R&D presentation for investors

Updated on 7 February 2018

ORION
Building well-being

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.

Focus areas of Orion's R&D

Proprietary Products

- CNS
- 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 Diagnostica

- QuikRead test system
- GenRead test system

Together we can achieve 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				Collaboration with partners		

DZNE Deutsches Zentrum für Neurodegenerative Erkrankungen in der Helmholtz-Gemeinschaft

AsahiKASEI

WISCONSIN UNIVERSITY OF WISCONSIN–MADISON

janssen PHARMACEUTICAL COMPANIES OF Johnson & Johnson

BAYER

Several academic and other collaborations both in early and late phase of development

GEDEON RICHTER

Building the R&D future success

2016 | 2017 | 2018 | 2019 | 2020 | 2021 | 2022 | 2023 | 2024 | 2025 | 2026

- Innovation system
- Competence base
- Therapy area work

ROADMAP

ODM-207
ODM-109
ODM-203
ODM-104
ORM-12741
tiotropium
Darolutamide

Bringing treatments to patients addressing unmet needs also in the future require capability to discover and develop less validated targets, new treatment concepts and increasing collaboration with academic partners

Clinical development pipeline

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Key clinical pharmaceutical development projects

Project	Indication	PHASE			Registration
Easyhaler® salmeterol-fluticasone	Asthma, COPD	Bioequivalence study			Registration
Easyhaler® tiotropium	COPD	Bioequivalence study			
Darolutamide (ODM-201) [1)]	Prostate cancer (nmCRPC)	I	II	III	
Darolutamide (ODM-201) [1)]	Prostate cancer (mHSPC)	I	II	III	
ODM-109 (oral levosimendan)	ALS	I	II		
ORM-12741 (alpha-2c adrenoceptor antagonist) [2)]	Alzheimer's disease	I	IIa		
ODM-104 (more effective COMT inhibitor)	Parkinson's disease	I	II		
ODM-203 (targeted FGFR+VEGFR inhibitor)	Solid tumours	I	II		
ODM-207 (BET protein inhibitor)	Cancer	I			

[1)] In collaboration with Bayer
[2)] In collaboration with Janssen Pharmaceuticals, Inc. The research results will be evaluated together with Janssen Pharmaceuticals, Inc. and the decision on continuation of the project will be taken later.
More info about R&D projects at: http://www.orion.fi/en/rd/orion-rd/pipeline/

= Phase completed
= Phase ongoing
= Status changed

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Vision for the future

Orion: a company with the brain power and muscle of Big Pharma but with the agility of small biotech

Making Orion capable of delivering novel proprietary small molecule therapeutics and biologics

Through internal work and partnering activities build and maintain a balanced pipeline that can deliver clinically meaningful differentiation/patient benefit long-term

Increase Orion's visibility within the academic community and being capable of recruiting and retaining "the best and the brightest"

Being a preferred partner for Big Pharma, Biotech and Academia

Being a significant contributor to the global scientific community

Darolutamide (ODM-201)

A novel second generation androgen receptor (AR) inhibitor for the treatment of prostate cancer
In collaboration with Bayer

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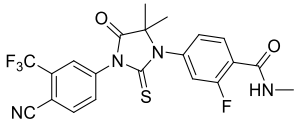
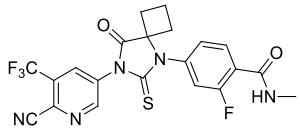
Darolutamide (ODM-201): Partnership with Bayer - Financial terms

- Orion and Bayer will jointly develop darolutamide, with Bayer contributing a major share of the costs of future development.
- Bayer will commercialise darolutamide globally and Orion has the option to co-promote darolultamide in Europe.
- Orion is eligible to receive milestone payments from Bayer upon achievement of certain development, tech transfer and commercialization milestones.
- Orion will receive substantial royalties on future sales.
- Orion will be responsible for manufacturing of the product.

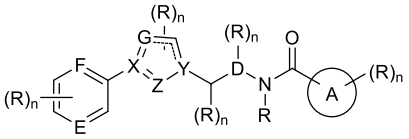
Darolutamide (ODM-201) has a unique profile



Enzalutamide



ARN-509



Darolutamide general structure

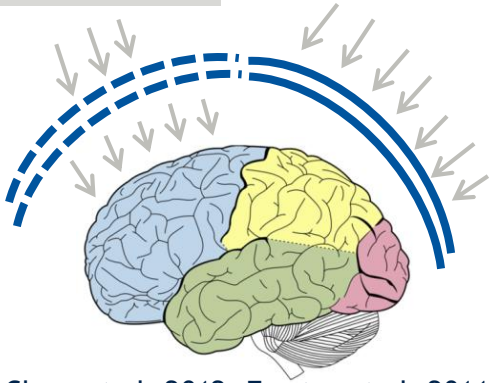
Compound	AR affinity Ki (nM)	Antagonism IC50 (nM)				Proliferation VCaP IC50 (nM)
		WT AR	AR (F876L)	AR (T877A)	AR (W741L)	
Bicalutamide	12	150	218	957	Agonist	
Enzalutamide	86	155	Agonist	296	>10000	400
ARN-509	68	168	Agonist	1130	>10000	300
Darolutamide	9	65	66	1782	1500	500

- Darolutamide blocks the function of androgen receptor in both biochemical and cell assays with equal or better potency compared to enzalutamide and ARN-509
- Low likelihood for brain entry demonstrated in preclinical models

Enzalutamide **19%***

ARN-509 **29%***

Darolutamide **3% ****



*Refs. Clegg et al, 2012; Forster at al, 2011
** Rat autoradiography (QWBA confirms brain/plasma ratio of 14C-ODM-201 related radioactivity was 0.04-0.06, indicating negligible penetration to the brain)

Darolutamide clinical studies

Study	Phase	Populations	N	Daily Dose (mg)	Status	ClinicalTrials.gov identifier
ARADES	I/II	mCRPC* • Chemo/CYP17 naïve • Post chemo/ CYP17 naïve • Post CYP17	134	200-1800	Completed	NCT01317641
ARADES ext	II	mCRPC* • Chemo/CYP17 naïve • Post chemo/ CYP17 naïve • Post CYP17	76	200-1800	Completed	NCT01317641
ARAFOR	I	Chemo-naïve mCRPC*	30	1200	Ongoing	NCT01784757
ARIADME	I	Healthy subjects	12	300	Completed	NCT02418650
ARAMIS	III	nmCRPC**	1500	1200	Ongoing	NCT02200614
ARASENS	III	mHSPC***	1300	1200	Ongoing	NCT02799602

* metastatic Castration Resistant Prostate Cancer
** non-metastatic Castration Resistant Prostate Cancer
*** metastatic Hormone Sensitive Prostate Cancer

Darolutamide Phase III study ongoing in non-metastatic castration resistant prostate cancer (nmCRPC)

- nmCRPC patients who are at high risk for developing metastatic disease are included
- Primary endpoint
  - Darolutamide over placebo in metastasis-free survival (MFS)
- Secondary endpoints
  - Overall survival, time to first symptomatic skeletal event (SSE), time to first initiation of cytotoxic chemotherapy, time to pain progression, and to characterize the safety and tolerability of darolutamide
- The study is proceeding as planned with estimated completion in 2018.

ARAMIS
Androgen Receptor inhibiting Agent for Metastatic-free Survival

ClinicalTrials.gov identifier: NCT02200614

Darolutamide Phase III study ongoing in metastatic hormone sensitive prostate cancer (mHSPC)

- mHSPC patients candidate for ADT (hormonal therapy) and docetaxel (chemotherapy) are included. Treatment Darolutamide with ADT and six cycles of docetaxel
- Primary endpoint
  - Darolutamide over placebo in overall survival
- Secondary endpoints
  - Time to castration resistance, time to antineoplastic therapy, time to first symptomatic skeletal event, time to initiation of opioids, time to pain progression, and to characterize the safety and tolerability of darolutamide
- The study is proceeding as planned with estimated completion in 2022.

ARASENS

ClinicalTrials.gov identifier: NCT02799602

ODM-203

A unique and selective dual FGFR+VEGFR inhibitor for FGFR-dependent tumors

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Angiogenic indications with altered FGFR* signalling

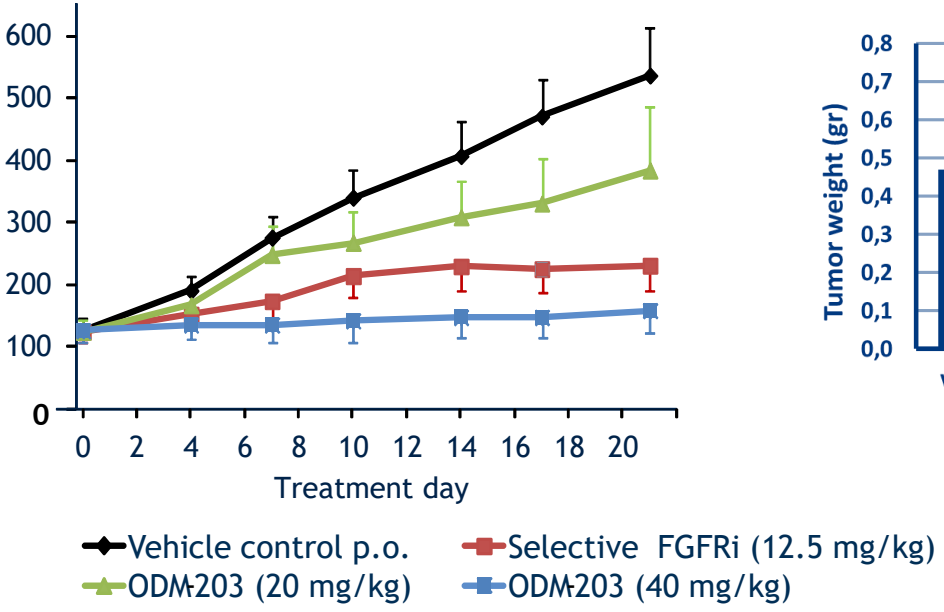
Tumor type	Genomic alterations of FGFRs and FGFs
Breast (luminal)	~35% (FGFR1 amp, FGFR2 amp, FGFR4 amp, FGFs)
NSCLC-SCC	~20% (FGFR1 amp, FGFR2 amp)
Bladder (invasive)	~15% (FGFR3 fusions, FGFR1 amp, FGFs)
Prostate	~14% (FGFR1 amp, FGFR2&3 fusions)
Colorectal	~10% (FGFR1 amp, FGFR3 mut)
Endometrial	~10% (FGFR2 mut)
Gastric	~7% (FGFR2 amp)
Renal	~6% (FGFR4 amp)

* Fibroblast Growth Factor Receptor

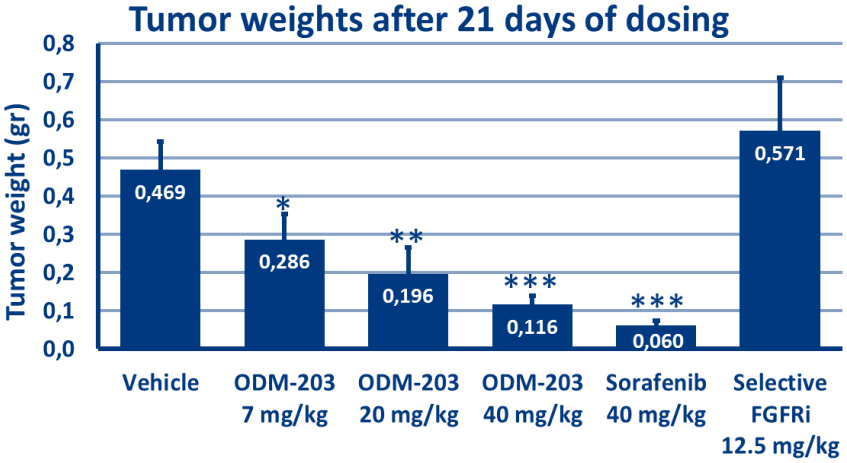
ODM-203 has strong in vivo antitumor activity

ODM-203 (targeted FGFR+VEGFR inhibitor)	Solid tumours	I	II

FGFR xenograft model (RT4)



Angiogenic kidney cancer model (Renca)



ClinicalTrials.gov identifier: NCT02264418

Rationale for combining FGFR* and VEGFR** inhibition

- Constitutively active FGFRs are oncogenic in non-clinical studies
- Both VEGFR and FGFRs are drivers for angiogenesis, a hallmark of tumorigenesis
- FGFR amplifications have an impact on patient survival in studied cancer types (breast, lung, and gastric)
- VEGFR expression correlates with survival or progression in tumor types with high incidence of FGFR alterations (bladder, breast, lung, gastric)
- FGFR signaling is a known escape mechanism for anti-VEGFR treatments

* Fibroblast Growth Factor Receptor
** Vascular Endothelial Growth Factor Receptor

ODM-203 – current status

ODM-203 (targeted FGFR+VEGFR inhibitor)	Solid tumours	I	II

KIDES trial with Phase II expansion ongoing

- The trial is investigating
  - Safety and tolerability of ODM-203 in subjects with advanced solid tumours
  - Efficacy of ODM-203 in slowing the growth of solid cancerous tumours in patients in which FGFR changes in cancerous tumours have been detected

ClinicalTrials.gov identifier: NCT02264418

ODM-207

Unique BET inhibitor for solid tumors

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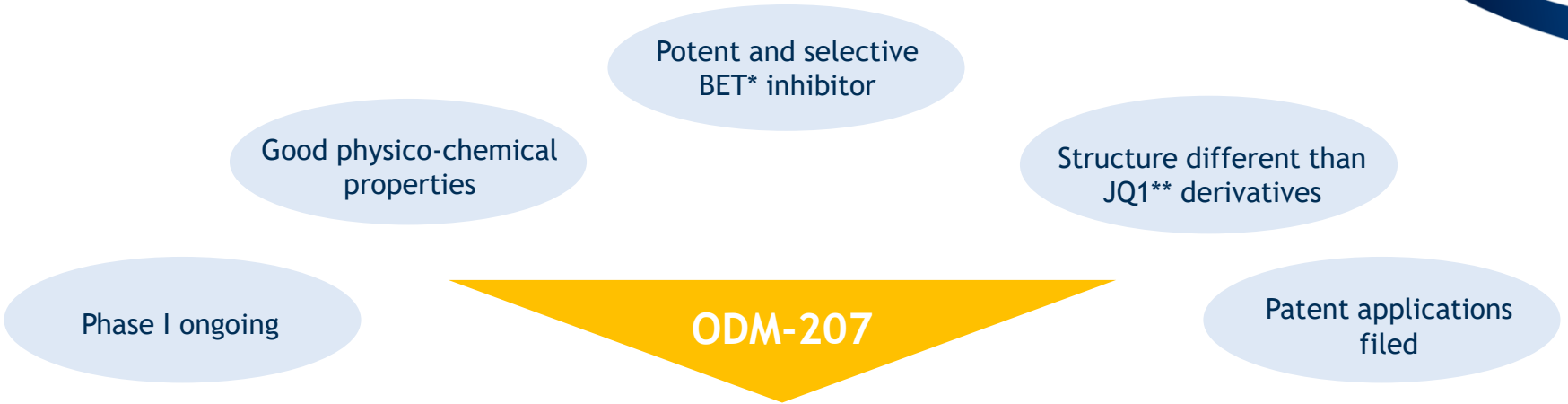
ODM-207 – A unique BET* inhibitor for solid tumours



- ODM-207 is an investigational small molecule that has a unique chemical structure designed to block the growth of cancer cells through potent and selective inhibition of BET* family proteins.
- In preclinical studies, ODM-207 has shown antiproliferative effects in several haematological and solid tumour cell lines.

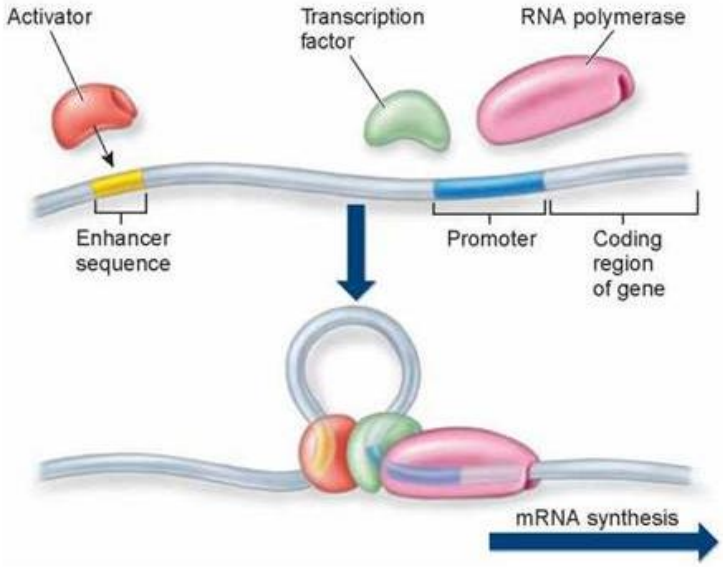
* Bromodomain and Extra-Terminal
** JQ1 is a BET inhibitor reference compound

Target: BET proteins which regulate expression of oncogenes

- BET proteins occupy regulatory elements of DNA (superenhancers) in many key oncogenes
  - They increase the expression target oncogenes
- BET target genes include: **Myc**, MycN

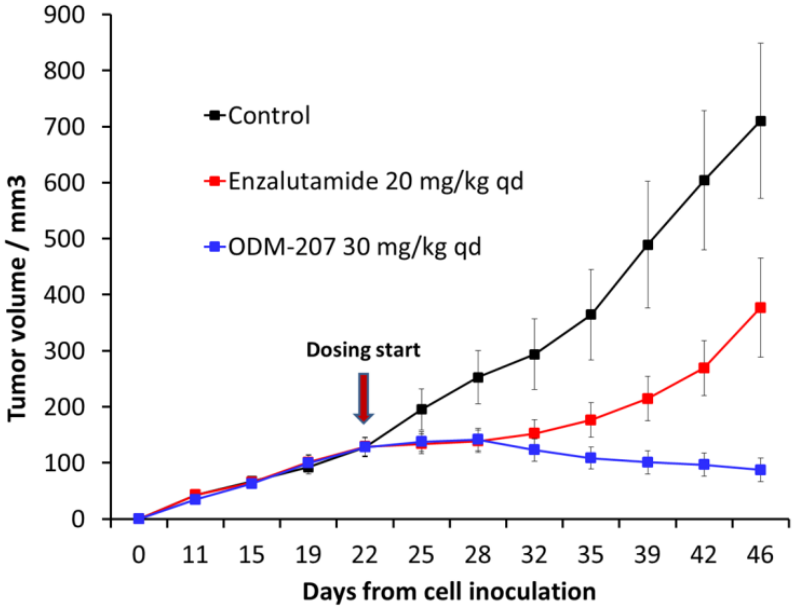
ODM-207

- Binds to BET proteins
- Inhibits transcription of key oncogenes such as Myc and MycN in many cancers



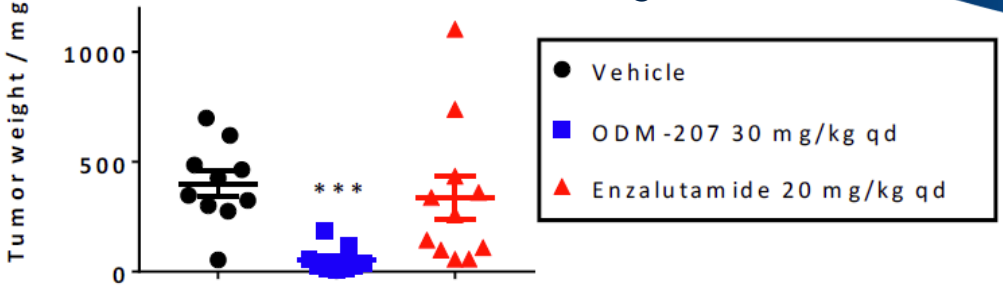
ODM-207 inhibits the tumour growth in enzalutamide-resistant 22Rv1 prostate cancer xenograft

Effect of ODM-207 on tumour volumes

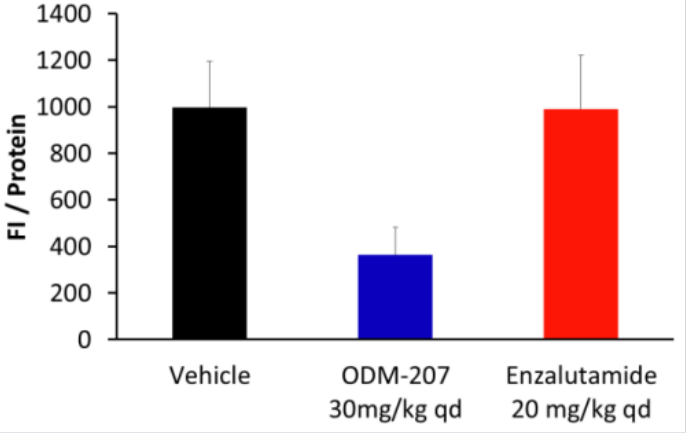


From poster Björkman et al., presented in EORTC-NCI-AACR in 11-12/2016

Effect of ODM-207 on tumour weights



ODM-207 inhibits Myc in *in vivo* efficacy study



ODM-207 – current status

ODM-207 (BET protein inhibitor)	Cancer	I

BETIDES phase I/II trial ongoing

- The trial is investigating
  - PK, safety and tolerability, and antitumour activity of ODM-207 in subjects with advanced solid tumours

ClinicalTrials.gov identifier: NCT03035591

ORM-12741

Alpha-2C adrenoceptor antagonist for symptomatic treatment of Alzheimer's disease
In collaboration with Janssen

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Phase IIa clinical trial completed – the efficacy objectives not met

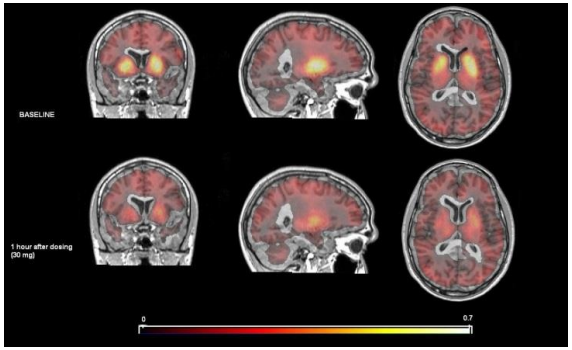
- Orion has completed a Phase IIa clinical trial in the development of an alpha-2c adrenoceptor antagonist (ORM-12741).
- The trial, conducted in collaboration with Janssen Pharmaceuticals, Inc., investigated the efficacy of two different drug formulations in treatment of agitation and aggression symptoms related to Alzheimer's disease. In addition, the efficacy on cognitive performance as well as safety of the compound was evaluated.
- The trial did not meet the efficacy objectives set for the product. The results will be evaluated together with Janssen Pharmaceuticals, Inc. and the decision on the continuation of the project will be made later.

Collaboration with Janssen

- Licence agreement announced on 19 December 2013 (ORM-12741 and other compounds).
- Orion received USD 31 million upfront payment which is mainly used against current ongoing additional Phase IIa study costs.
- Orion is eligible to receive milestone payments from Janssen upon successful completion of certain development and commercialisation events, as well as royalties on future sales.
- Orion has exclusive commercialisation rights in Europe.
- Janssen has worldwide exclusive license to develop ORM-12741 and an exclusive right to commercialise it outside Europe.

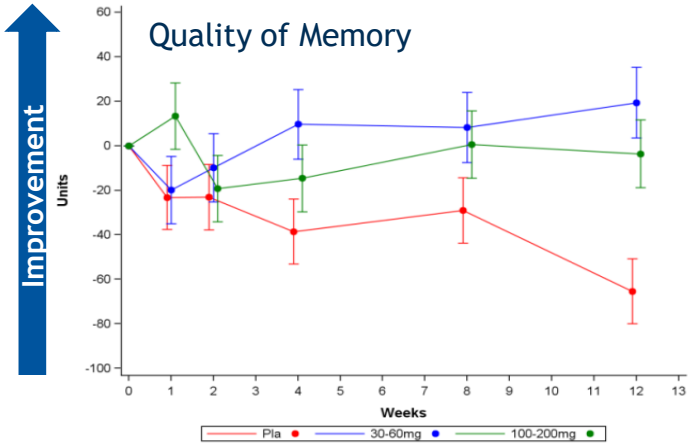
ORM-12741

- Highly potent and selective alpha-2C adrenoceptor antagonist
- Rodent models predict beneficial effects on cognition and neuropsychiatric symptoms (NPS)
- Phase 1 studies (healthy subjects)
  - Possible to administer orally
  - Well tolerated
  - Displacement of an alpha-2C PET tracer
- Phase 2a study in Alzheimer's disease patients
  - Positive signals of efficacy in
  - Episodic and working memory
  - Neuropsychiatric symptoms



Baseline

1 hour after dosing (30 mg)



Phase 2 study on efficacy of ORM-12741 in AD

ORM-12741 (alpha-2c adrenoceptor antagonist)	Alzheimer's disease	I	IIa

- New formulation improving pharmacokinetic (PK) properties of ORM-12741 was used in the Phase 2a study

Objectives

To evaluate efficacy of ORM-12741 on agitation & aggression and other neuropsychiatric symptoms

To evaluate efficacy of ORM-12741 on cognitive performance

To evaluate safety

Design and methodology

Randomised, double-blind, placebo-controlled, parallel-group, Phase 2 study

Patients with mild to moderately severe Alzheimer's disease

2 dose levels of ORM-12741 and placebo

Sample size

100/group = ~300

ClinicalTrials.gov identifier: NCT02471196

ODM-104

New COMT-Inhibitor for Parkinson's Disease

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New COMT-inhibitor ODM-104 for Parkinson's disease treatment

ODM-104 (more effective COMT inhibitor)	Parkinson's disease	I	II

- In phase I, ODM-104 has been in well tolerated and superior to entacapone by improving COMT inhibition and levodopa pharmacokinetics in man.
- Optimized carbidopa component further improves ODM-104 effect with double action on levodopa PK - levodopa exposure (AUC*) increased over 30% when compared to entacapone.
- Phase II: ODM-104/optimized carbidopa/long-acting levodopa will be compared with Stalevo® (levodopa/carbidopa/entacapone combination) in PD patients with end-of-dose wearing-off symptoms The Phase 2 study is ongoing.

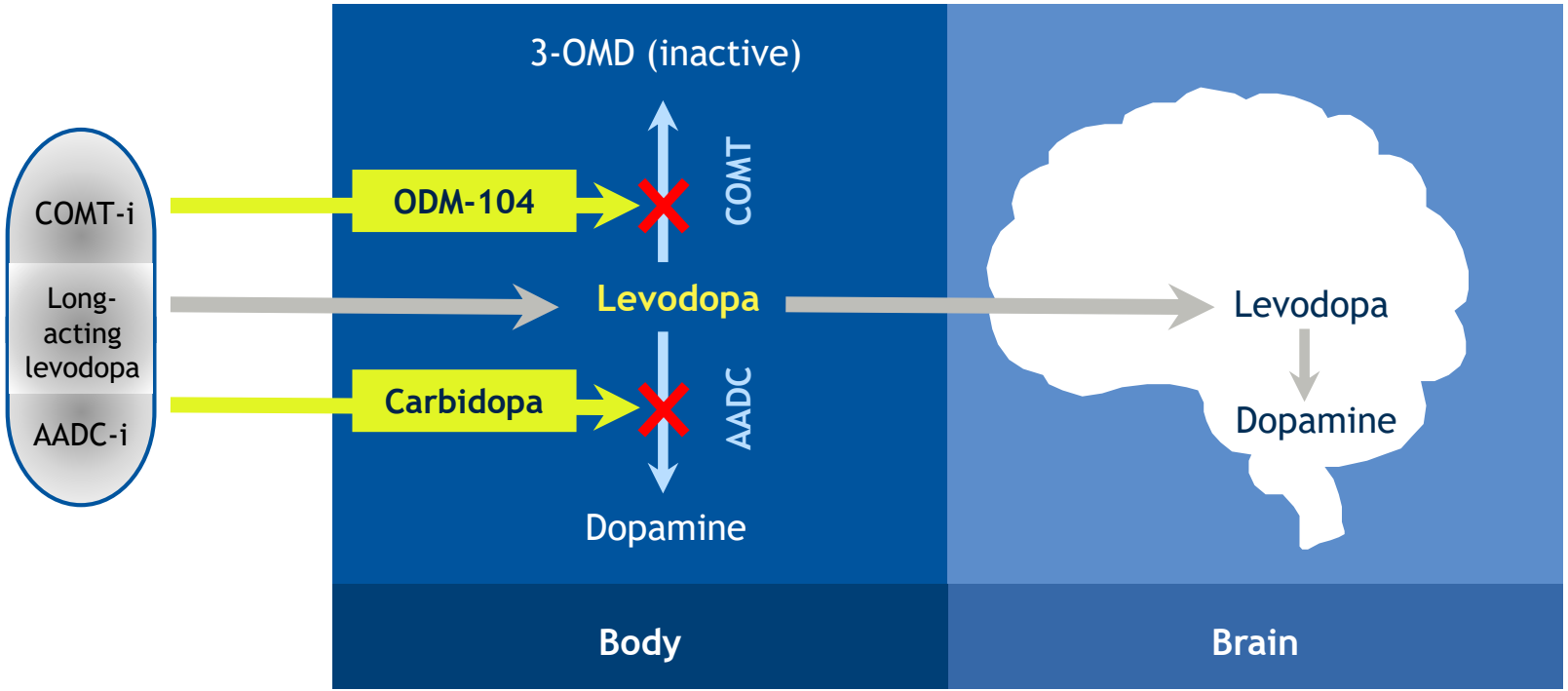
ClinicalTrials.gov identifier: NCT02764125

* Area Under the Curve

Treatment of Parkinson's disease with levodopa

- Levodopa is the most effective medicine for treating Parkinson's disease (PD).
- As PD progresses, most people will eventually require the use of levodopa (85% of PD patients receive levodopa).
- However, like all medicines, levodopa is not perfect – short acting levodopa can lead to motor complications.
- Longer acting levodopa with more stable plasma concentrations is an unmet need for PD treatment.

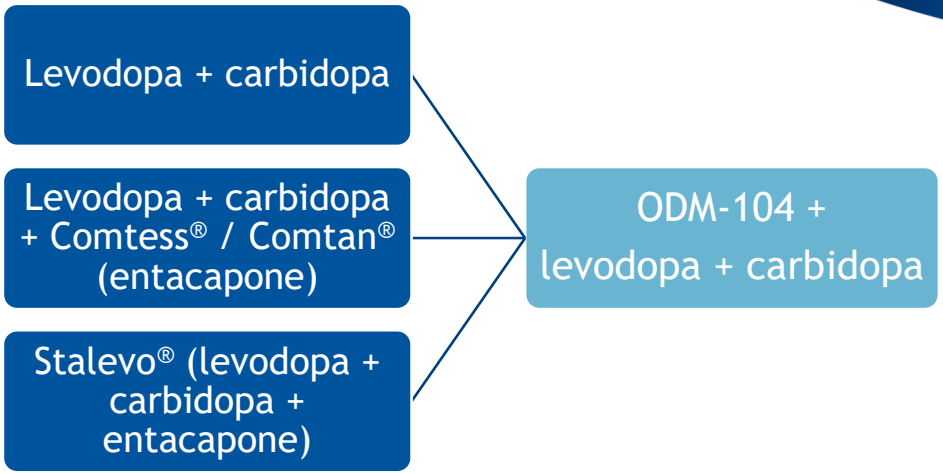
Levodopa elimination can be reduced and treatment effect improved by inhibiting breakdown enzymes AADC and COMT



AADC = Aromatic amino acid decarboxylase COMT = Catechol-O-methyltransferase 3-OMD = 3-O-Methyldopa

Target indication

- The target indication of ODM-104 is Parkinson´s disease with end-of-dose motor fluctuations - the same as the currently approved indications of Comtess®/Comtan® and Stalevo®.
- Patients on levodopa/AADC inhibitor treatment with or without entacapone can be directly switched to the new combination product (ODM-104/optimized carbidopa/long-acting levodopa).



ODM-109

Best symptomatic treatment for Amyotrophic Lateral Sclerosis (ALS)

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LEVALS phase II study - levosimendan in ALS patients

ODM-109 (oral levosimendan)	ALS	I	II

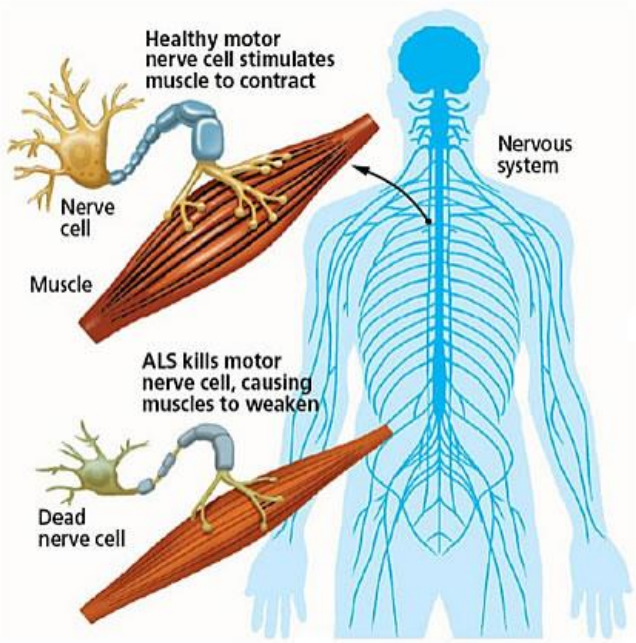
- The first phase II study aimed to demonstrate beneficial effects on respiratory function.
- Double-blind, cross-over design with 3 treatment periods.
- Cross-over part of the study is followed by an open-label part for 6 months – an opportunity to study long term effects.
- The cross-over part of Phase II clinical trial with orally administered levosimendan (ODM-109) for treatment of patients with ALS has been completed.
- Although the trial did not achieve its primary objective, the findings were, however, promising.
- Based on the findings, we are planning to continue the development programme.

Amyotrophic lateral sclerosis - ALS

- Orphan disease with prevalence of

  ~1 patient/25,000
- Degeneration of motoneuron leads to skeletal muscle weakness including diaphragm.
- Causes premature death (3 years median survival time from symptom onset).
- Decreases Quality of Life of both patient and caregiver.
- No symptomatic treatments for muscle function available.

A clear unmet need in ALS for a drug that improves diaphragm/skeletal muscle function and endurance.



Picture from: ALS Foundation for life
http://www.alsfoundation.org/learn/

Data supporting development of ODM-109 for ALS

- Levosimendan enhances force generation of diaphragm muscle fibers obtained from a rat model of heart failure and from COPD and non-COPD patients (ex vivo experiments).
- Levosimendan improves human diaphragm function in healthy subjects *in vivo*.
- Levosimendan show a positive effect on skeletal muscle function (endurance) in Myasthenia Gravis rat model functionally mimicking ALS.

By increasing skeletal muscle force and endurance, levosimendan has potential to improve respiratory function, muscle fatigue and QoL* in ALS patients.

*)QoL = Quality of Life

Easyhaler product family

Easyhalers for treatment of asthma and COPD

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Easyhaler® portfolio expanding

Salmeterol-fluticasone Easyhaler®

- In registration phase in Europe since 4/2017
- Favorable bioequivalency study results at the end of 2016
- Learnings from budesonide-formoterol Easyhaler® development utilised, which have significantly increased our understanding of the regulatory requirements.

Tiotropium Easyhaler®

- Orion has commenced a new project to develop a tiotropium formulation for European markets.
- Triotropium is a long-acting anticholinergic bronchodilator for treatmenent in chronic obstructive pulmonary disease.

2014 budesonide-formoterol Easyhaler®

2004 formoterol Easyhaler®

1994 beclomethasone Easyhaler®

salmeterol-fluticasone Easyhaler®

2002 budesonide Easyhaler®

1993 salbutamol Easyhaler®

tiotropium Easyhaler®

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