurodegenerative Erkrankungen in der Helmholtz-Gemeinschaft

AsahiKASEI

BUSINESS FINLAND

UNIVERSITÄT BONN

Collaboration with partners

HUS

UNIVERSITY OF TURKU

imi

BAYER

More focused R&D

Building long-term growth in R&D helping patients with unmet needs

Key actions:

- Increase the number of promising research projects
- Extend beyond small molecules in R&D
- Focus on disease biology
- Balance between known robust targets and entirely new ideas

Changes over the last 2 years

- Restructured R&D from process focus to Therapy Areas
- In-house capability to discover protein drugs (monoclonal antibodies)
- Made some key recruitment (from Finland and abroad) and continue to do that
- Focused our two main R&D sites (Espoo and Turku)

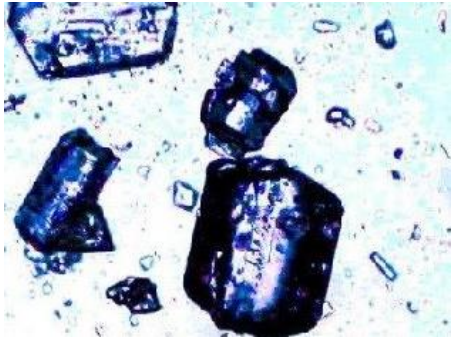
Focus areas of Orion's R&D

Proprietary products

- Central nervous system
- Oncology
- Respiratory
  (Easyhaler product family)

Animal Health

- Orion utilises the R&D of proprietary products to develop new medicines for animals



Fermion

- APIs to Orion's proprietary products
- Generic APIs
- Contract development for pharmaceutical companies

Orion's key clinical drug development programs

Project	Indication	Phase	Registration
Easyhaler® tiotropium	COPD	Bioequivalence study	
Darolutamide [1)]	Prostate cancer (nmCRPC)	I, II, III	FDA Priority Review
Darolutamide [1)]	Prostate cancer (mHSPC)	I, II, III	
ODM-109 (oral levosimendan)	ALS	I, II, III	
ODM-203 (targeted FGFR+VEGFR inhibitor)	Solid tumours	I, II	
ODM-207 (BET protein inhibitor)	Cancer	I	
ODM-208 (CYP11A1 inhibitor)	Prostate cancer (CRPC)	I	
ODM-209 (CYP11A1 inhibitor)	Prostate cancer (CRPC), breast cancer	I	

[1)] In collaboration with Bayer

More information on R&D projects: www.orion.fi/en/rd/orion-rd/pipeline/

= Completed

= Ongoing

= Status changed

Interesting non-clinical projects under investigation to ensure long-term success

CNS Therapy Area

- Parkinson's disease (PD), amyotrophic lateral sclerosis (ALS) and chronic pain
- Currently primarily symptomatic treatments

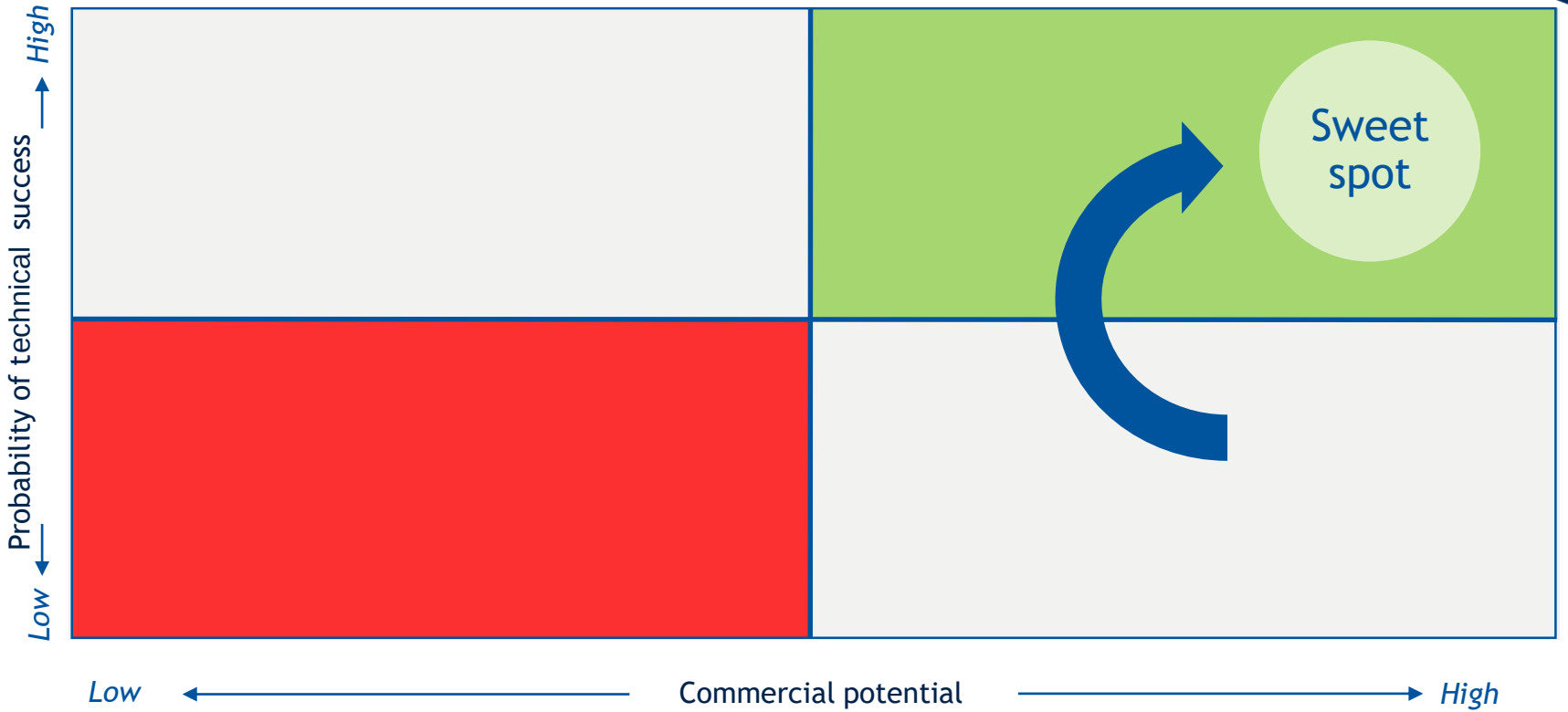
Oncology Therapy Area

- Common cancer types, such as steroid hormone-dependent prostate cancer and breast cancer, but also the treatment of some rare cancer types.

Rare Disease Therapy Area

- Progressive, **serious**, life-limiting and life-threatening diseases, where affected patients are lacking adequate treatment.
- At the first, priority on Finnish Heritage Diseases, but will not limited to these.

R&D balancing between technical probability and commercial potential

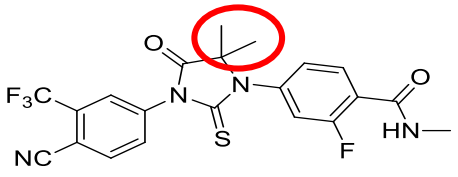


Darolutamide (ODM-201) for prostate cancer

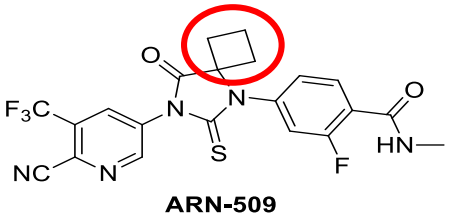
Prof. Heikki Joensuu
VP, Therapy Area Oncology

Darolutamide: Invented at Orion, co-developed with Bayer

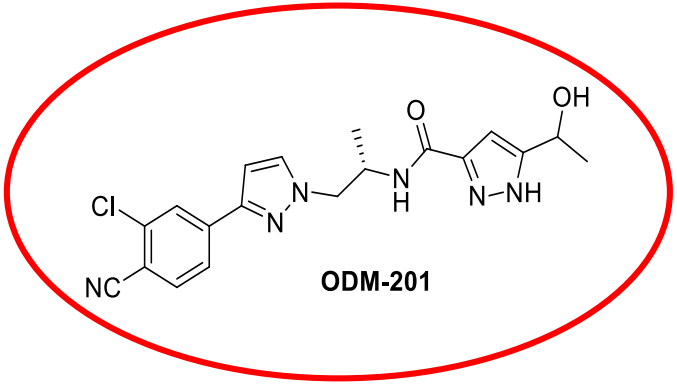
- A structurally unique androgen-receptor antagonist
- Under development for the treatment of prostate cancer
- Preclinical studies indicate a low risk for drug-drug interactions



Enzalutamide
(Pfizer, Astellas)



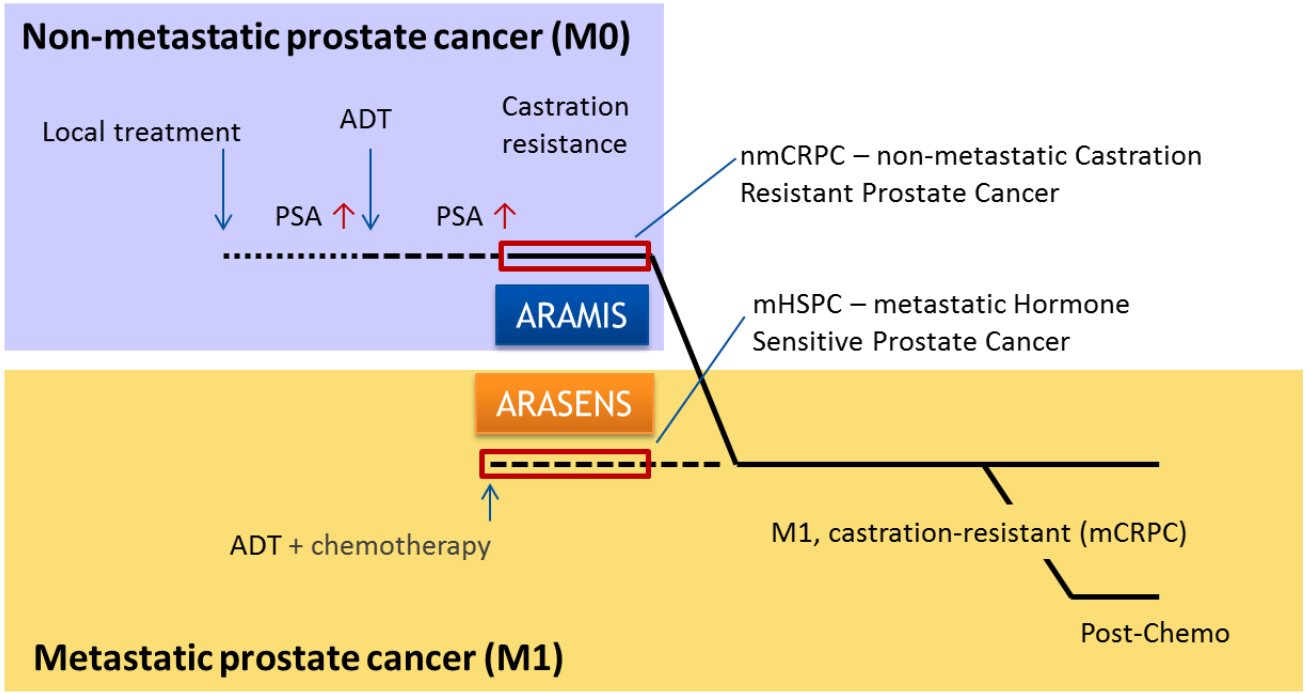
Apalutamide
(Janssen)



Darolutamide*
(Orion)

* Development phase product

Two Phase III studies with darolutamide ongoing: ARAMIS and ARASENS



PSA – prostate-specific antigen
ADT – androgen deprivation therapy

ARAMIS target population:

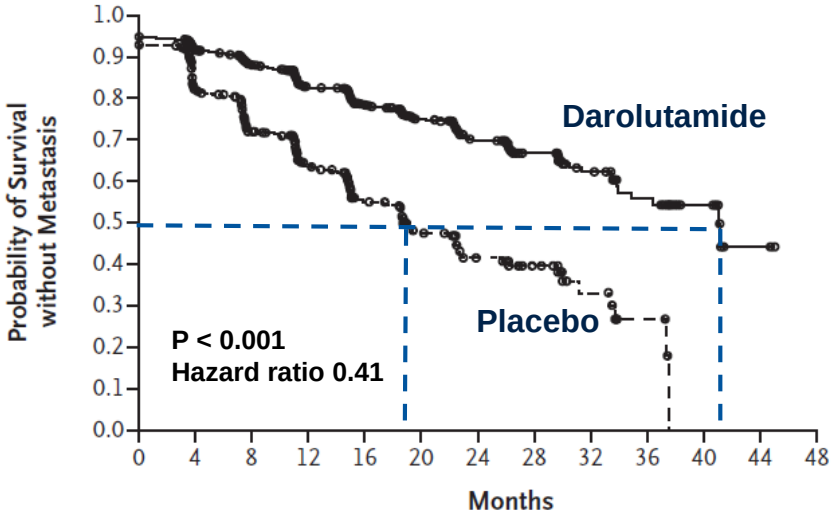
Localized prostate cancer that *no longer responds* to chemical (or surgical) castration

ARASENS target population:

Overtly metastatic prostate cancer that is *sensitive* to chemical (or surgical) castration

ARAMIS: Darolutamide vs. placebo in the treatment of hormone-insensitive localized prostate cancer1

Median metastasis-free survival improved from 18 months (placebo) to 40 months (darolutamide)



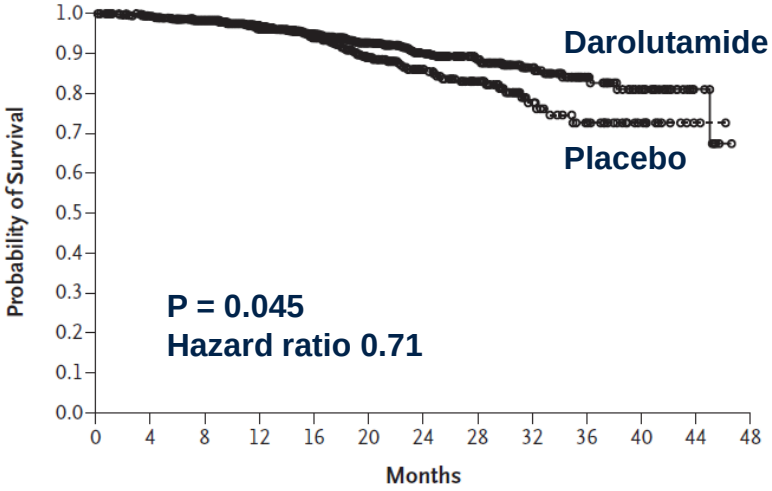
No. at Risk

Darolutamide	955	817	675	506	377	262	189	116	68	37	18	2	0
Placebo	554	368	275	180	117	75	50	29	12	4	0	0	0

[1]Fizazi K, Shore N, Tammela TL, et al. N Engl J Med 2019;380:1235-46

ARAMIS: Darolutamide vs. placebo in the treatment of hormone-insensitive localized prostate cancer1

A strong trend for improved overall survival in favor of darolutamide



No. at Risk													
Darolutamide	955	932	880	737	586	428	302	218	123	64	35	8	0
Placebo	554	529	467	394	307	214	154	110	56	34	14	2	0

[1]Fizazi K, Shore N, Tammela TL, et al. N Engl J Med 2019;380:1235-46

Key messages from the ARAMIS trial

The NEW ENGLAND JOURNAL of MEDICINE

Fizazi K ym. NEJM 2019; 380:1235-46

- Darolutamide has substantial efficacy (like enzalutamide and apalutamide)
- Darolutamide has an excellent safety profile: parallels placebo
  - No side effect occurred in >10% of the patients except fatigue (darolutamide 12%, placebo 9%)
  - Discontinuation rate was similar in both groups (darolutamide 9%, placebo 9%)
  - No increase in dizziness, cognitive disorders, falls, fractures, or skin rash (darolutamide concentrations low in the central nervous system)

U.S. FDA accepts New Drug Application for review and grants Priority Review for darolutamide

Orion Corporation Press release 29 April 2019 at 3.00 p.m. EEST

U.S. FDA accepts New Drug Application for review and grants Priority Review for darolutamide

Orion Corporation and Bayer today announced that the U.S. Food and Drug Administration (FDA) has accepted the New Drug Application (NDA) for review and granted Priority Review for darolutamide for the treatment of non-metastatic castration-resistant prostate cancer (nmCRPC) in the U.S.

ORAL levosimendan (ODM-109) in ALS

The REFALS phase 3 study

Levosimendan in Amyotropic Lateral Sclerosis (ALS)

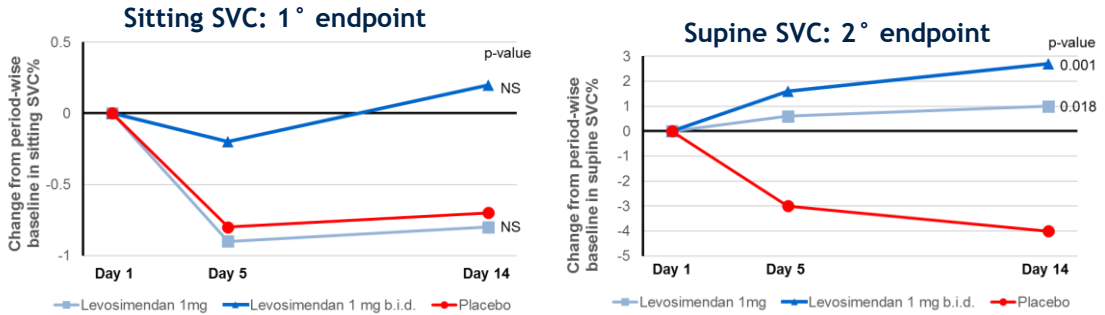
1. IV levosimendan (Simdax®) has been used for short-term treatment of acutely decompensated severe chronic heart failure (CHF), since 2000
2. ALS is a rare, devastating, neurodegenerative disorder with few treatment options, causing progressive weakness and paralysis. Death typically occurs within 3-5 years due to respiratory failure
3. Oral levosimendan improved respiratory function in a 2 week pilot study vs. placebo on ALS patients (LEVALS study) (post-hoc analysis of supine slow vital capacity)
4. Ongoing REFALS phase 3 trial will be the basis for approval for oral levosimendan in the USA and elsewhere to improve symptoms of ALS

Parissis et al Heart Fail Rev (2009) 14:265–275

The LEVALS phase 2 study of oral levosimendan

- Pilot crossover study to establish proof of concept
- Primary endpoint (sitting slow vital capacity SVC) was negative but there was a significant change in supine slow vital capacity
- Supine vital capacity correlates better with diaphragmatic weakness and is a better predictor of survival than that measured in upright position
- Duration of treatment was too short to assess changes in overall function.
- Levosimendan was well-tolerated - headache and tachycardia were the expected adverse effects

LEVALS demonstrated a significant effect on pulmonary function during only 2 weeks dosing that supports progression to phase 3



Period-wise baseline used (post-hoc)

Al-Chalabi, Shaw, Leigh, van den Berg, Hardiman, Ludolph, Sarapohja, Kuoppamäki
International Symposium on ALS/MND, Boston, December 2017

The REFALS study of oral levosimendan in ALS

Objectives

- Demonstrate benefit of oral levosimendan on respiratory and overall function in ALS
- Safety in prolonged use in ALS patients

Methodology

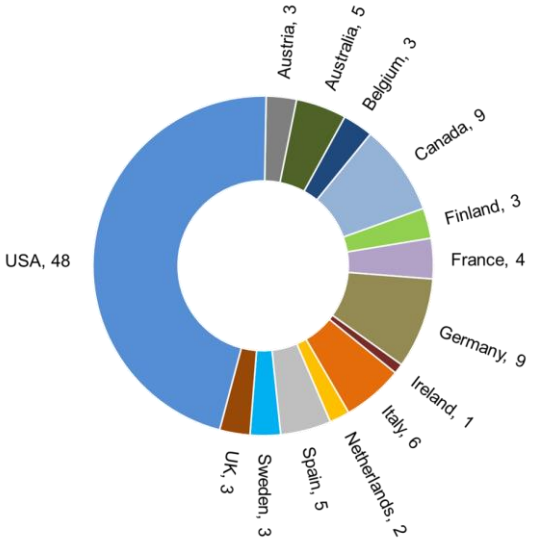
- Phase 3 randomised, double-blind, placebo-controlled
- 450 patients with ALS, 2:1 randomisation, who already have some degree of respiratory dysfunction (SVC 60-90% predicted)
- 48 weeks study treatment (levosimendan 1-2 mg/day or placebo), added to existing therapy (riluzole and/or edaravone)
- Optional long-term extension (REFALS-ES study)

Efficacy endpoints

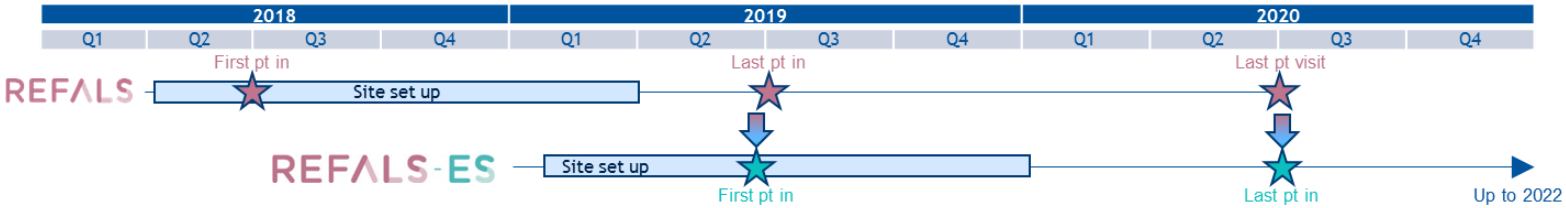
- **PRIMARY**
  Supine slow vital capacity at 12 weeks
- SECONDARY
  - ALS Functional Rating Scale (ALSFRS-R) adjusted for survival (CAFS) through 48 weeks
  - Time to respiratory event
  - Dyspnoea, sleep and sleepiness scales
- Safety

REFALS study progress

104 ALS centres in 14 countries



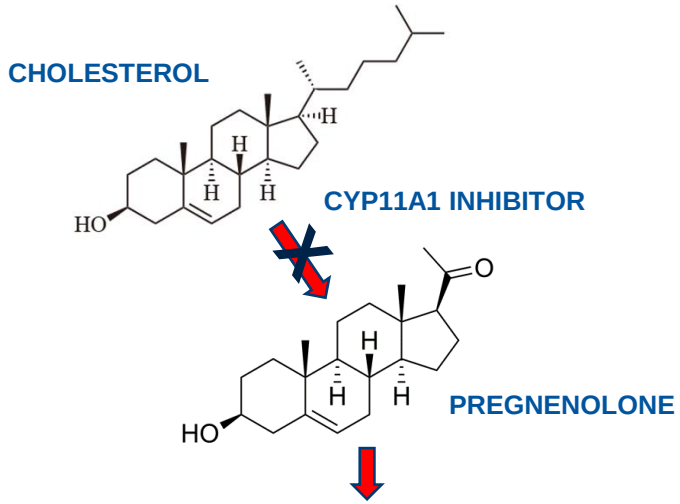
- REFALS is an Orion study,
- 1st patient randomised July 2018
- Patient accrual is rapid
  - Last patient randomisation is expected July 2019
  - Last patient visit expected July 2020
  - Study results 2nd half 2020
- REFALS-ES on schedule to accept 1st patient June 2019



Update on CYP11A1 platform (ODM-208/209)

CYP11A1 inhibitors (ODM-208 and ODM-209)

- First-in-class compounds
- Orion leads the development in the world
- CYP11A1-inhibitors prevent the synthesis of ALL steroid hormones
- Glucocorticoids and mineralocorticoids need to be replaced during therapy



All other steroid hormones

- Sex hormones (E.g. estrogen, progesterone, testosterone
- Glucocorticoids (E.g. hydrocortisone)
- Mineralocorticoids (E.g. aldosterone)

CYP11A1 inhibitors have wide potential indications

- Prostate cancer (1.3 million cases/year; the 2nd most common cancer in males in the world[1])
- 70% of breast cancers (estrogen receptor-positive cancers; 1.5 million cases/year; the most common cancer in females[1])
- Endometrial cancer of the uterus (0.4 million cases/year[1])
- Adrenocortical carcinoma (very rare, 1 case/million/year)
- Some hormone-producing benign tumors

[1]Bray F ym. CA Cancer J Clin 2018; 68:394-424

Orion investigates CYP11A1 inhibitors in two first-in-human Phase I-II trials

The CYPIDES trial (ODM-208)

- Advanced prostate cancer that progressed during ≥1 novel hormonal therapy and chemotherapy
- Opened up for patient enrollment on March 19, 2018
- Continues to accrue patients in Finland, France, and the U.K.

The STESIDES trial (ODM-209)

- Advanced prostate cancer that progressed during one or more novel hormonal therapy and chemotherapy
- Advanced breast cancer that progressed during two or more systemic treatments
- Opened up for patient accrual in April 2019

Update on ODM-203 and ODM-207

Update on ODM-203 and ODM-207

ODM-203

- A tyrosine kinase inhibitor (FGFRs and VEGF)
- KIDES Phase I-II trial:
  - 84 patients, various types of cancers
  - 9% of the patients responded, 45% had disease stabilization, 35% achieved target lesion reduction
  - Clinical benefit rate 52%
  - Most side effects mild
- Partnering activities ongoing

ODM-207

- A BET inhibitor (inhibits key oncogenes, such as Myc)
- A unique structure
- BETIDES Phase I-II trial:
  - Various types of solid tumors
  - Generally well tolerated
- Partnering activities ongoing

FGFR= Fibrobalst growth factor receptor, VEGF= Vascular endothelial growth factor, BET = bromodomain and extra-terminal motif

Update on Easyhaler development projects

Orion continues investing in Easyhaler®

Tiotropium Easyhaler

- We are developing a new second entry product for COPD (Chronic obstructive pulmonary disease) indication
- Tiotropium Easyhaler is in bioequivalence studies
- We have utilized the learnings from budesonide-formoterol and salmeterol-fluticasone Easyhaler® which have significantly increased our understanding of development

Connected Easyhaler

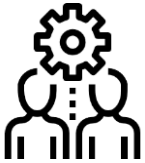
Our aim is to

- Increase treatment adherence
- Strengthen patient-physician relationships
- Reduce hospitalisations

Improve disease control and Quality of Life

Orion's R&D vision for the future success

Brain power and muscle combined with agility of a small biotech.



A preferred partner for other pharma companies and research institutions.

Increased visibility within the academic community and capabilities to recruit and retain "the best and the brightest".

A balanced pipeline that can deliver clinically meaningful differentiation and patient benefit.

Capability to deliver novel proprietary small molecule therapeutics and biologics.

A significant contributor to the global scientific community.

Thank you!