# Orion Capital Markets Day 2015

26 May 2015 Helsinki

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# Agenda

| | |
|---|---|
| CEO's review | Timo Lappalainen, President & CEO |
| R&D pipeline review, part I | Reijo Salonen, SVP, Research & Development |
| Break | |
| Proprietary Products update | Markku Huhta-Koivisto, SVP, Proprietary Products |
| Specialty Products update | Liisa Hurme, SVP, Proprietary Products |
| CFO's presentation | Jari Karlson, CFO |
| Break | |
| Animal Health | Niclas Lindstedt, Vice President, Animal Health |
| Fermion | Arto Toivonen, President, Fermion |
| Orion Diagnostica | Jaakko Rissanen, President, Orion Diagnostica |
| R&D pipeline review, part II | Reijo Salonen, SVP, Research & Development |
| Closing remarks and Q&A | |
| Lunch | |

*Short Q&A sessions will be held after each presentation*

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.

# CEO's presentation

CEO Timo Lappalainen

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# Development since CMD in 2013

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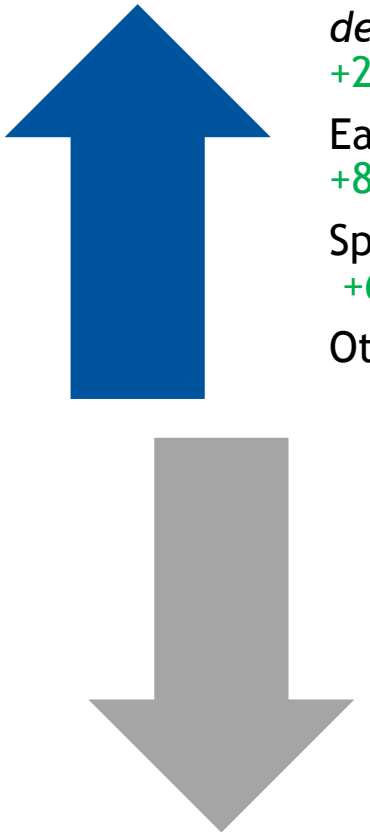
# Key developments 2012 to 2014



*dexdor®*
+22 MEUR

Easyhaler
+8 MEUR

Specialty Products
+60 MEUR

Other business +41 MEUR

Branded PD
-81 MEUR

Precedex
-15 MEUR

+ Partnerships with Janssen and Bayer
+ 7 new projects in clinical developement pipeline
+ Stalevo for Japan
+ First approvals of Bufomix
– 3 development projects discontinued (2 back-ups)
– Expansion of Stalevo generic competition
– Generic competition for Precedex in the USA



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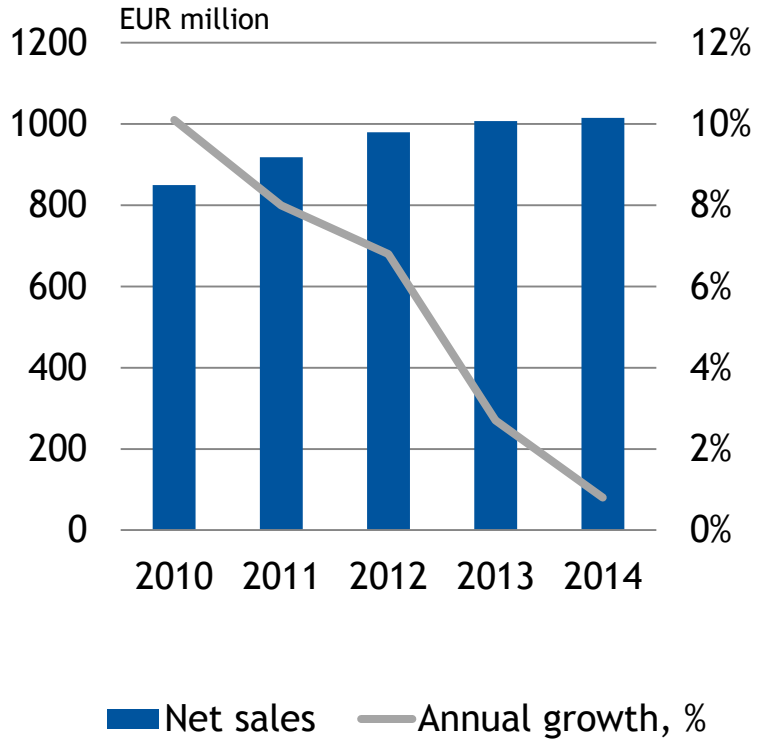
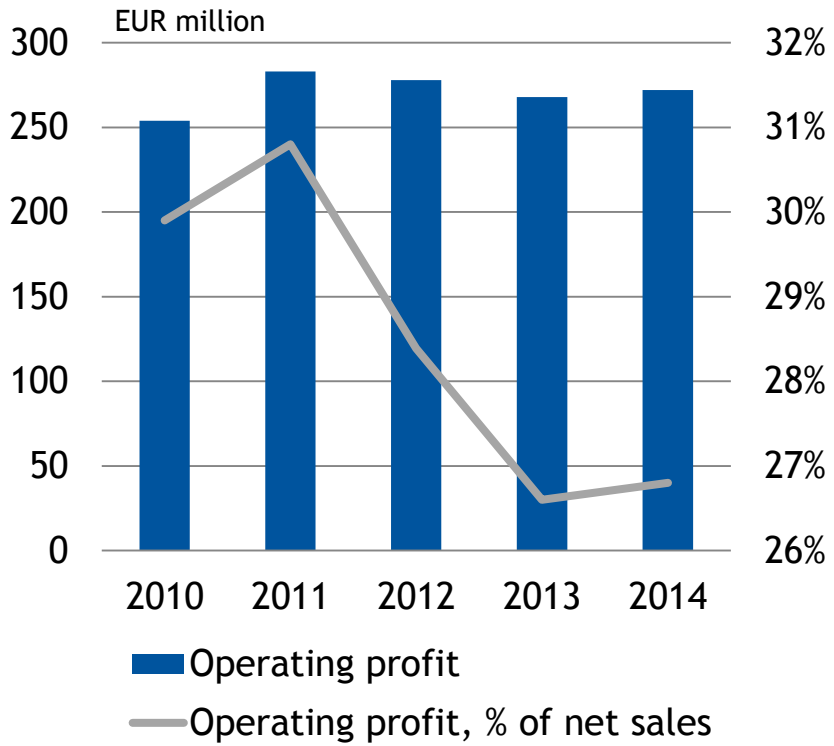
# Financial performance in 2010-2014

## Net Sales 2010-2014




CAGR 5%

## Operating Profit 2010-2014




CAGR 2%



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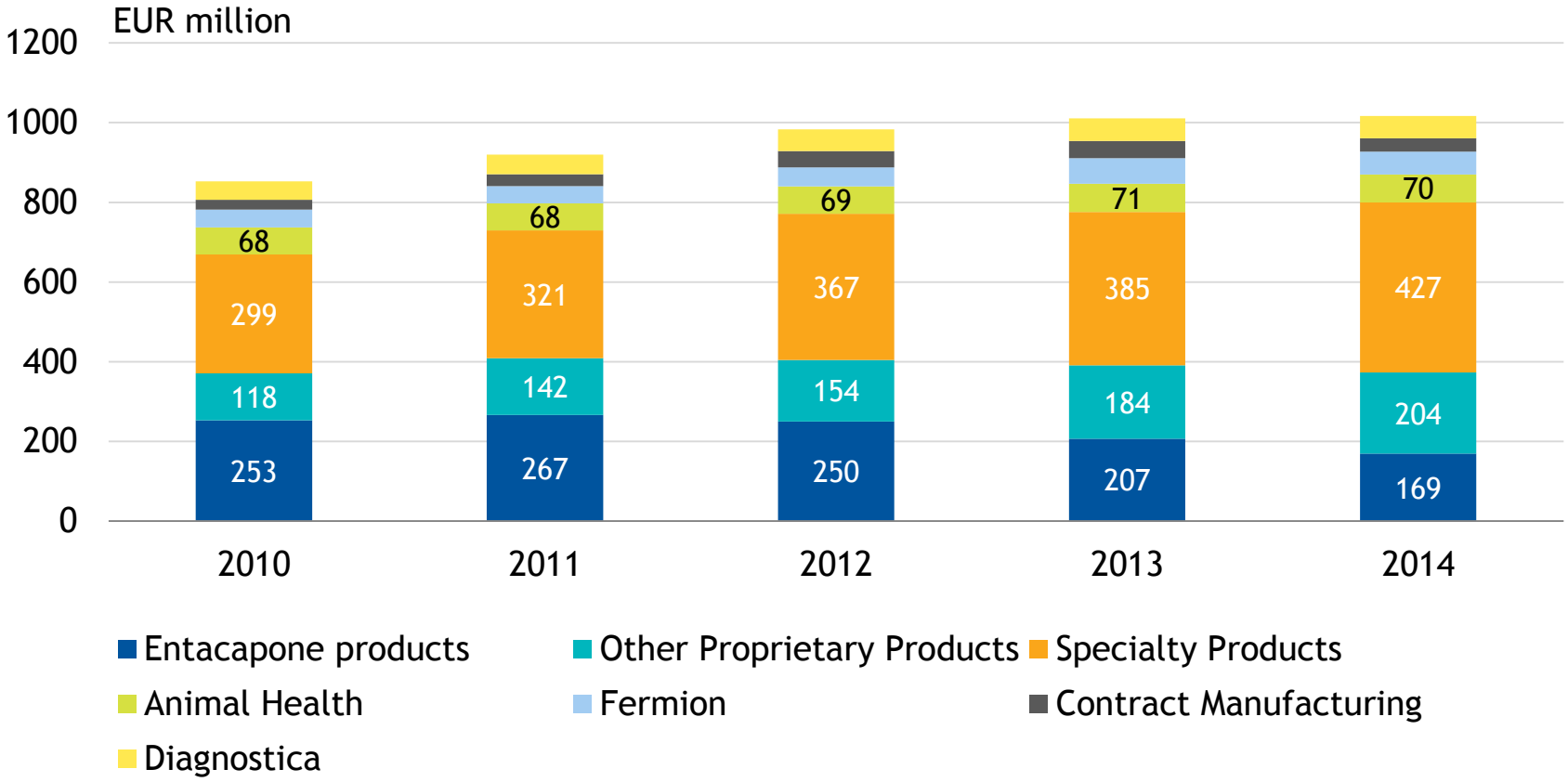
# Net sales by business division 2010-2014




Proprietary Products CAGR 0%
Specialty Products CAGR 9%



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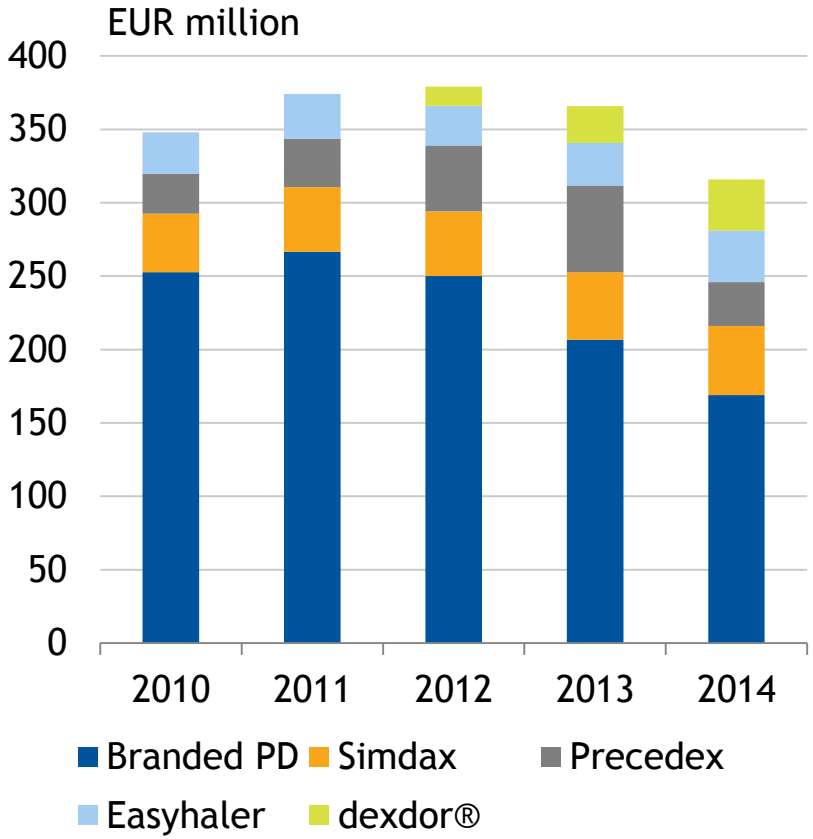
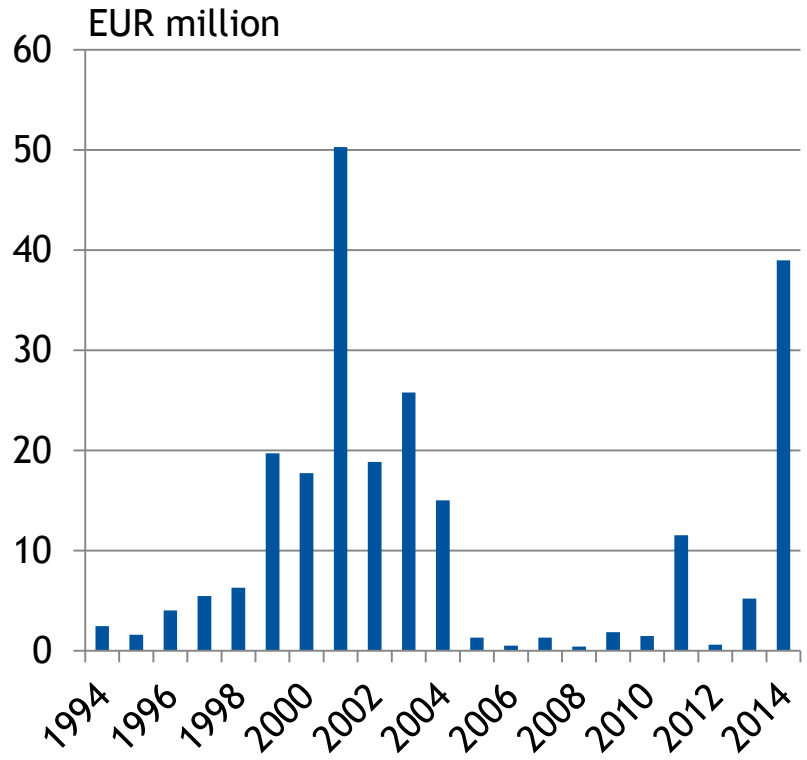
# Development of key PP products and milestones




Orion milestone history*




*) essential milestones



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# The way forward - Orion's strategy

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# Balancing mid-term – building long-term

Long-term growth opportunities from R&D pipeline. Milestone payments.

Generic competition for Parkinson's franchise and Precedex.

Timing of milestone payments.

Generic drugs and self-care products.

Easyhaler® combinations and *dexdor*® for European markets.

Global pricing pressure, especially on new products.

Operational flexibility and efficiency.



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# R&D pipeline review part I

Reijo Salonen
SVP, Research & Development

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# Best R&D Pipeline

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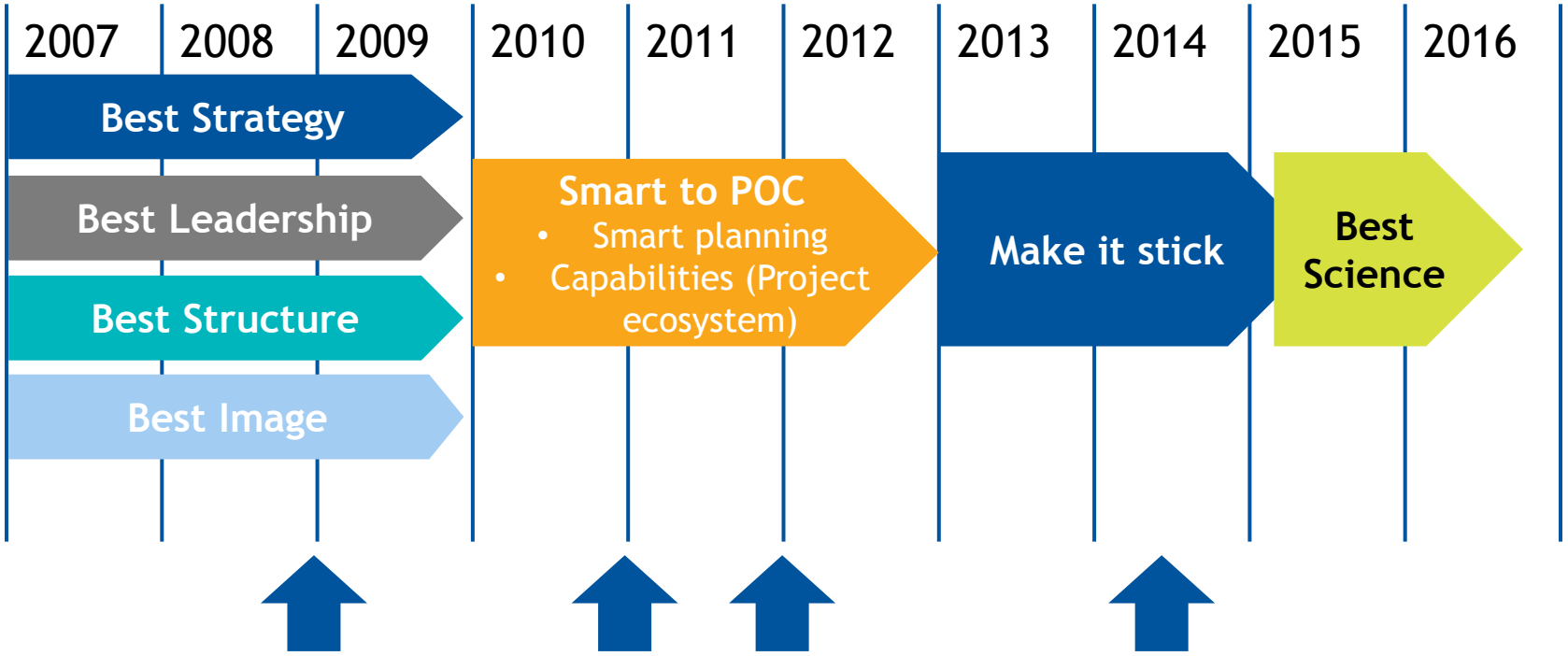
# Transformation journey of Orion Pharma R&D toward the Best R&D in the world 2017




Continous reorganizations have reshaped the project centric matrix organisation to support the cultural change

*R.Thong and T. Lotta: Creating a Culture of Productivity and Collaborative Innovation- Orion's R&D Transformation. This article was published in Research-Technology Management (RTM), Vol. 58, No. 3 (2015), pp. 41-50. Available online at www.iriweb.org/rtm*



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# Pharmaceutical R&D portfolio 2015 1/2

| Project | Indication | PHASE | Registration |
|---|---|---|---|
| Bufomix Easyhaler® (budesonide-formoterol) [1] | Asthma, COPD | I II III | |
| Easyhaler® salmeterol-fluticasone | Asthma, COPD | I II III | |
| ODM-201 (androgen receptor inhibitor) [2] | Prostate cancer | I II III | |
| Levosimendan [3] | Low Cardiac Output Syndrome | I II III | |
| ORM-12741 (alpha-2c adrenoceptor antagonist) [4] | Alzheimer's disease | I IIa | |
| Dexmedetomidine (intranasal) [5] | Treatment of pain | I IIb | |
| ODM-109 (oral levosimendan) | ALS | I II | |

[1] Aim is to obtain marketing authorisation for product in at least some European countries not included in decentralised marketing authorisation application process.
[2] In collaboration with Bayer
[3] Partner: Tenax Therapeutics, Inc.
[4] In collaboration with Janssen Pharmaceuticals
[5] Partner: Recro Pharma, Inc.

= Phase completed
= Phase ongoing

More info at: http://www.orion.fi/en/rd/orion-rd/pipeline/



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# Pharmaceutical R&D portfolio 2015 2/2

| Project | Indication | PHASE | | | Registration |
|---|---|---|---|---|---|
| ODM-104 (more effective COMT inhibitor) | Parkinson's disease | I | | | |
| ODM-203 (targeted FGFR+VEGFR inhibitor) | Solid tumours | I | | | |
| ODM-204 (CYP17 enzyme and androgen receptor inhibitor) | Prostate cancer | I | | | |
| ODM-106 (GABA-B receptor positive allosteric modulator) | Essential tremor | I | | | |
| ODM-108 (negative allosteric modulator of TRPA1 ion channel) | Neuropathic pain | I | | | |

= Phase completed

= Phase ongoing

More info at: http://www.orion.fi/en/rd/orion-rd/pipeline/


# Easyhaler

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# Bufomix Easyhaler®

- Application for marketing authorisations in some countries left out from the 1st DCP round for 160/4.5 and 320/9 µg/inhal. strengths
- The further development plans are based on experiences from the 1st DCP round and authority consultations increasing our confidence in obtaining authorisations in at least some remaining countries




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# BUFODIL study

| Bufomix Easyhaler® (budesonide-formoterol) | Asthma, COPD | I | II | III |
|---|---|---|---|---|

- A study to confirm equivalent bronchodilator efficacy of Bufomix Easyhaler compared to Symbicort Turbuhaler in adult asthmatics
- Randomised, double-blind, double-dummy, multicentre, single dose, crossover study
- Asthmatic patients who demonstrate reversible airway obstruction, have prebronchodilator forced expiratory volume in 1 second (FEV1) 45-90% of the predicted value and who have stable asthma will be included
- Clinical phase is on-going and estimated to be completed in 2015


ClinicalTrials.gov identifier: NCT02308098



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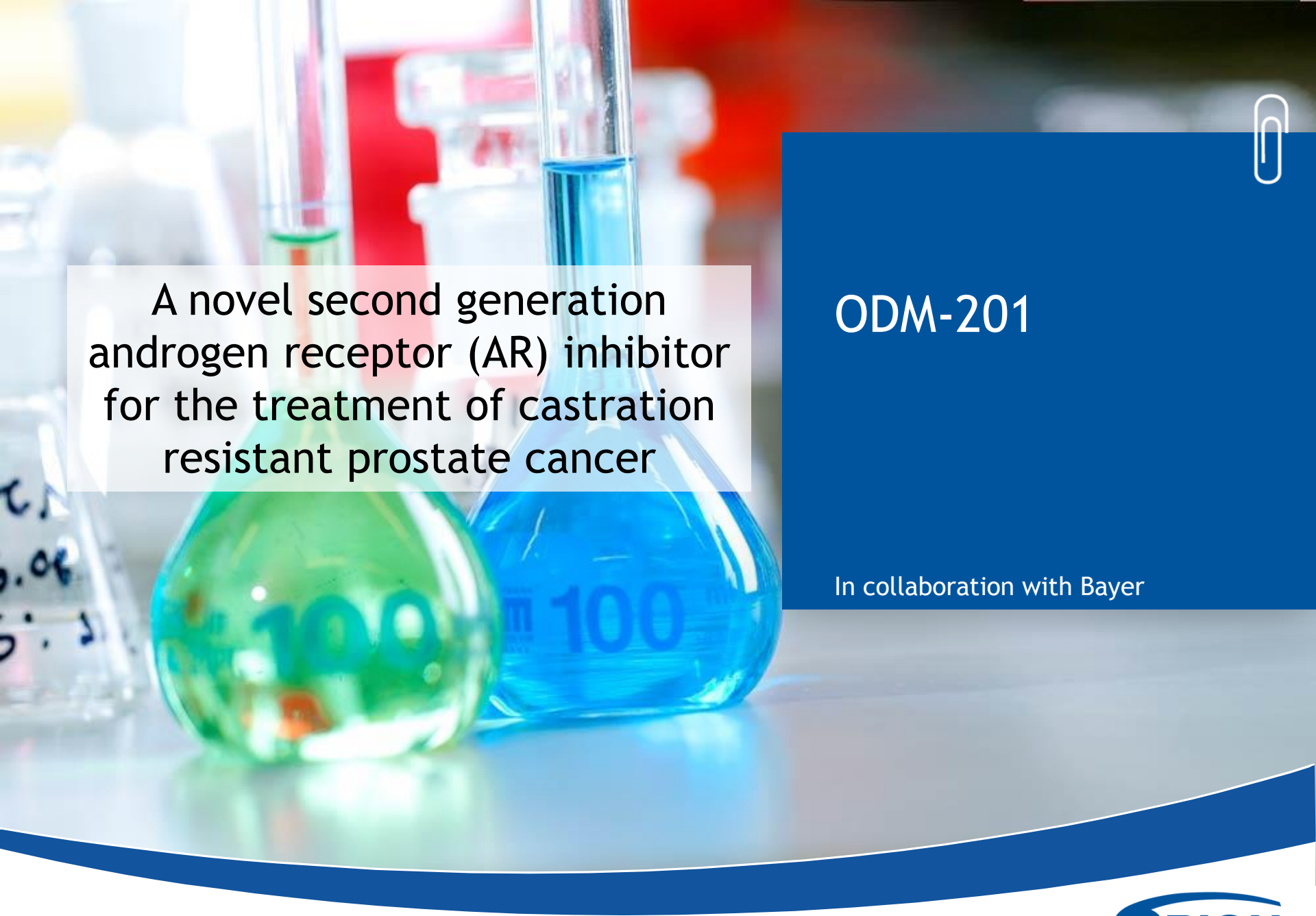
# Salmeterol-Fluticasone Easyhaler®

| Easyhaler® salmeterol-fluticasone | Asthma, COPD | I | II | III |
|---|---|---|---|---|

- Development of Salmeterol-Fluticasone Easyhaler® is in clinical phase
- We have utilized the learnings from Bufomix Easyhaler® development which have significantly increased our understanding of the regulatory requirements. This is believed to smoothen the regulatory phase

ClinicalTrials.gov identifier: NCT02162485



A novel second generation androgen receptor (AR) inhibitor for the treatment of castration resistant prostate cancer

# ODM-201

In collaboration with Bayer

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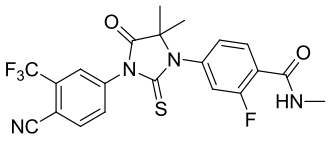
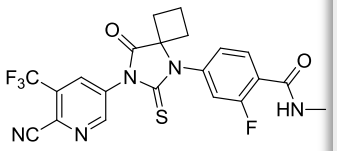
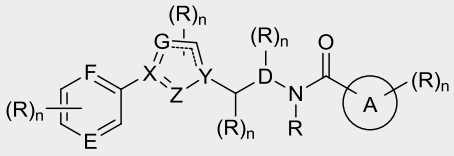
# ODM-201 has a unique profile



Enzalutamide

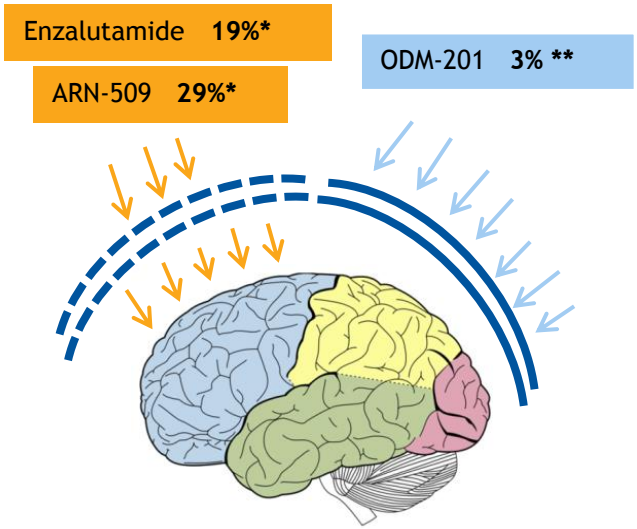


ARN-509



ODM-201 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 |
| ODM-201 | 9 | 65 | 66 | 1782 | 1500 | 500 |




*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)

- ODM-201 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



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# ODM-201 Clinical studies

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

* metastatic castration resistant prostate cancer
** non-metastatic castration resistant prostate cancer



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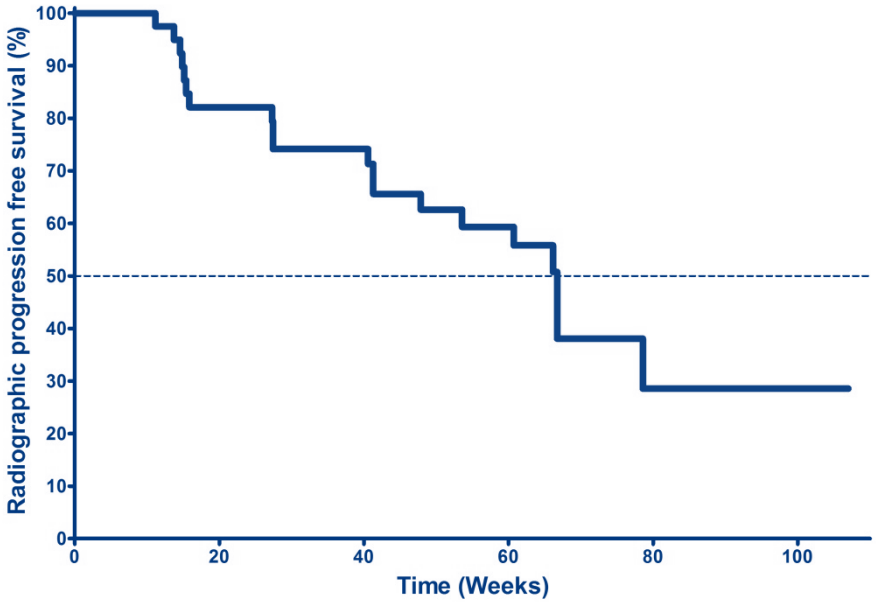
# ODM-201 provided antitumour activity with mCRPC patients in phase I/II studies (ARADES and ARAFOR)

Radiographic progression, product-limit survival estimate with number of subjects at risk




ODM-201 with daily doses between 1200-1800 mg was well tolerated and provided antitumor activity in patients with mCRPC who were naïve for chemotherapy and CYP17-inhibitor treatment.

Median time to radiographic progression was 66.7 weeks (95% CI 41.3 - not reached).

Source: EAU2015 - Study poster 567
”Safety and antitumor activity of ODM-201 in chemotherapy and CYP17-inhibitor naïve patients from the ARADES and the ARAFOR trials”



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# ODM-201 Phase III study ongoing in non-metastatic castration resistant prostate cancer (nmCRPC)

| | | | | |
|---|---|---|---|---|
| ODM-201 (androgen receptor inhibitor) [2)] | Prostate cancer | I | II | III |

- nmCRPC patients who are at high risk for developing metastatic disease are included (n=1500)
- Primary endpoint
  - ODM-201 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 ODM-201.
- Operational responsibility transferred from Orion to Bayer in December 2014
- The study is proceeding as planned with estimated completion in 2018

ARAMIS
Androgen Receptor inhibiting Agent for Metastatic-free Survival

ClinicalTrials.gov identifier: NCT02200614



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# ODM-203

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

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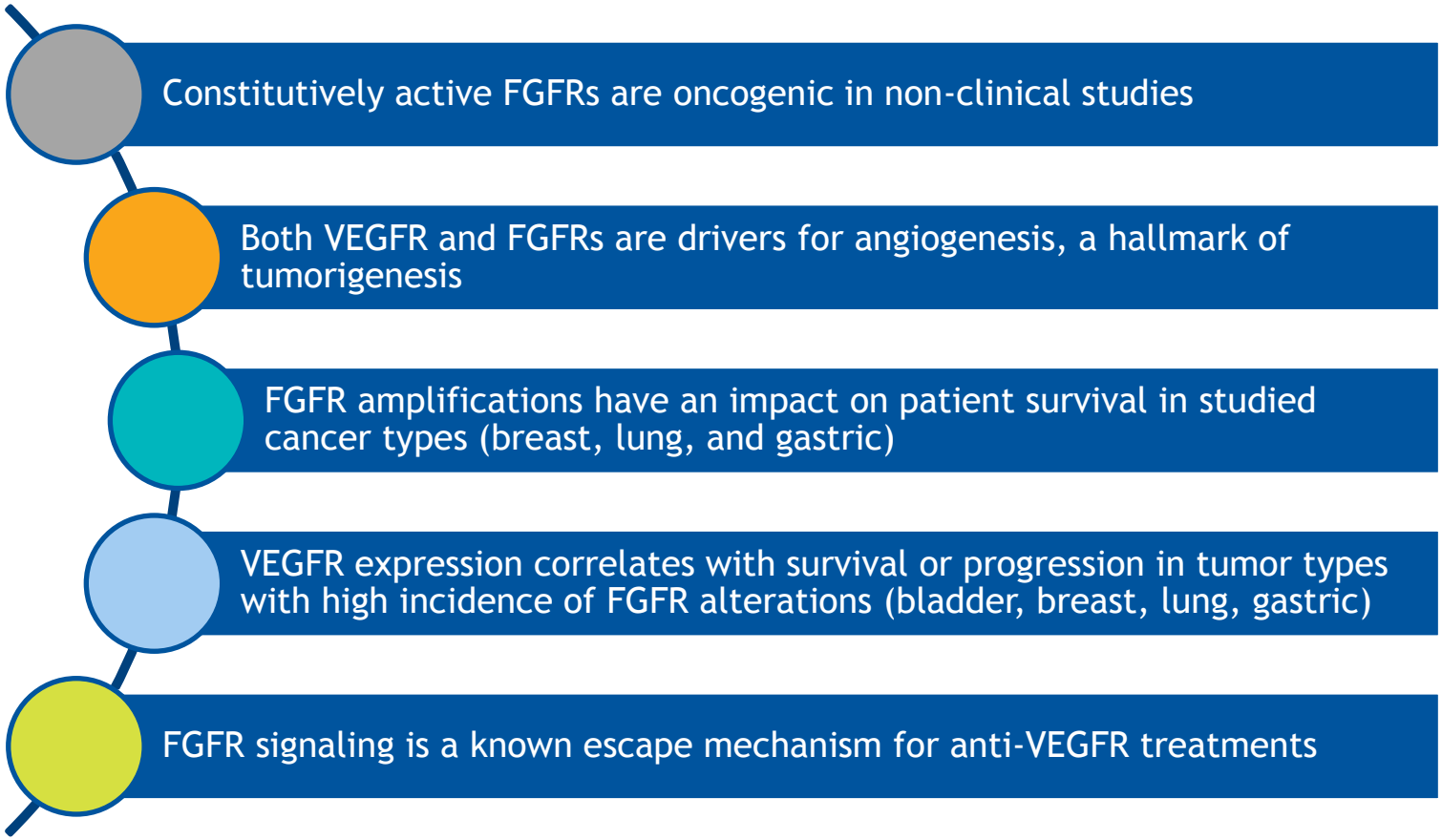
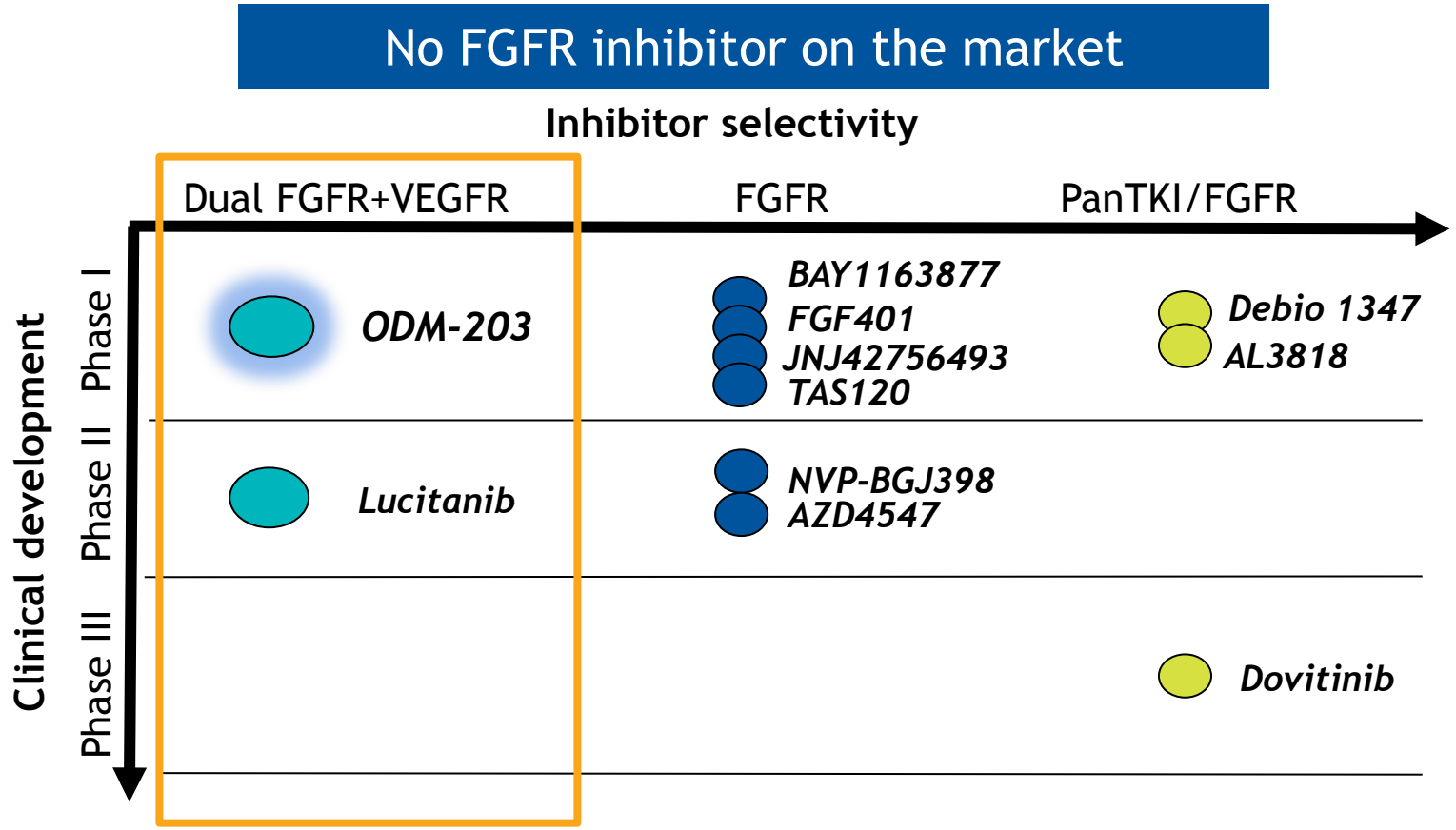
# Rationale for combining FGFR and VEGFR inhibition



# 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) |

# Current competitive landscape for small molecule FGFR inhibitors



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# ODM-203 seems to be the only equally balanced selective dual FGFR/VEGFR inhibitor

**In vitro kinase activity**

| Ratio | ODM-203 | Lucitanib |
|---|---|---|
| FGFR1/VEGFR2 | 1:1 | 1:6 |

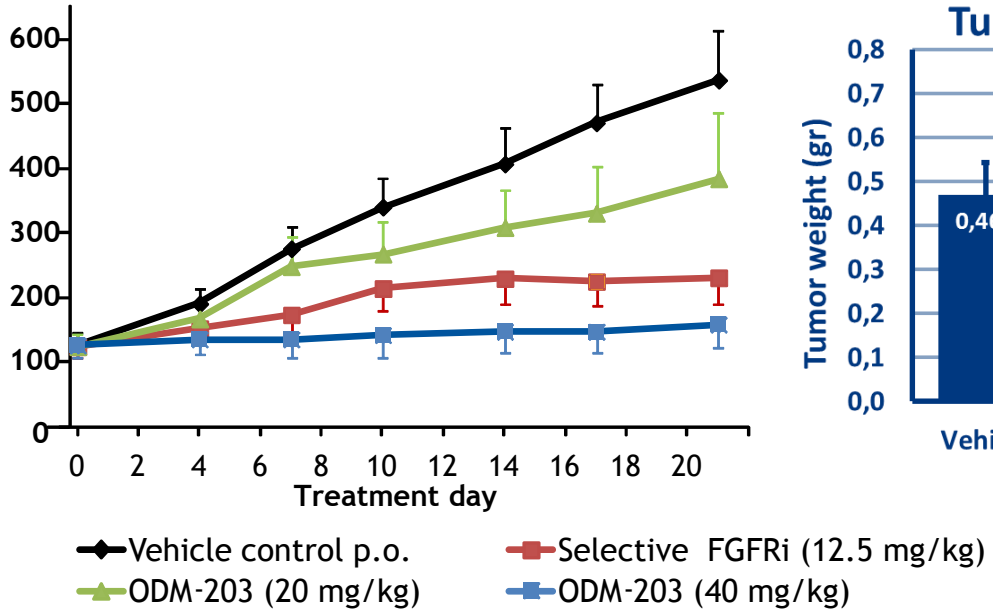
**Cell based activity**

| Cell line (receptor), Ratio | ODM-203 | Lucitanib |
|---|---|---|
| FGFR/Angiogenesis | 1:2 | 1:100 |

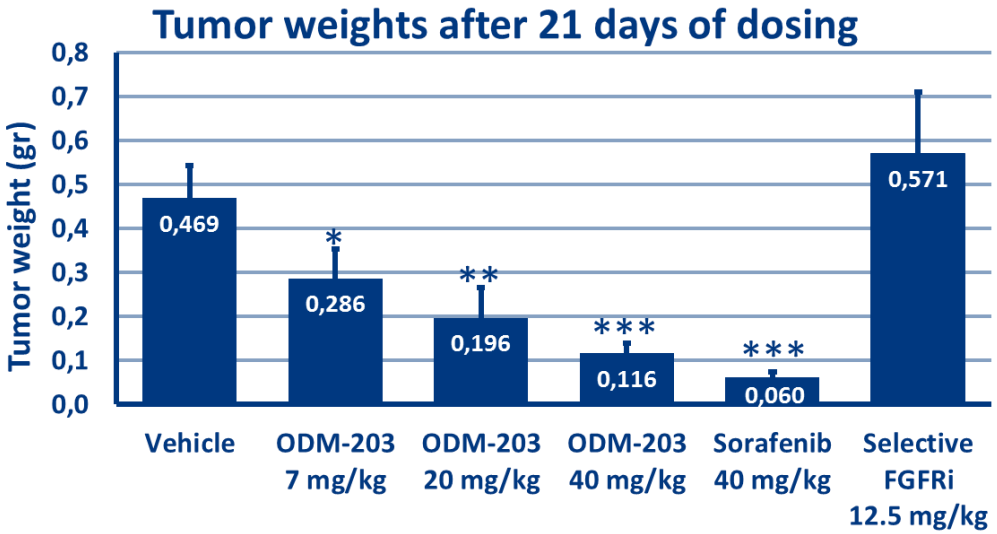
- ODM-203 has very high kinase selectivity against FGFR1-4 and VEGFR1-3
- Equally balanced inhibition may provide better efficacy/safety profile

# ODM-203 has strong in vivo antitumor activity

FGFR xenograft model (RT4)




Angiogenic kidney cancer model (Renca)




- Superior activity in angiogenic tumor models
- Strong antitumor activity in several FGFR dependent models
  - No effect in a FGFR and VEGFR *independent* xenograft model



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# ODM-203 – current status

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

- Phase I KIDES trial ongoing
- Safety and Tolerability of ODM-203 in Subjects With Advanced Solid Tumours (KIDES-203)

ClinicalTrials.gov identifier: NCT02264418

Target:
Best-in-class treatment for metastatic Castration Resistant Prostate Cancer (mCRPC)

# ODM-204

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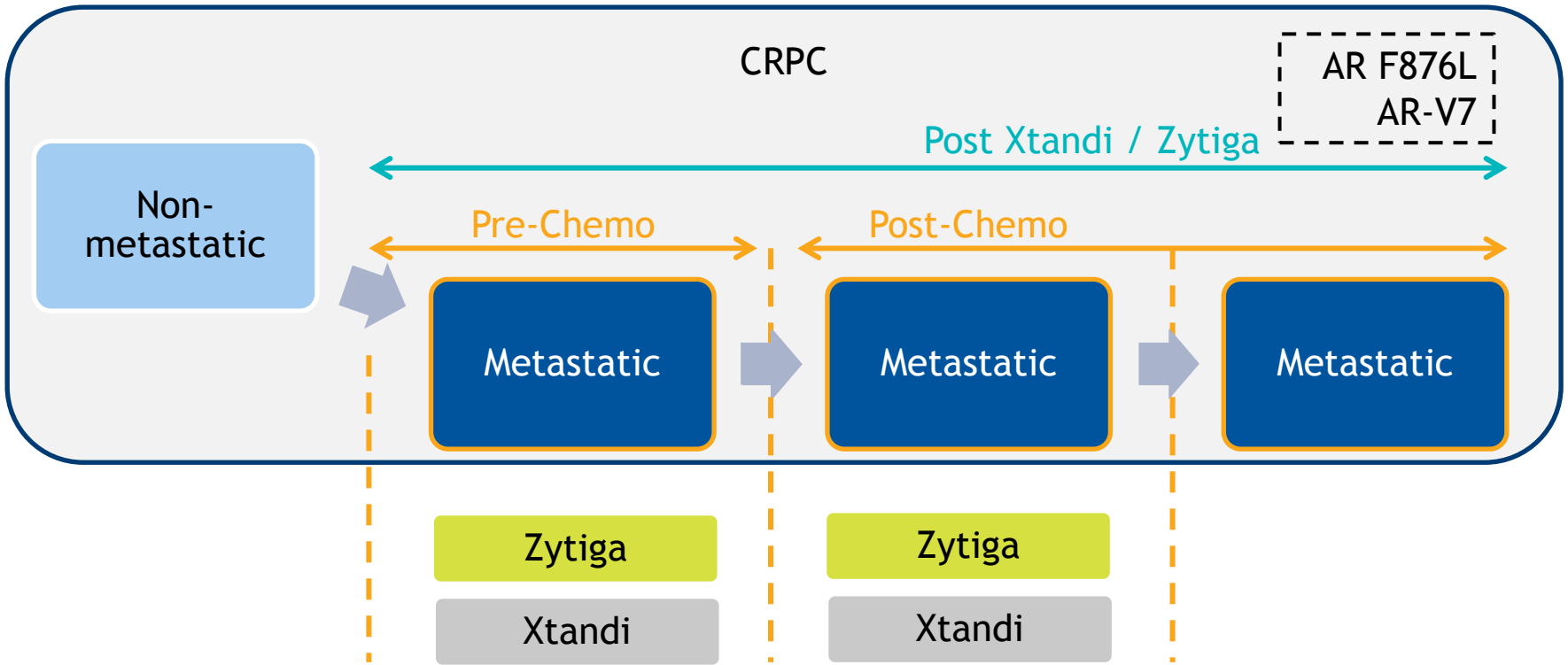
# Positioning of ODM-204




Note: Zytiga/Xtandi combination trials are ongoing



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# Target product profile in mCRPC*

| | ODM-204 | Xtandi (Enzalutamide) | Zytiga (Abiraterone) | Galeterone (TOK-001) |
|---|---|---|---|---|
| Mechanism | CYP17A1 inhibitor+ AR inhibitor | AR inhibitor | CYP17A1 inhibitor | CYP17A1 inhibitor |
| CYP17A1 inhibition | ++ | - | +++ | ++ |
| AR binding/activity | +++ | ++ | - | (+) |
| In vitro efficacy in VCaP cells | +++ | + | + | - |
| Antagonist in AR mutations and overexpression | +++ | ++ | - | - |
| Bioavailability and stability | +++ | +++ | + | + |
| Significant inhibition of androgenic steroid production in preclinical models | +++ | - | +++ | ++ |

*) Orion internal data with ODM-204 and competitors

# ODM-204 – current status

| | | |
|---|---|---|
| ODM-204 (CYP17 enzyme and androgen receptor inhibitor) | Prostate cancer | I |

- Phase I/II DUALIDES trial ongoing
  - Safety and Pharmacokinetics of ODM-204 in Patients With Metastatic Castration-Resistant Prostate Cancer (DUALIDES)
  - Subgroups:

| Number of subjects (approx.) | Chemotherapy | Second-generation AR inhibitor (e.g. enzalutamide) | CYP17A1i (e.g. abiraterone acetate) |
|---|---|---|---|
| 15 | Naive | Naive | Naive |
| 15 | Naive or pre-treated | Naive | Pre-treated |
| 15 | Naive or pre-treated | Pre-treated | Naive |

ClinicalTrials.gov identifier: NCT02344017

## Orion signs cooperation agreement with HUCH Comprehensive Cancer Center

**26 Mar 2015 | Orion Corporation and the HUCH Comprehensive Cancer Center have entered into an extensive cooperation agreement. The agreement will bring all the clinical cancer drug studies launched by Orion to HUCH and also enable more comprehensive research cooperation in the development of drug candidates.**



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# Break


PROFIT
DEVELOPMENT
SALES
OPERATING
NET
PRODUCT
ORION
GENERIC
EASYHALER
CLINICAL
MARKETING
BUFOMIX
PRECEDEX
PHASE
COLLABORATION
SIMILAR
INTENSIVE
DRUGS
BAYER
GROWTH
MILESTONE
LEVEL
FAMILY
INHIBITOR
PROPRIETARY
OUTLOOK
STEADILY
STRONGLY
ESPECIALLY
DEXDOR
CANCER
HIGHER
CONTINUED
PARTNERS
ORM
NOVARTIS
ROYALTIES
REVIEW
ADDITION
MILLION
GOOD
SIGNIFICANT
PLANNED
CLEARLY
DISEASE
ANDROGEN
CERTAIN
PERIOD
GREW
COMPOUND
PLEASED
RECEPTOR
LEVOSIMENDAN
ENTACAPONE
DELIVERIES
QUARTER
INVESTMENT
ORGANISATION
PARTICULAR
CASTRATION
PUBLISHED
FINANCIAL
OBJECTIVES
INFORMATION
PORTFOLIO
POSITIVE
UPDATED
COMPENSATE
SAFETY
ANTICIPATED
FOLLOWING
SYMPTOMS
STRONG
BEGINNING
MODULATOR
HOSPIRA
GRANTED
FUTURE
REGARDS
ANNOUNCED
EXTENSION
REORGANISATION
CHANGES
PROSTATE
ANTAGONIST
DECLINING
INCREASE
CARE
PROGRESSED
RELATED
INVESTIGATIONAL
ALLOSTERIC
ADRENOCEPTOR
SIMDAX
DEXMEDETOMIDINE.COM
REMAINS
CURRENT
RESPONSIBLE
GERMANY
NATIONAL
RECORDED
MOLECULE
NETWORK
GROW
RELIABILITY
CELEBRATED
EXPECTED
MAINTAINED

# Proprietary Products Update

Markku Huhta-Koivisto,
SVP Proprietary Products

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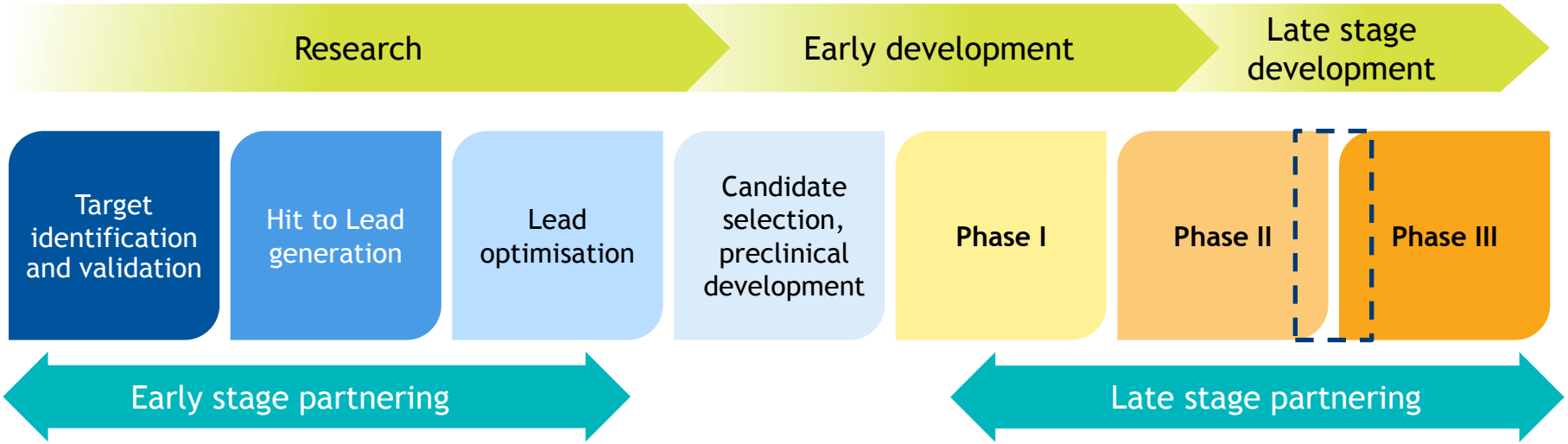
# Orion's partnering strategy is based on profitable growth and increased shareholder value whilst keeping business risk under control




## KEY CHARACTERISTICS OF LATE STAGE PARTNERING

- Late stage partnering typically after PoC
- Risk and reward sharing
- Partner has commercial capabilities especially in USA
- Potential for income before commercial sales in form of milestones



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# Key late stage development partnerships

## Partnership with Janssen on ORM-12741 for treatment of symptoms of AD

Commercial territories

- Orion: Europe
- Janssen: RoW

Development cost sharing

- Development co-funded after Orion has successfully completed additional phase IIa study

Financials

- Upfront payment of MEUR 23 (MEUR 20 to be used against Phase IIa costs)
- Orion entitled to milestones and royalties based on development and commercial success

## Partnership with Bayer on ODM-201 for treatment of prostate cancer

Commercial territories

- Bayer: Global rights
- Orion: Co-promotion option in Europe, manufacturing of the product

Development cost sharing

- Bayer contributes major share of development costs from 2015 onwards

Financials

- Upfront payment of MEUR 50 (MEUR 22 used for development costs in 2014)
- Orion entitled to milestones and royalties based on development and commercial success

# Partnering opportunities in the pipeline

| Project | Indication | PHASE | | | Registration |
|---|---|---|---|---|---|
| ODM-109 (oral levosimendan) | ALS | I | II | | |
| ODM-104 (more effective COMT inhibitor) | Parkinson's disease | I | | | |
| ODM-203 (targeted FGFR+VEGFR inhibitor) | Solid tumours | I | | | |
| ODM-204 (CYP17 enzyme and androgen receptor inhibitor) | Prostate cancer | I | | | |
| ODM-106 (GABA-B receptor positive allosteric modulator) | Essential tremor | I | | | |
| ODM-108 (negative allosteric modulator of TRPA1 ion channel) | Neuropathic pain | I | | | |

= Phase completed

= Phase ongoing

More info at: http://www.orion.fi/en/rd/orion-rd/pipeline/

# Sales of key proprietary products

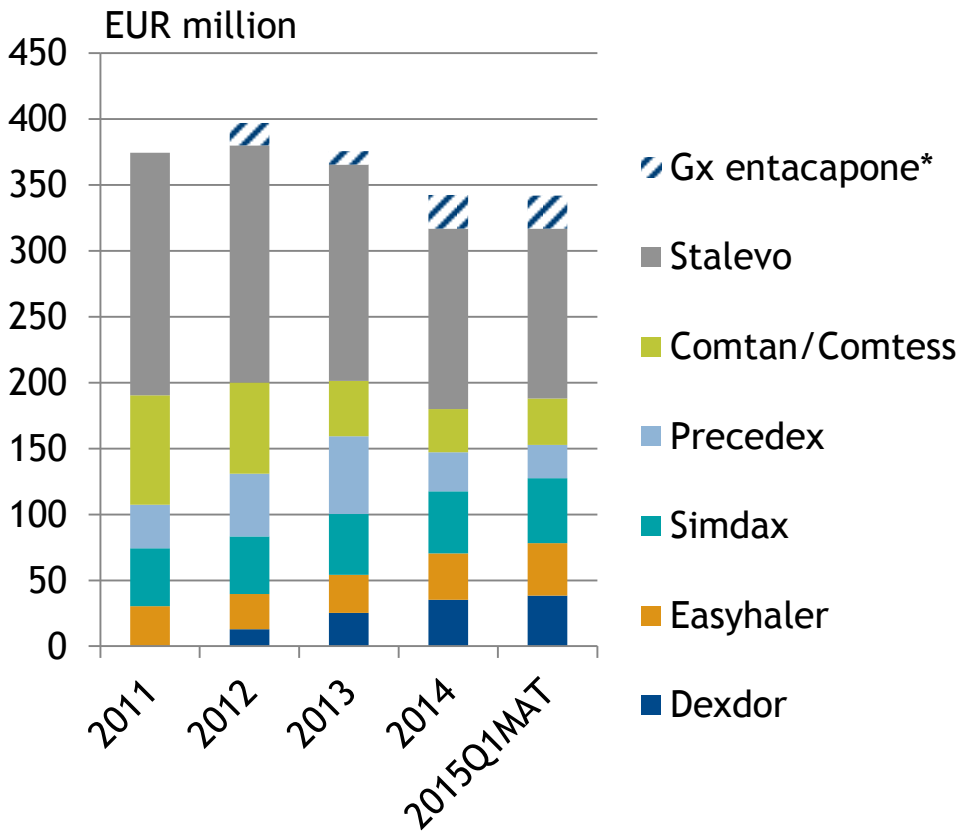
2011
Dexdor launched

2012
First generic Comtan in USA

2012
First generic Stalevo in USA

2012
Entacapone molecule patent expired in Europe

2013
Stalevo data exclusivity in EU expired




2014
First Bufomix MAs in Europe

2014
First generic Stalevo in Germany

2014
First generic Precedex in USA

2015
Stalevo launched in Japan

2015
Stalevo generic competition expected to extend in Europe

*) Gx entacapone is part of Orion's Specialty Products business



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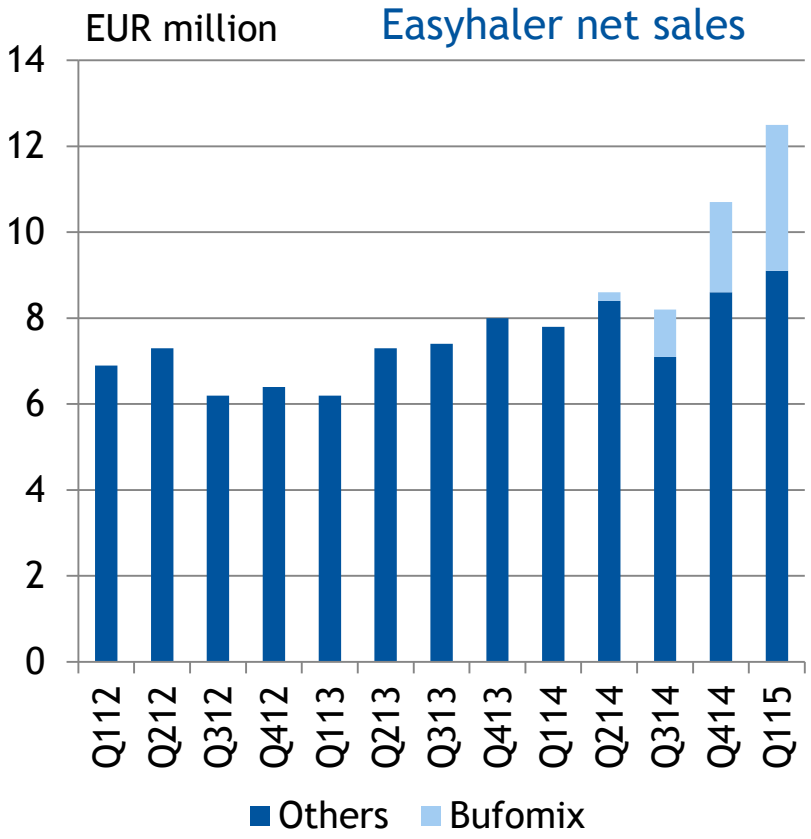
# Easyhaler update


## Bufomix

Available strengths:
160/4.5 µg/inhal
320/ µg/inhal

Sales started in more than 10 countries

MA in 23 countries (excluding Germany, France, UK, The Netherlands and Austria)




Easyhaler® salmeterol-fluticasone development project ongoing



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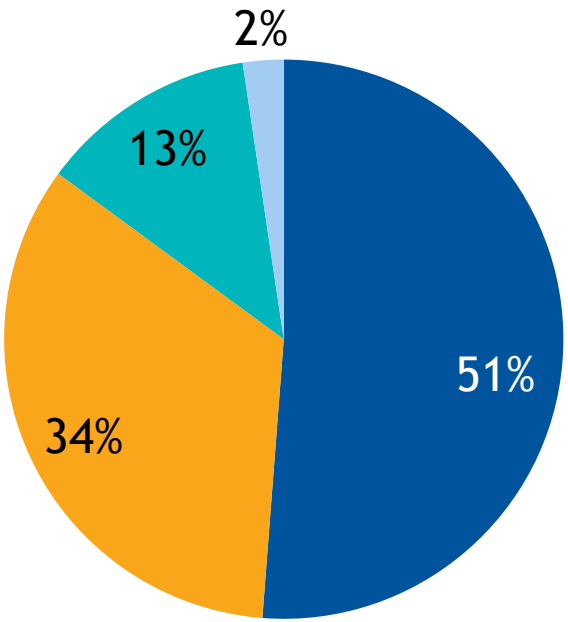
# Easyhaler combinations main target market

B2-STIMULANTS+CORTICOIDS CLASS (R3F)
SALES IN EUROPE 2014
Total market: EUR 3.4 billion (+0.7%)




- Salmeterol/fluticasone
- Budesonide/formoterol
- Beclometasone/formoterol
- Total Others (4)



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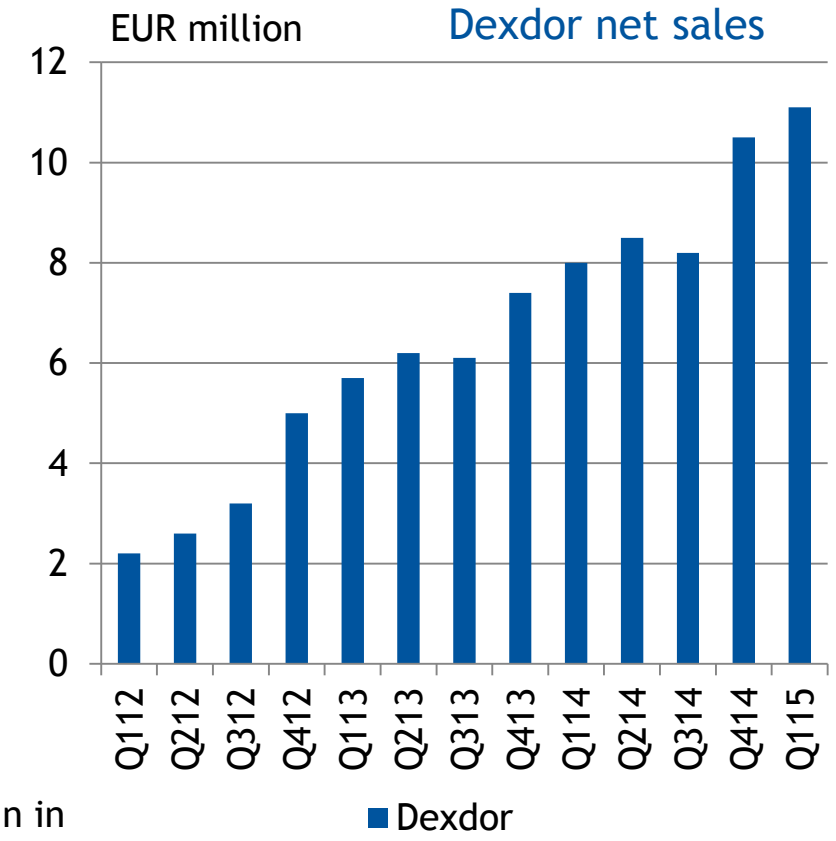
# Dexdor update

ICU patent until 2019

Data protection until 2021

Updated positioning to drug of choice to optimize PAD (pain, agitation & delirium) management

Added value justified by health economic publications and models




Dexmedetomidine non-i.v. under development for pain in USA by Recro Pharma(phase IIb). Top line results expected to be reported in summer 2015*.

*) Source: www.recropharma.com



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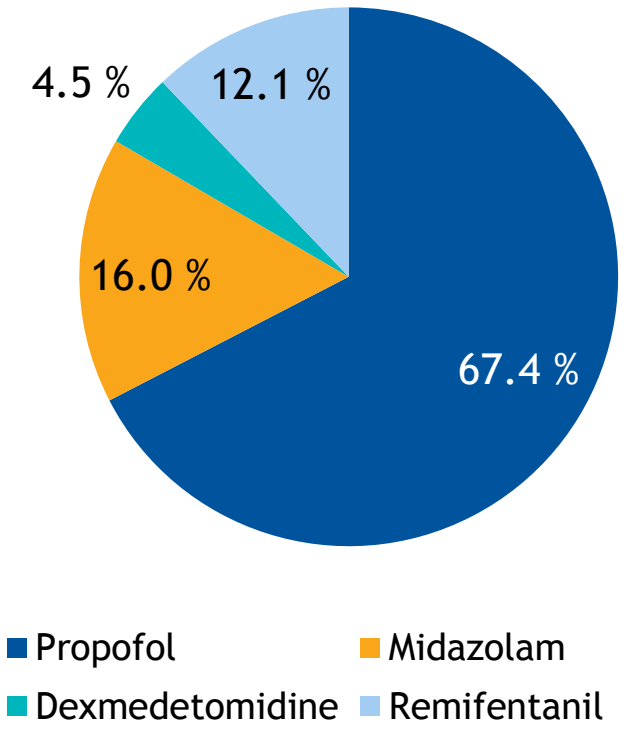
# Dexdor gaining market share

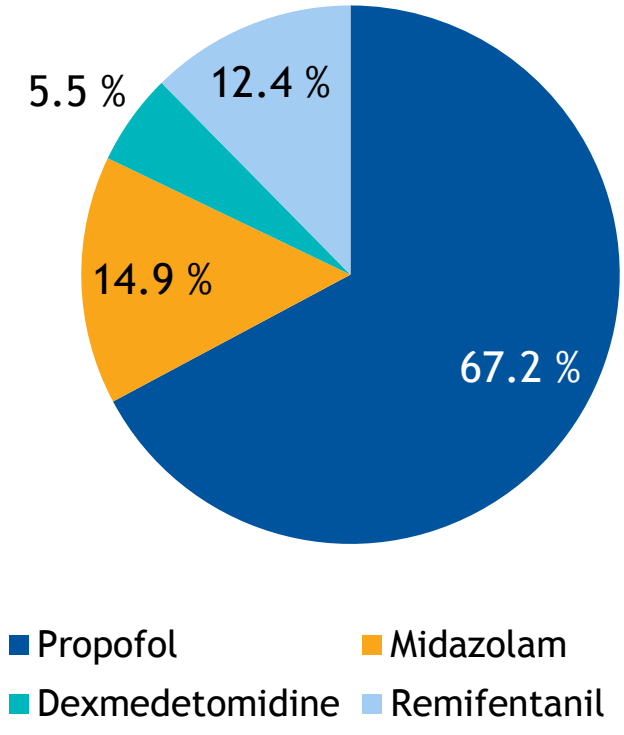
## European sedative market 2013

Total market value EUR 494 million




## European sedative market 2014

Total market value EUR 509 million




Source: IMS Health sales statistics 2013 and 2014



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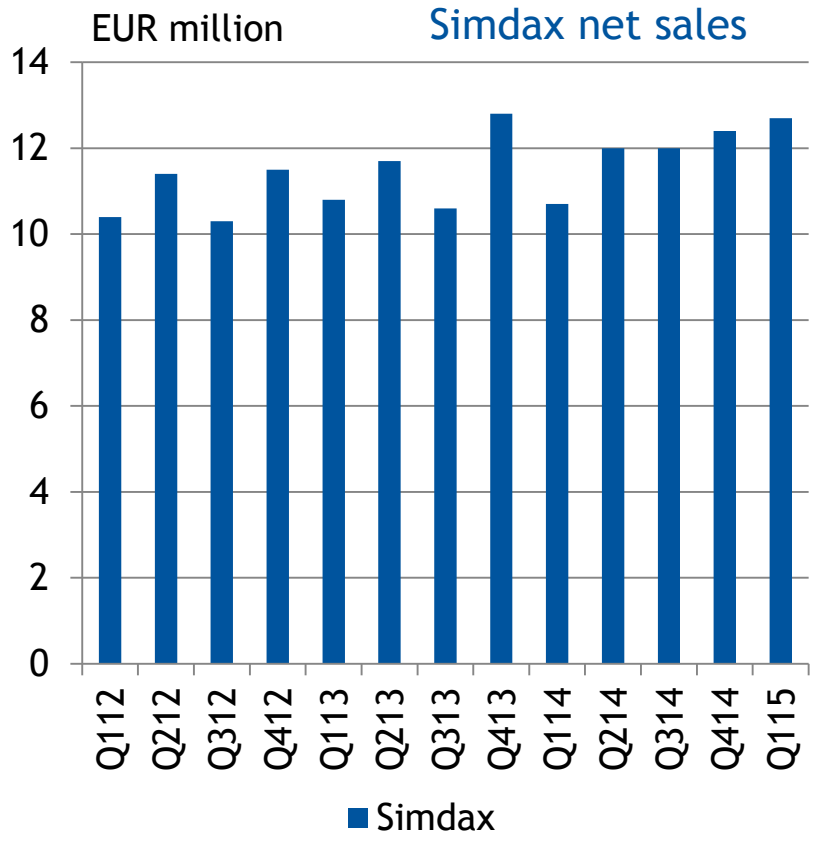
# Simdax update


Molecule patent expires Sep 2015

Formulation patent valid until Sep 2020

MA received in Germany and Switzerland Q4/2013




Study results available for Low Cardiac Output Syndrome (phase III in US by Tenax) in 1Q2016*. In addition Tenax is investigating possibility of gaining an additional indication of septic shock for levosimendan. *) Source: www.tenaxthera.com



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# Orion Specialty Products with strong foothold in Nordics

Liisa Hurme
SVP, Specialty Products
Chairman of the Board, Fermion

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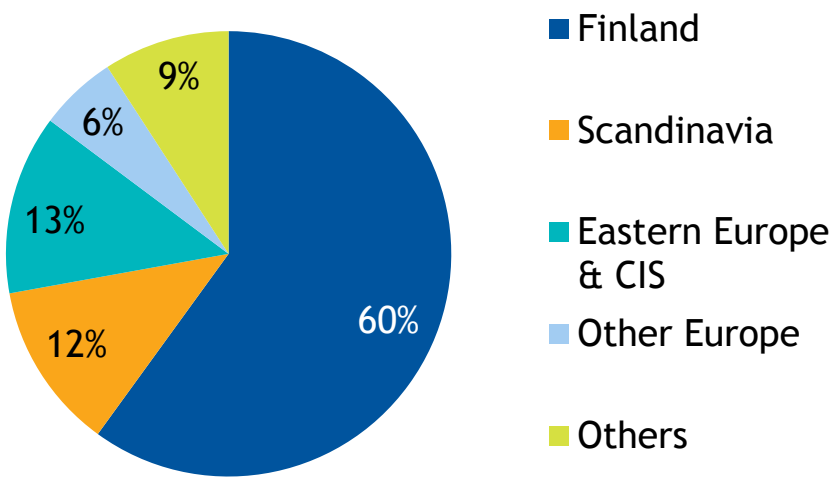
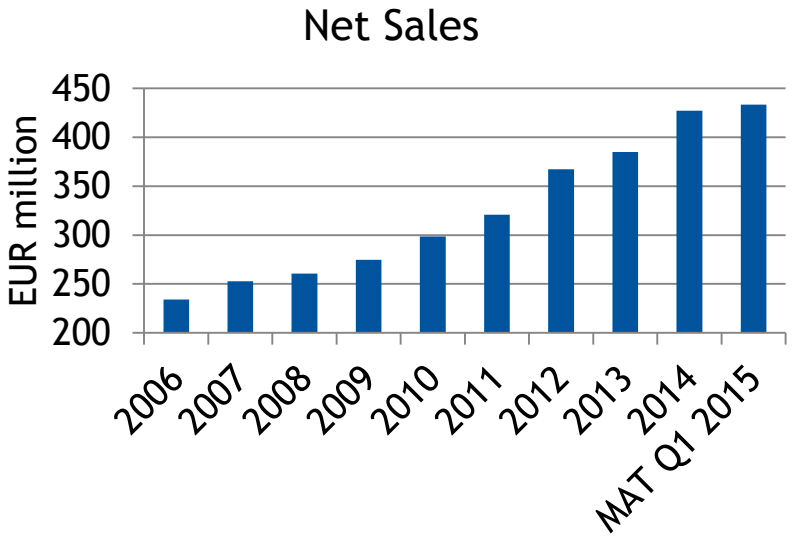
# SpP division has generated steady sales growth

Breakdown of SpP (Gx & OTC)net sales by geographic area MAT Q1 2015




Development of SpP net sales (Gx & OTC) from 2006 to MAT Q1 2015




## Key figures from 2014

2,418 MAs

3,310 SKUs

Net sales EUR 427 million



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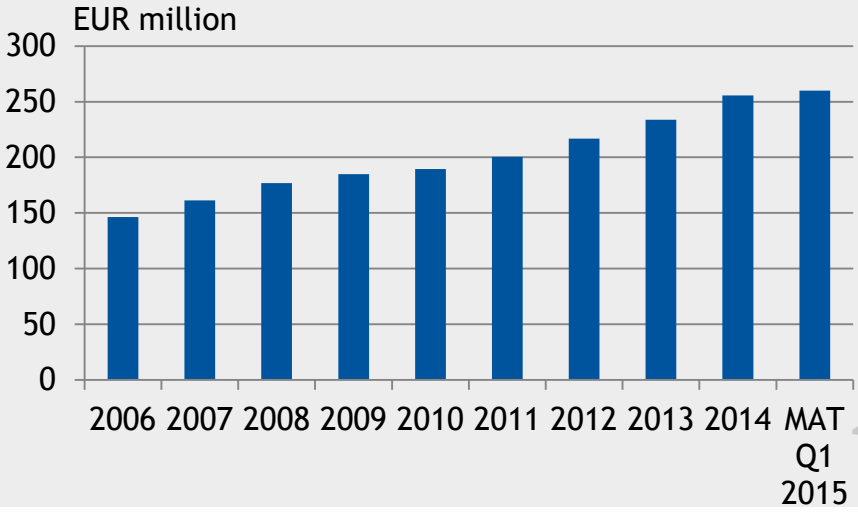
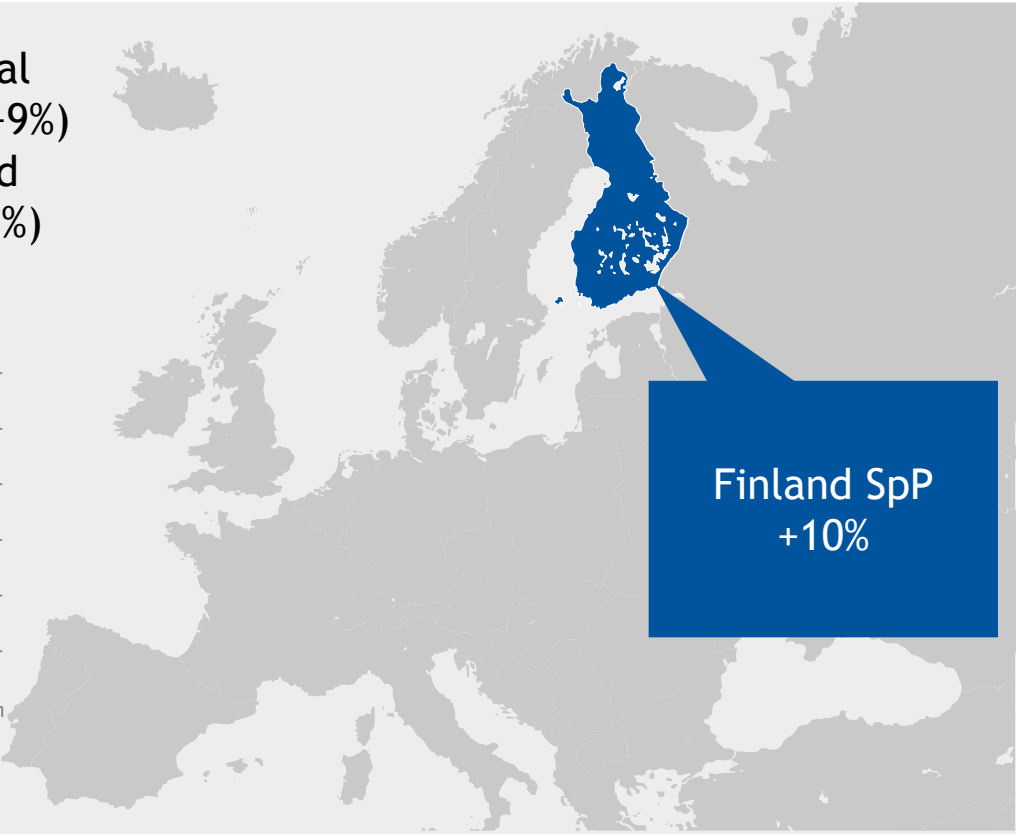
# Strong SpP growth in Finland with Gx and OTC

In MAT Q1 2015, Orion human pharmaceutical total sales in Finland was EUR 281 million (+9%) of which SpP was EUR 260 million (+10%) and out of that Self Care was EUR 87 million (+2%)



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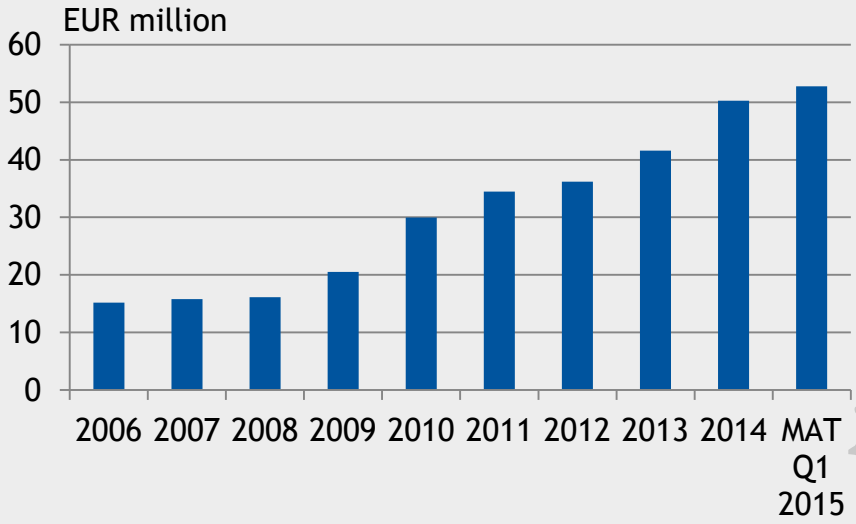
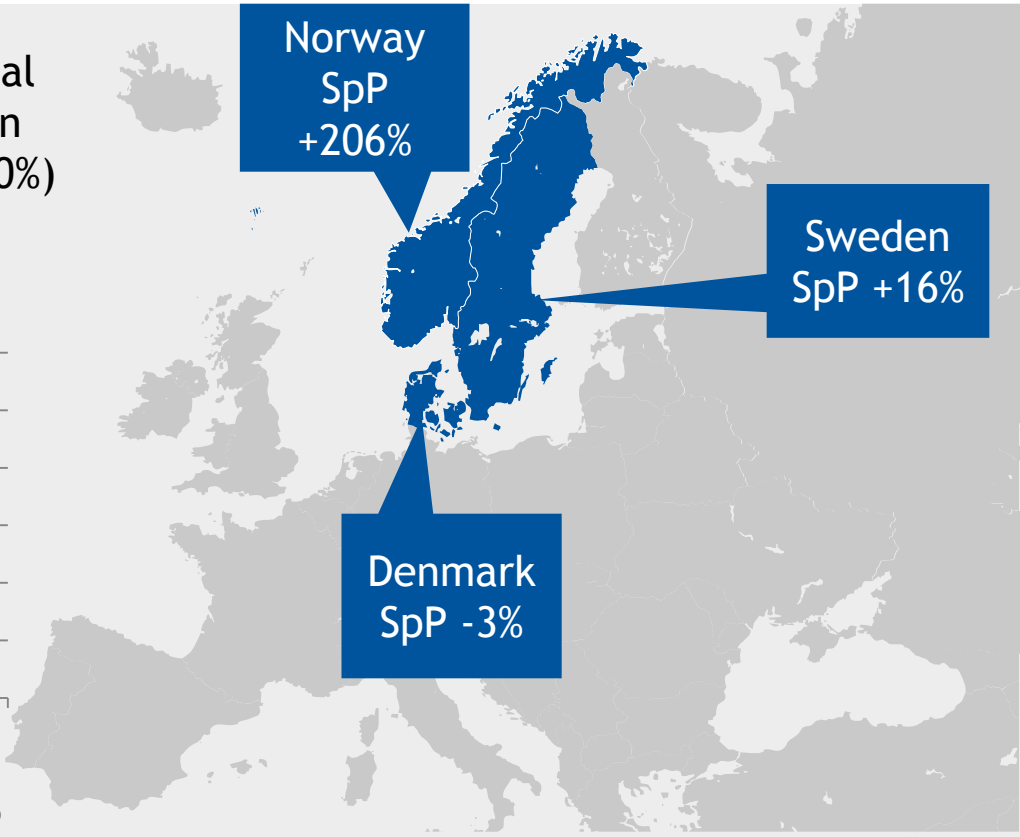
# Strong growth in  Scandinavia driven by Gx

In MAT Q1 2015, Orion human pharmaceutical total sales in Scandinavia was EUR 82 million (+14%) of which SpP was EUR 53 million (+20%) and mainly Gx driven



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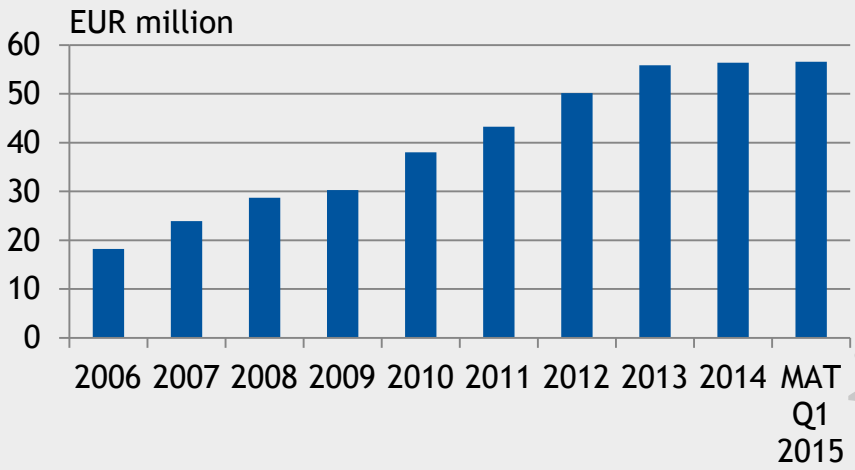
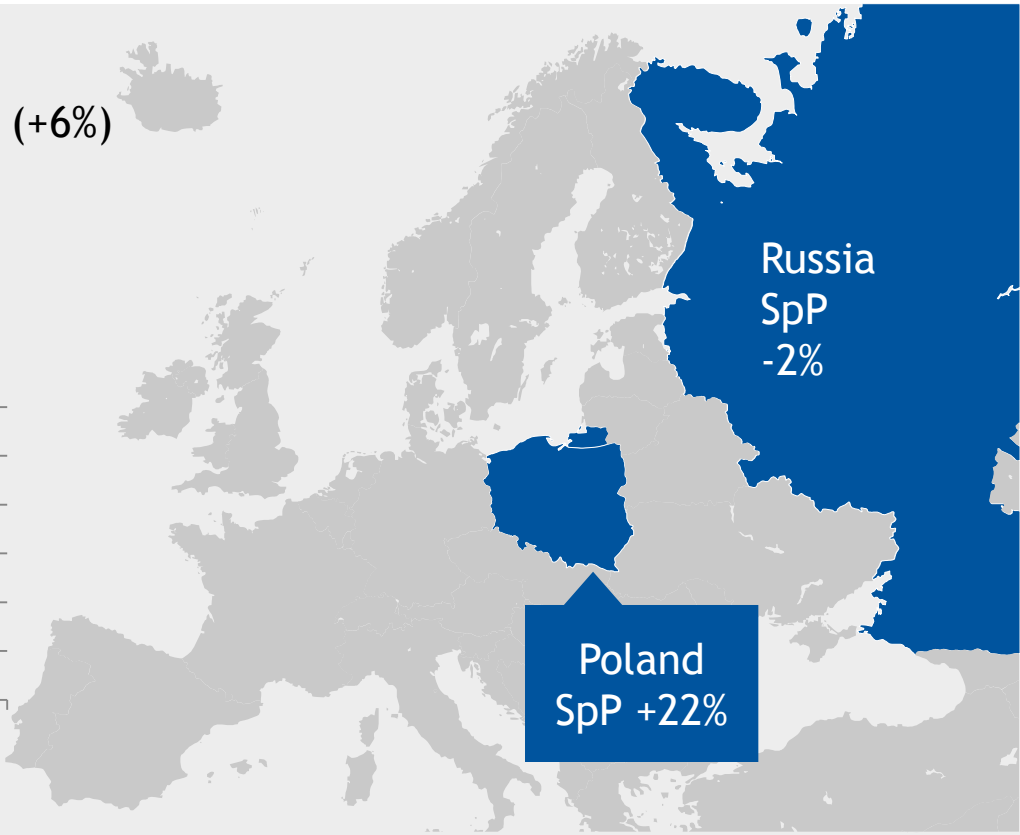
# Steady growth also throughout Eastern Europe

Orion human pharmaceutical total sales in Eastern Europe EUR 79 million MAT Q1 2015 (+6%) of which sales in top 2 SpP countries were:
Russia EUR 19 million
Poland EUR 19 million



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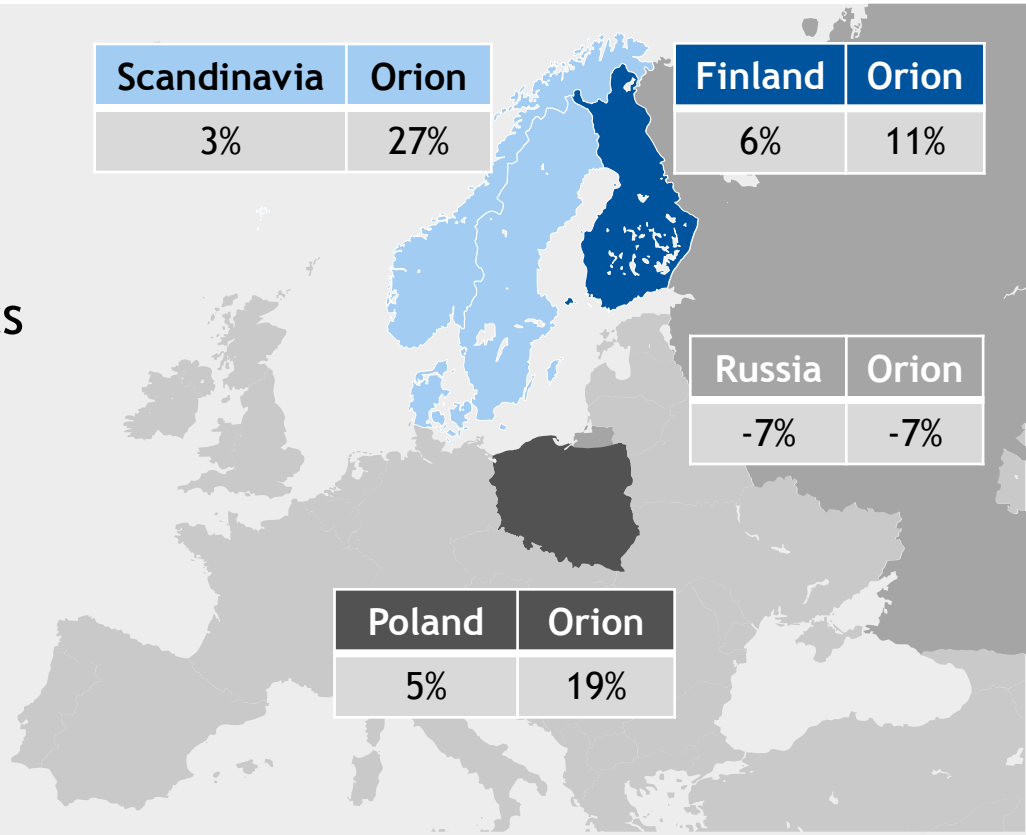
# Orion Gx business has outperformed market growth

- Nordic region is Orion's home base for generic products
- Orion has been able to grow faster than the market in Nordics
- Two digit growth in Poland exceeding the market
- In Russia we are at par with the market




Source: IMS Health, sales growth (2014 vs. 2013) in EUR, except Russia in USD, Gx total growth Russia from BMI in USD



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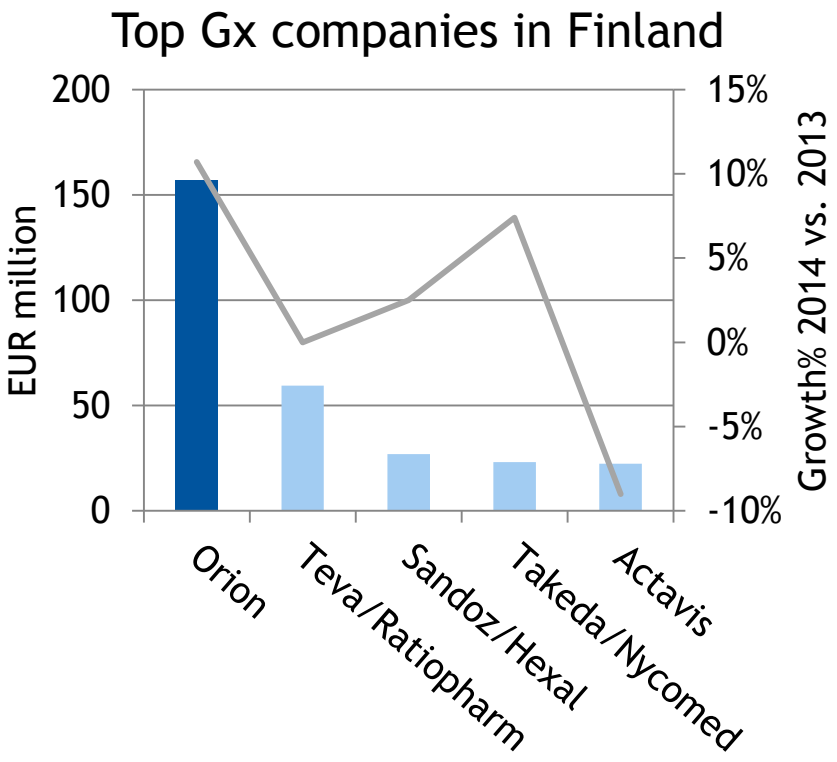
# Orion's position at Gx markets is well established




In Finland, Orion continues to be the leading generics player with 37% market share

Source: IMS Health, 2014

In Sweden Orion is one of the fastest growing Gx companies

| Ranking | Company | Gx Growth% |
|---|---|---|
| **Sweden** | | 10% |
| #1 | Sandoz | 39% |
| #8 | Orion | 33% |
| **Denmark** | | 6% |
| #1 | Sandoz | 5% |
| #7 | Orion | -5% |
| **Norway** | | 3% |
| #1 | Weifa | 6% |
| #7 | Orion | 262% |
| **Poland** | | 5% |
| #1 | Polfarma | 6% |
| #27 | Orion | 19% |

In Norway and Poland Orion clearly outperformed the leading Gx companies in 2014



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# Some key characteristics of Nordic Gx markets

| | Substitution system | Primary care pricing cycle and process | Distribution channel | Hospital market |
|---|---|---|---|---|
|  | YES | Reference priced Gx products with quarterly pricing and re-imbursement cycle | Single channel | 20 health care regions & 5-6 regional tenders |
|  | YES | Monthly pricing | Single channel | 21 health care regions & 9-11 regional tenders |
|  | YES | Bi-weekly pricing | Multichannel | National hospital tender |
|  | YES | Agreed maximum price levels | Multichannel | National hospital tender |



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# Key success factors of Scandinavian Gx business

- Broad customer base
- Several unique Rx products
- Entry into biosimilars
- Large portfolio
- Global network of quality suppliers
- Solid commercialisation and customer processes
- Throughput efficiency

Through the broad portfolio Orion has developed multichannel sales processes to meet the needs of our key customer groups in a very effective way (high throughput ratio)



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# Key success factors of Finnish Gx business

- Commercialisation and customer processes
- Strong OTC market share
- Fast growth of OTC non-medicinal portfolio
- Orion active with all customer groups
- Wide portfolio of hospital products
- Several Rx/OTC switches lately
- Large portfolio (~300 brands)
- Several unique Rx products



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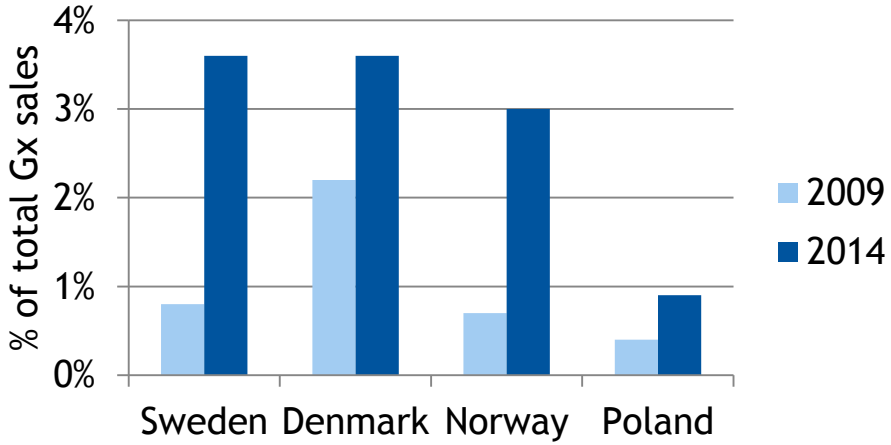
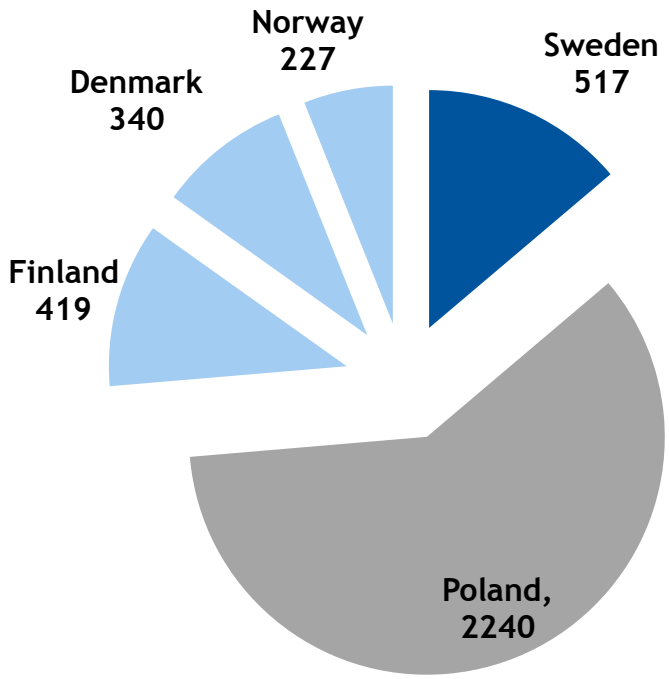
# Positive outlook for continued growth in all markets

Market share development of Orion Gx




Source: IMS Health 2009 vs. 2014

Gx market size in 2014 (mEUR)




Source: IMS Health 2014

Gx market growth estimates

| Gx Market | Growth 2014-2019 |
|---|---|
| Finland | +2.8% |
| Sweden | +3.2% |
| Poland | +4.5% |
| Russia | +10.9% |

Source: BMI, 2015, in local currency



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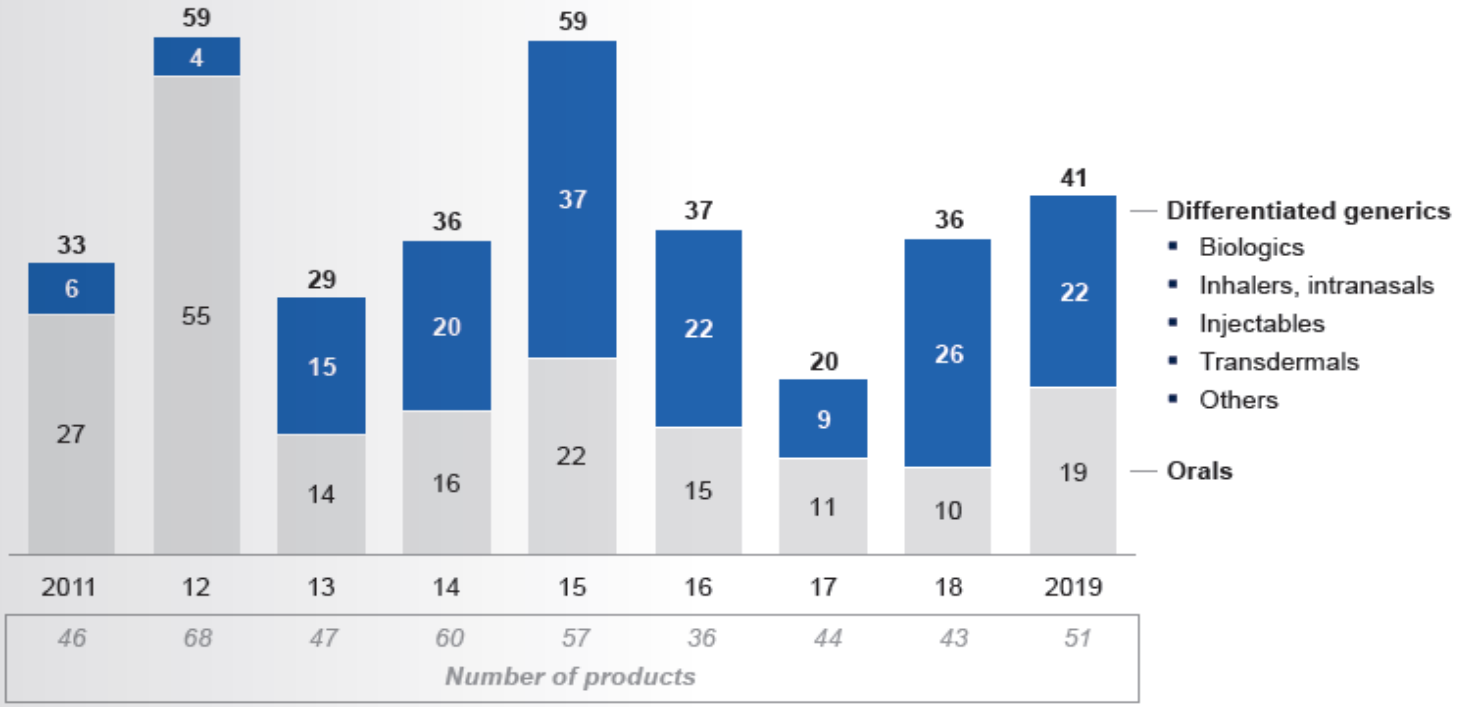
# Looking into the future of Gx business

## Upcoming LOE opportunities will be dominated by differentiated generics products

**Estimated worldwide sales of all products losing US patent protection in the year before patent expiry**
USD billions




SOURCE: Evaluate, 2013



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# Strategic actions for Specialty Products


OTC: Keep the market share and grasp the non-medicinal market trend with new products


Gx Pharmacy: Ensure constant flow and renewal of the porfolio with competitive COGS


Gx Hospital: Keep and grow



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# CFO's presentation

CFO
Jari Karlson

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# Orion’s financial objectives

**Increasing net sales.**
Achievement of this objective requires continuous investment in development of the product portfolio.

**Maintaining profitability at a good level.**
The aim is operating profit that exceeds 20% of net sales.

**Keeping the equity ratio at least 50%.**

**Distributing an annual dividend that in the next few years will be at least EUR 1.20 per share, and increasing the dividend in the long term.**

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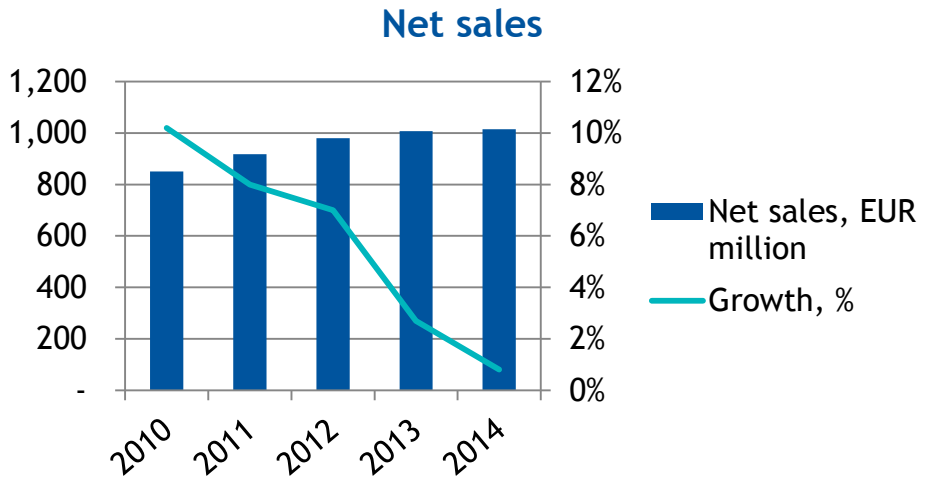
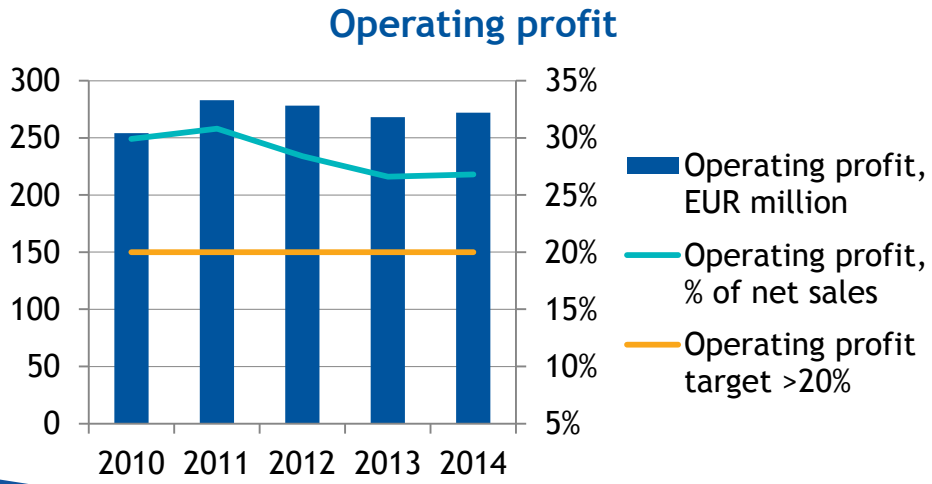
# Orion's financial objectives and outlook 2015




| | |
|---|---|
| **Net sales** | Net sales will be slightly lower than in 2014 (net sales were EUR 1,015 million in 2014). |




| | |
|---|---|
| **Operating profit** | Operating profit is estimated to exceed EUR 230 million. |



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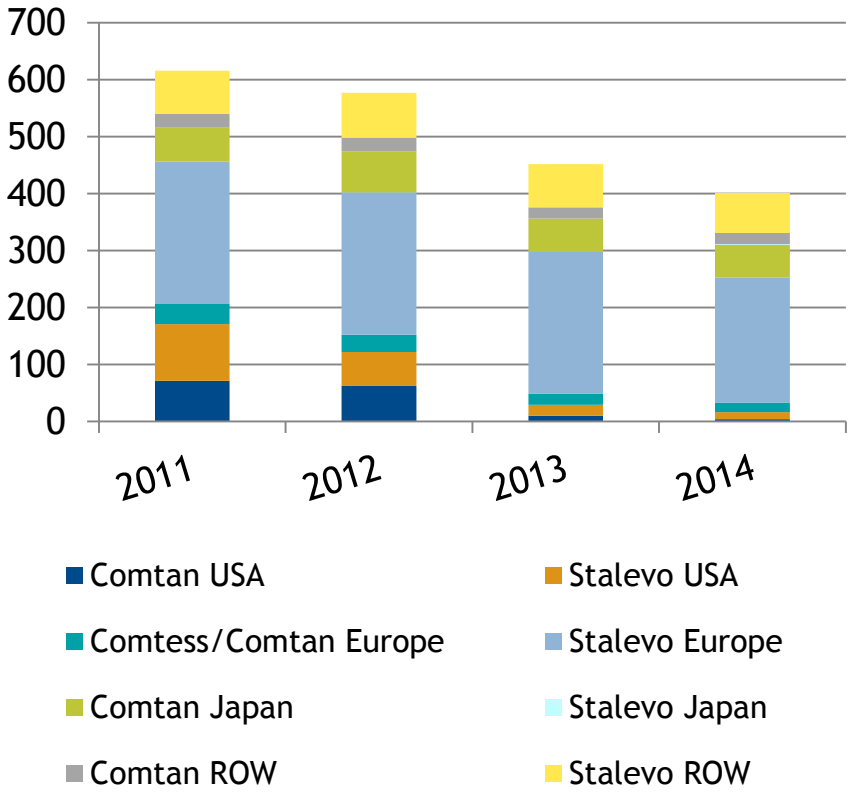
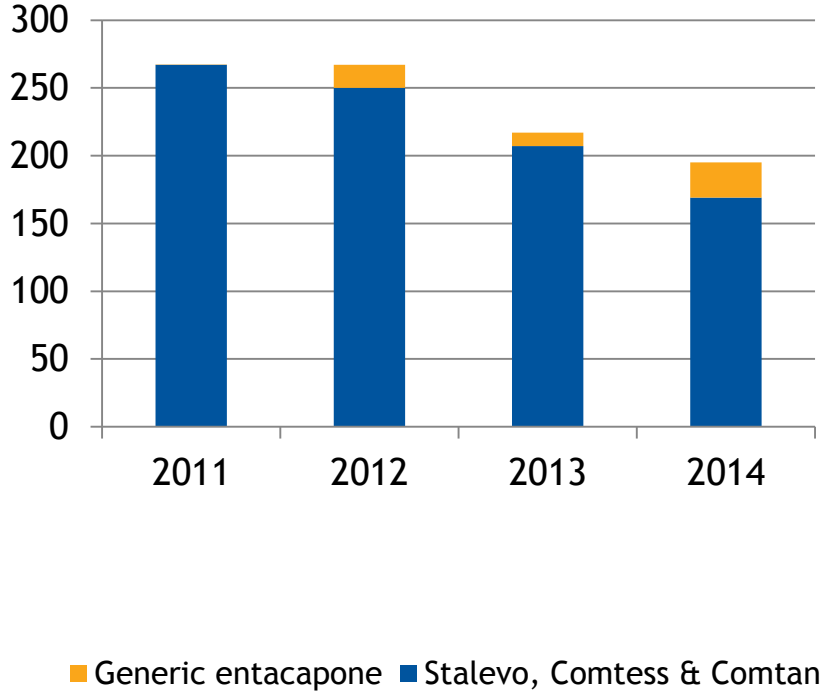
# Turning points of Parkinson's franchise

## Annual in-market sales, EUR million*




## Orion sales, EUR million




| | USA | EUROPE | JAPAN |
|---|---|---|---|
| STALEVO | First generics in April 2012 | First generics in Q2/2014 | |
| COMTESS/COMTAN | First generics in October 2012 | First generics in Q4/2012 | Data protection ended in January 2015 |

*) Source: IMS Health

# Balancing mid-term – building long-term

Long-term growth opportunities from R&D pipeline. Milestone payments.

Generic competition for Parkinson's franchise and Precedex.

Timing of milestone payments.

Generic drugs and self-care products.

Easyhaler® combinations and *dexdor*® for European markets.

Global pricing pressure, especially on new products.

Operational flexibility and efficiency.



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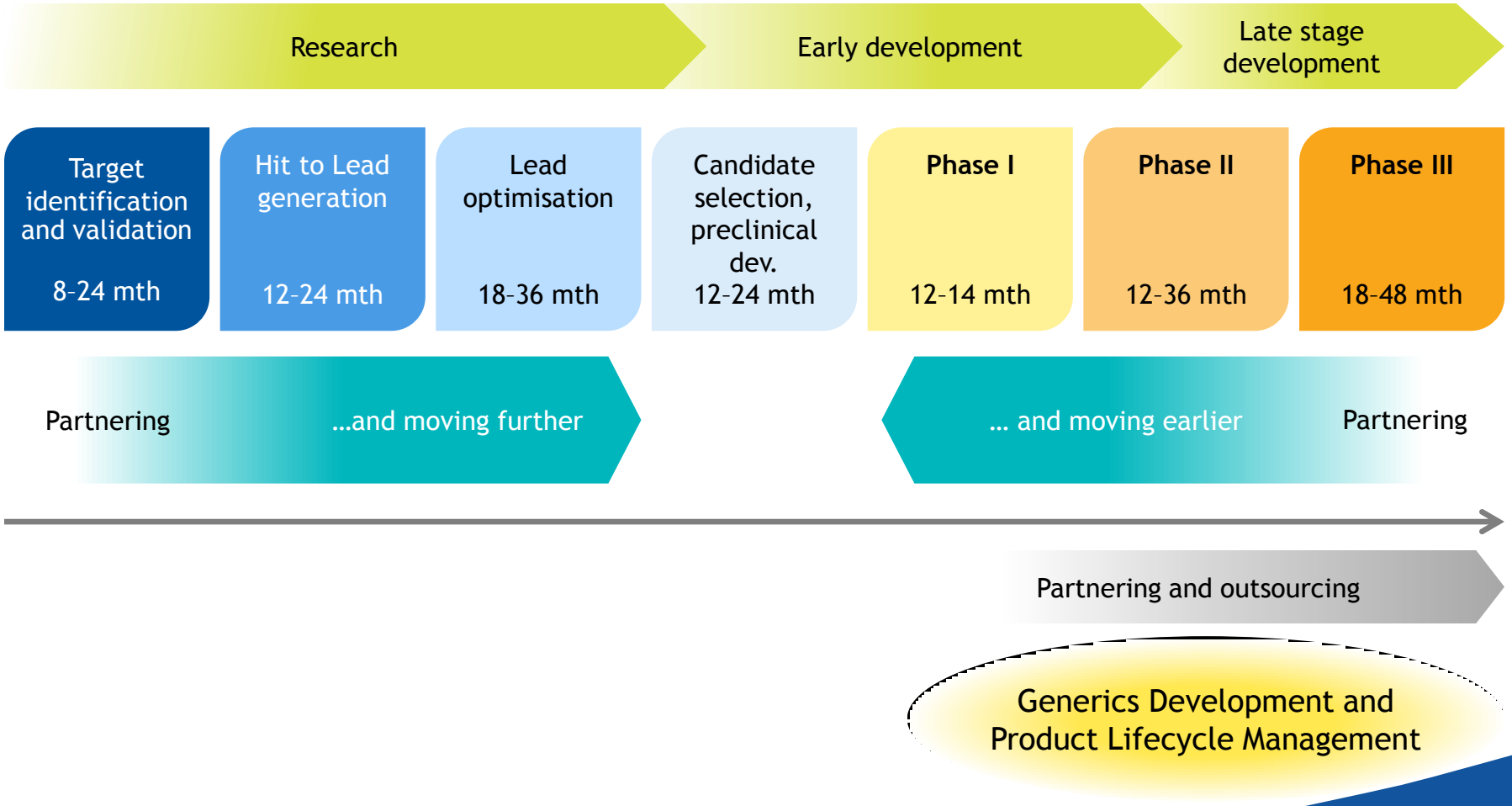
# Collaborative networks across the R&D value chain



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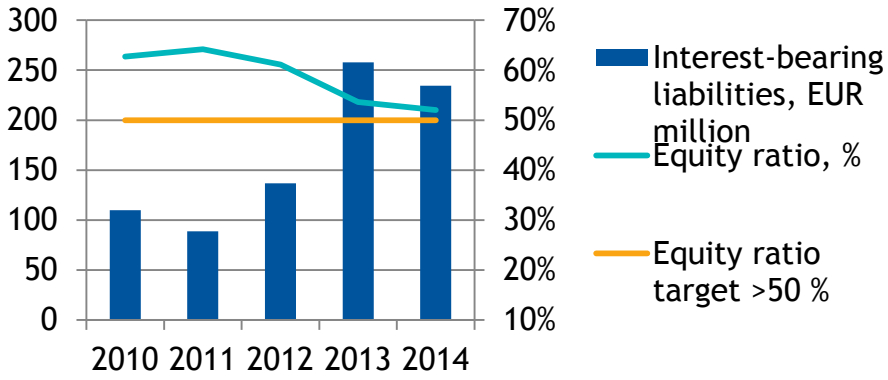
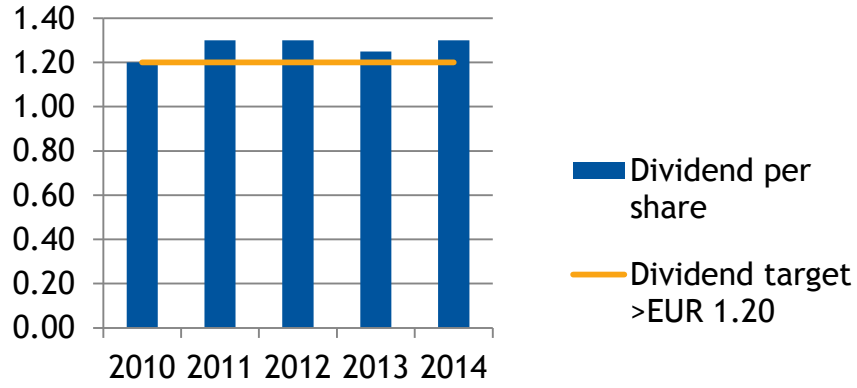
# Orion’s financial objectives and outlook 2015

**Equity ratio and interest-bearing liabilities**




**Dividend**




| | |
|---|---|
| **Group’s capital expenditure** | The Group’s capital expenditure will be about EUR 50 million excluding substantial corporate or product acquisitions (The Group’s capital expenditure was EUR 57 million in 2014). |



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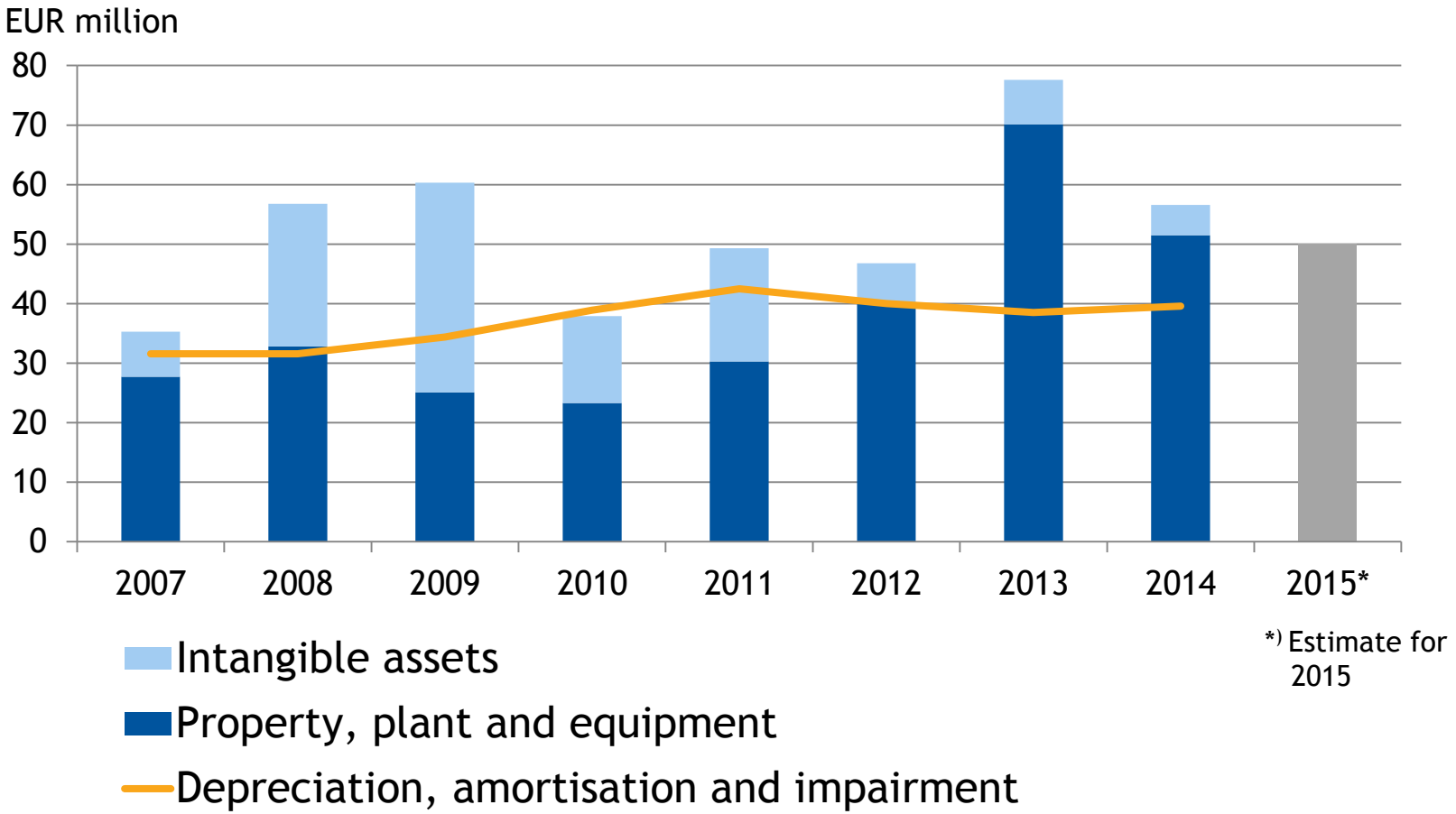
# Capex normalising after investment program




*) Estimate for 2015



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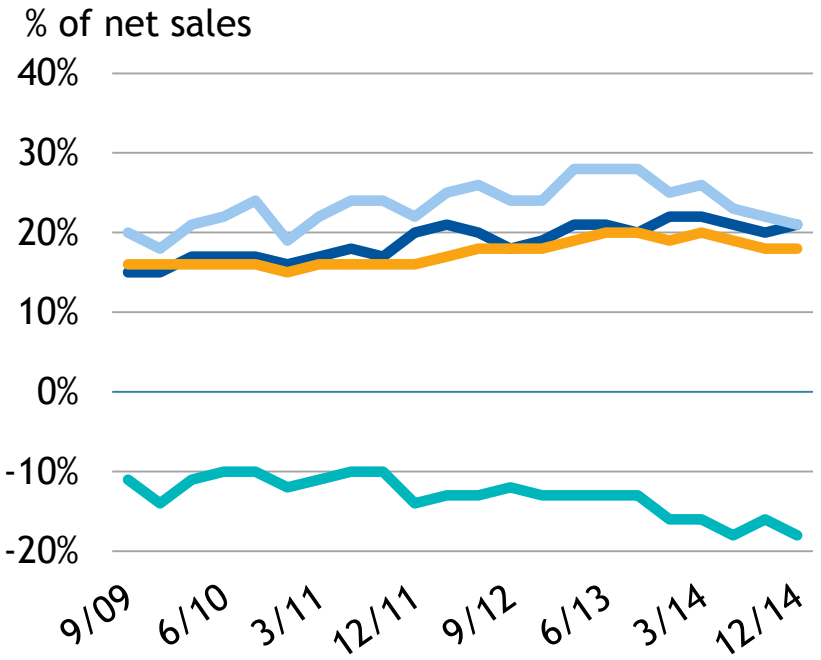
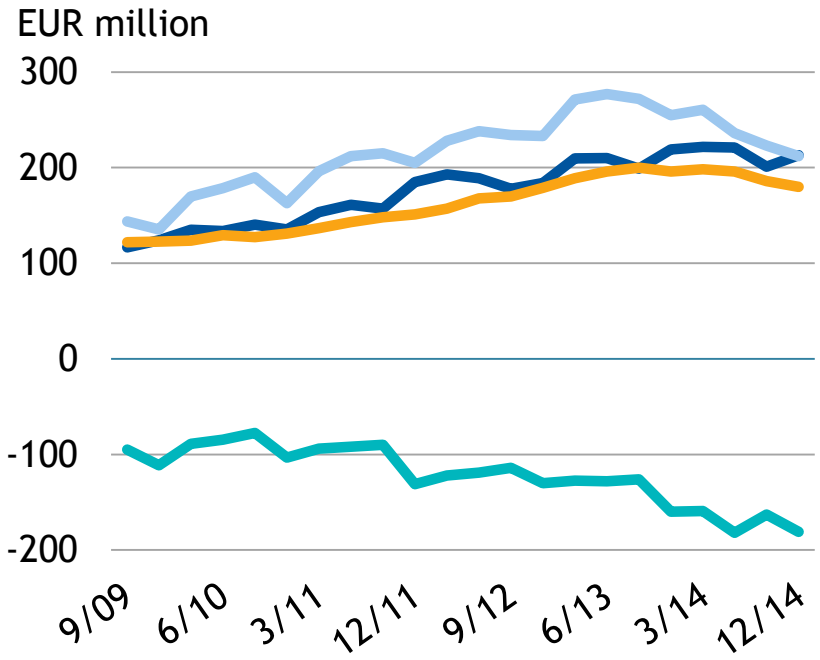
# Development of Net working capital



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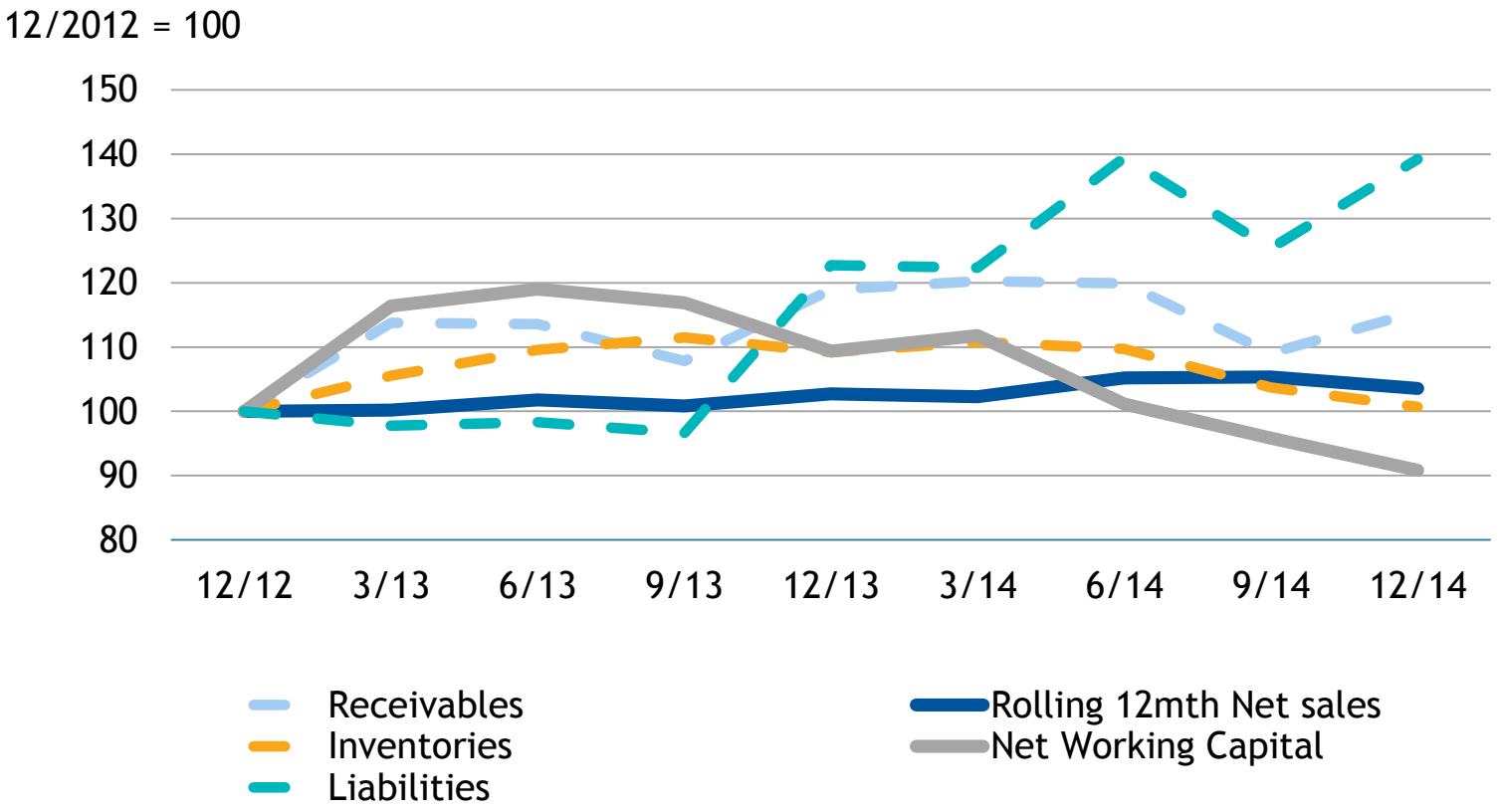
# Development of Net working capital
## (Indexed 12/2012=100)



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# Equity structure and Profit distribution

| 31 Dec 2014 (EUR million) | Orion Corporation | Orion Group |
|---|---|---|
| Share capital | 92.2 | 92.2 |
| Reserves | 1.4 | -44.4 |
| Retained earnings | | |
| Orion Corporation | 254.6 | 254.6 |
| Subsidiaries | | 75.7 |
| Consolidation and IFRS adjustments | | 142.2 |
| Translation adjustments | | -5.4 |
| Non-controlling interests | | 0.0 |
| **Total equity** | **348.2** | **514.9** |

Of these 183 million was distributed in March 2015 → left EUR 0,51/share

IFRS and consolidation items not available for profit distribution



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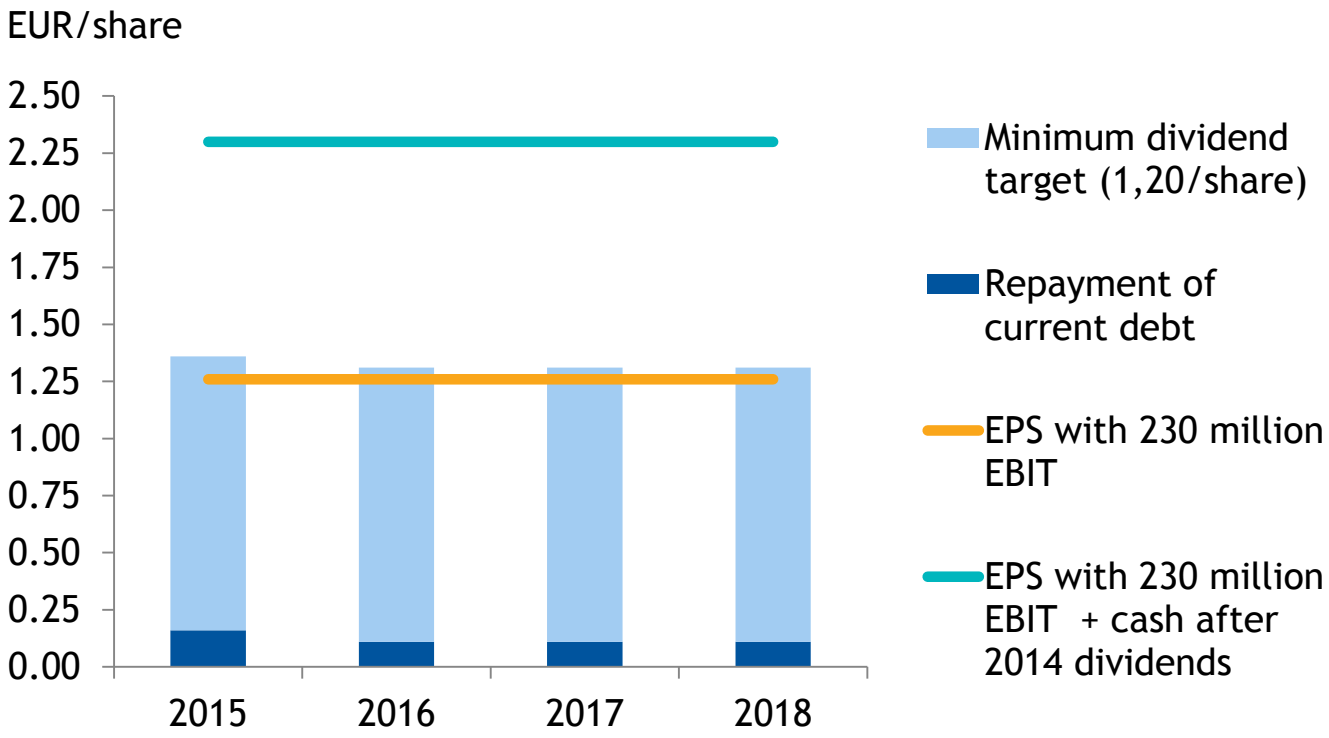
# Funding of dividends




EPS to be quite close to free cash flow assuming

- Capital expenditure is quite close to depreciation
- Net working capital management is successful



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# Break


PROFIT
DEVELOPMENT
SALES
OPERATING
NET
PRODUCT
ORION
GENERIC
EASYHALER
CLINICAL
MARKETING
BUFOMIX
PHASE
PRECEDEX
SIMILAR
COLLABORATION
INTENSIVE
DRUGS
BAYER
GROWTH
ORM
PARTNERS
SIMDAX
INHIBITOR
CANCER
DEXDOR
ROYALTIES
NOVARTIS
MILLION
HIGHER
CONTINUED
PROGRESSED
CARE
INCREASE
DECLINING
REVIEW
ADDITION
MILESTONE
LEVEL
FAMILY
SIGNIFICANT
GOOD
PERIOD
GREW
COMPOUND
RECEPTOR
PLEASED
EXPECTED
MAINTAINED
CURRENT
REMAINS
NETWORK
GERMANY
NATIONAL
RECORDED
LEVOSIMENDAN
ENTACAPONE
DELIVERIES
QUARTER
INVESTMENT
PARTICULAR
CASTRATION
CERTAIN
DISEASE
CLEARLY
ANDROGEN
PUBLISHED
FINANCIAL
PLANNED
STEADILY
OUTLOOK
PROPRIETARY
ESPECIALLY
STRONGLY
BEGINNING
STRONG
SYMPTOMS
FOLLOWING
ANTICIPATED
SAFETY
COMPENSATE
PORTFOLIO
POSITIVE
UPDATED
GRANTED
FUTURE
REGARDS
ANNOUNCED
EXTENSION
REORGANISATION
MODULATOR
HOSPIRA
PROSTATE
ANTAGONIST
CHANGES
MOLECULE
RESPONSIBLE
ORGANISATION
OBJECTIVES
INVESTIGATIONAL
RELATED
ALLOSTERIC
ADRENOCEPTOR
DEXMEDETOMIDINE.COM

# Orion Animal Health

Niclas Lindstedt
Vice President

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# Orion Pharma Animal Health

- 2014 sales EUR 71.5 million
- Part of the top 30 Animal Health Companies Globally*
- Animal Health division of Orion consists of 68 people, in 8 countries
  - 40 people in sales in Nordics
  - 20 people in sales in CEE
  - 8 people HQ function

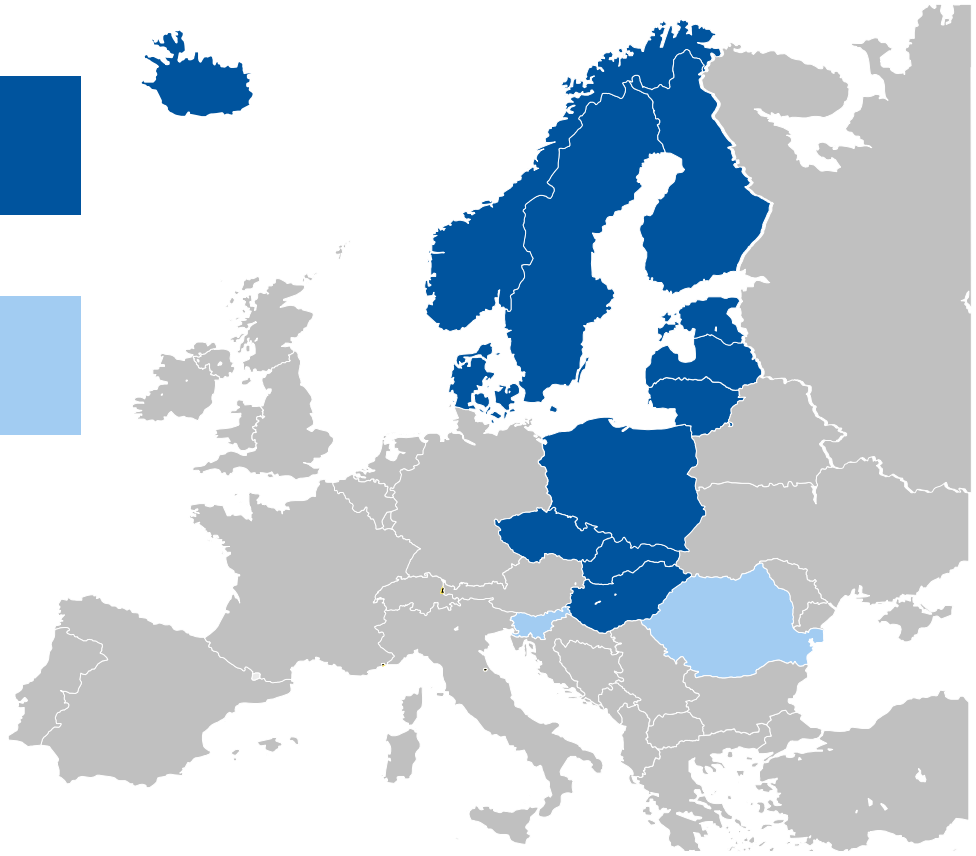
- Sales by species: 60% companion animal, 40 % livestock
- Majority part of sales is in-licensed products (65%)
- R&D, logistics - supply chain , finance, HR and all other support functions common with Orion Corporation

*Animal Pharm Top 30: 2013 Edition

# Orion Pharma Animal Health European presence

Orion Pharma Animal Health Captive Market

Romania and Slovenia: through a distributor



Our product portfolio consists of both medicinal and non-medicinal products for animals.



ORION Building well-being

# Partners

Bayer HealthCare Animal Health

ZENOAQ is a leading company for developing, manufacturing, importing, and selling veterinary pharmaceutical products in Japan.

Vétoquinol a Sign of Passion

zoetis

Ceva

DOPHARMA HOLDING

Provet Vet.-med. Center Ein Unternehmen der HENRY SCHEIN® Gruppe

Norbrook®

Virbac ANIMAL HEALTH

Boehringer Ingelheim

ecuphar® Animal Healthcare

nimrod

Elanco

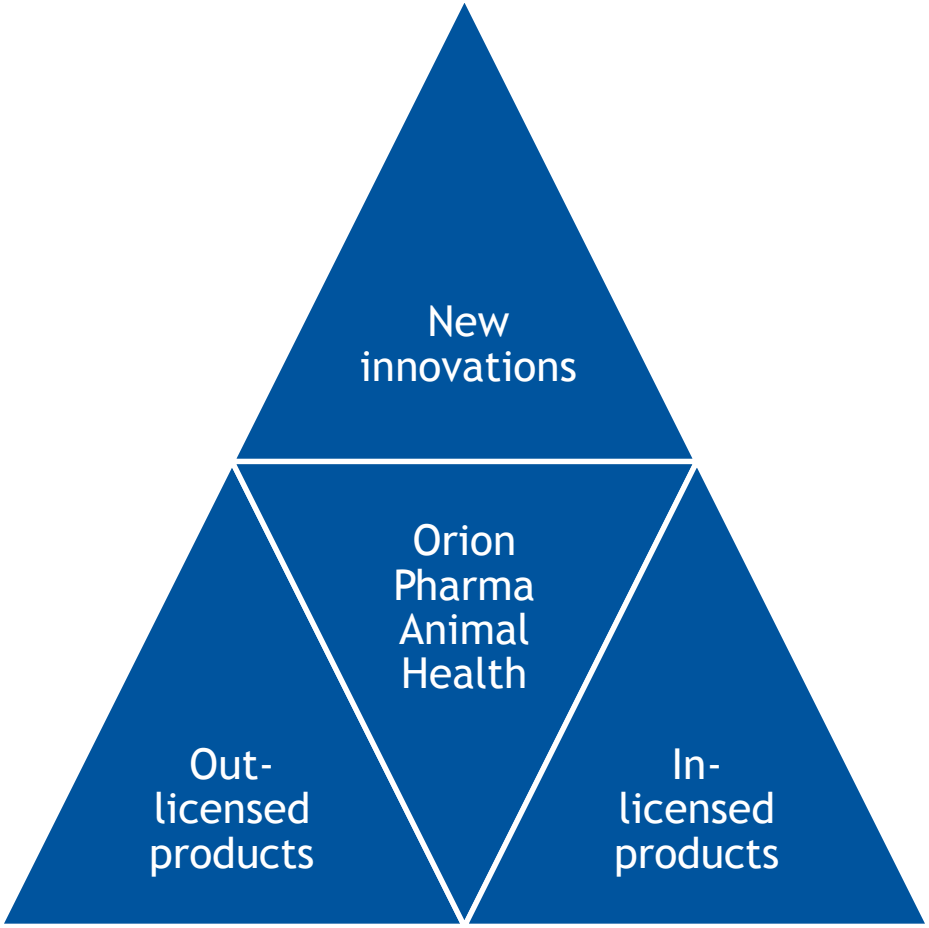
ilender Pharmaceutical Corporation

chanelle VETERINARY



ORION Building well-being

# Orion Pharma Animal Health






Building well-being


Sileo®
alleviates acute fear and anxiety associated with noise

# Sileo®
# First approved medicine for noise anxiety in dogs

**SILEO INDICATION: Alleviation of acute anxiety and fear associated with noise in dogs**

- Positive opinion for marketing authorisation from the European Committee of Medicinal Products for Veterinary Use received 10th April 2015
- Dog owners are actively seeking solutions to this welfare problem. Common noise events are e.g. fireworks, thunderstorms, traffic noise, construction work, festivals etc.
  - Distressed reactions to noises are one of the most common behavioral concerns for pet dogs
- Currently no licensed veterinary medicines on the market for this indication
  - Non medicinal products exist

# ODM-105

## Orally active alpha-2 agonist

ORION
Building well-being

# ODM-105

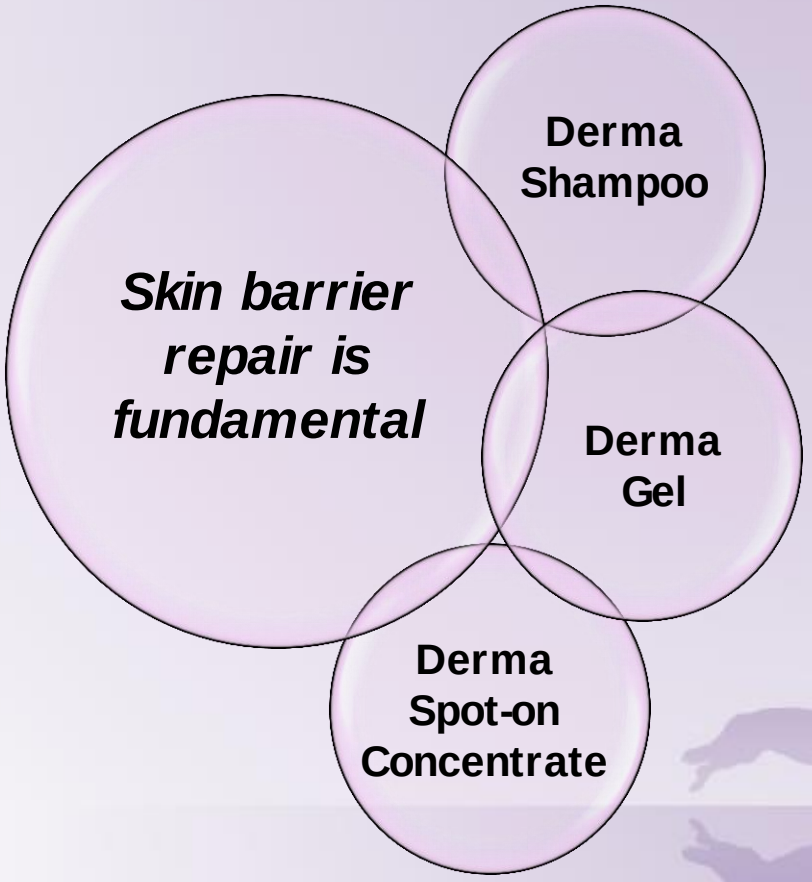
- First alpha-2 agonist that is active even when swallowed
- Target species: dog and cat
- Part of Orion´s own research and development pipeline
- Several potential indication areas in behavior, pain management and sedation / anesthesia

# Aptus®

## Non-medicinal portfolio

- Joints & mobility
- Digestion
- Skin & Fur
- Eye & Ear
- Wound Healing
- Mouth Hygiene
- Energy & Nutritional Supplements

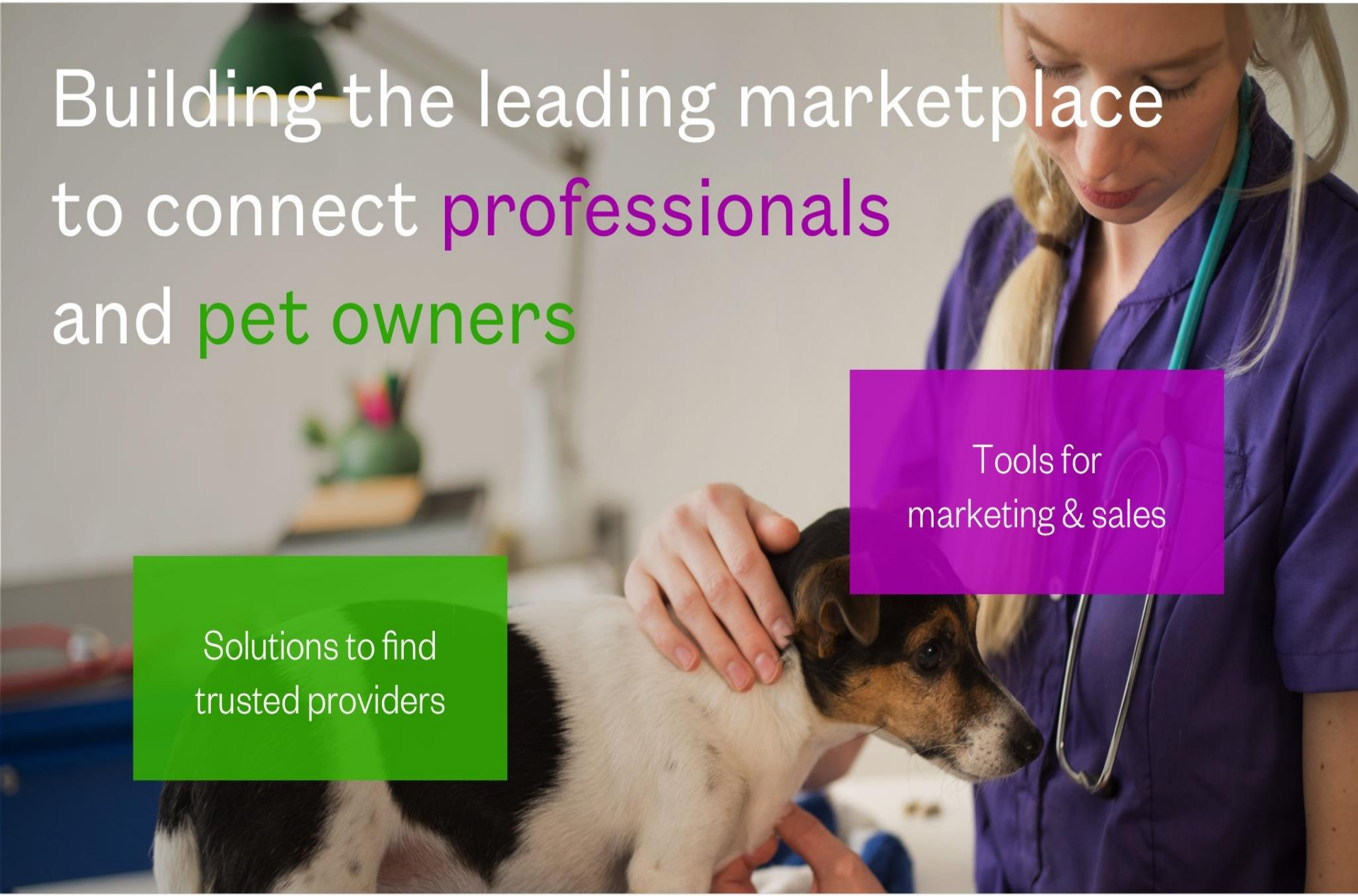
# Orion development in Aptus® Derma line




Created by a leading Swedish dermatologist,
an innovative, high-quality therapy approach
targeting the root cause of sensitive skin;
strengthening the skin barrier,
effective combination of antimicrobial components
and
restoring the humidity of the skin

ORION PHARMA

Morrr®



ORION

Building well-being


# Fermion

Arto Toivonen
President

fermion

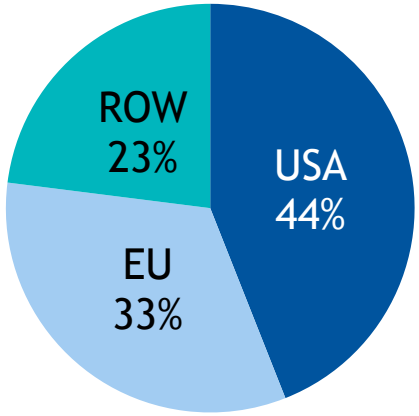
# Fermion in Brief

Fully owned subsidiary of Orion Corporation
Develops, manufactures and sells active pharmaceutical ingredients (APIs)
Business segments:

- NCEs for Orion's existing and new proprietary products
- Generics to Orion and other pharmaceutical companies worldwide
- Custom development and manufacturing for innovators with focus on high potency APIs

| Fermion in 2014 |
| --- |
| Net sales: EUR 57 million excluding supply to Orion |
| Main markets: USA, EU and Japan, ca. 100 customers |
| Ca. 35 products, both innovative and generic APIs |
| Head office, R&D, bench scale production, regulatory department in Espoo |
| Two manufacturing sites: Hanko and Oulu |
| Personnel: 326 |

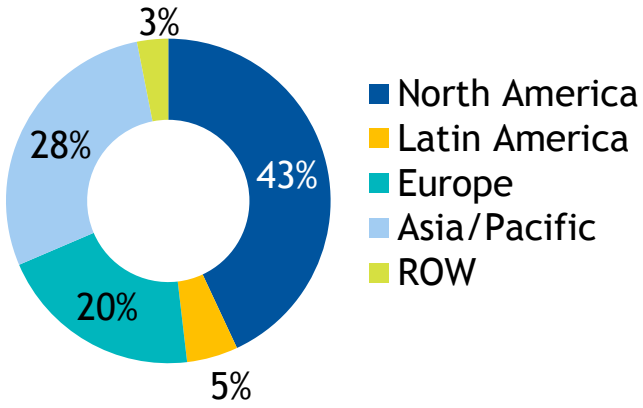
Sales split



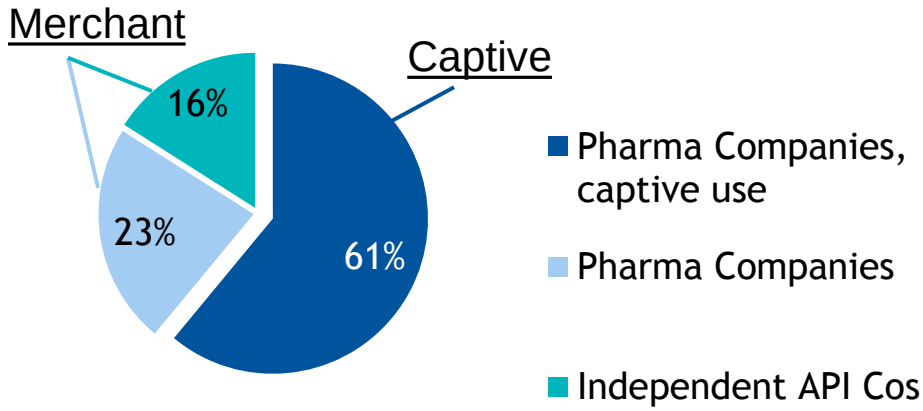
# Global API Market

- 113 B$ in 2012 of which ca. 61% is captive and 39% merchant
- Annual growth rates 2008-2012: 13.9% Asia-Pacific, 3.8% N-America, 2.5% W-Europe
- Growth rate high > 20% in oncology
- High potency APIs (HAPIs) is a fast growing segment
- Global market estimated to reach ca. 144 B$ in 2016 and 190 B$ in 2020

## API consumption




## Supply of APIs




- 62% of the generic API supply to merchant market comes from Asia-Pacific (esp. India and China)



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# Fermion Production - Chemistry in Pharmaceutical Environment

Strong regulatory authorities' (FDA, FIMEA, PMDA, MOH, KFDA, ANVISA) inspection track record

## HANKO

- Fully automated
- High volume products
- Reactor capacity 240 $m^3$


## OULU

- Fully automated
- Specialty products
- Both cytotoxics and non-cytotoxics HAPIs up to OEB class V
- Reactor capacity 76 $m^3$



ORION Building well-being

# Captive Business –Strategic fit with Orion Pharma creating valuable synergy

## Exclusive supply of APIs for Orion's proprietary products:

- Atipamezole HCl
- Detomidine HCl
- Dexmedetomidine HCl
- Entacapone
- Medetomidine HCl
- Levosimendan
- Toremifene citrate

Orion's strengthened clinical pipeline → Significant API process development, optimisation and industrialisation effort on-going with ODM-201, 203, 204, 104, 105, 106, 108, 109 and ORM-12741

# Strong Market Position with a Number of Generic APIs

## Antineoplastic

- Mercaptopurine*
- Methotrexate*
- Flutamide*
- Azathioprine*
- Irinotecan HCl

## Central Nervous System

- Buspirone HCl*
- Fluoxetine HCl
- Trazodone HCl
- Alprazolam
- Quetiapine Fumarate
- Carbidopa

## Cardiovascular

- Propafenone HCl
- Nadolol*
- Diltiazem HCl

## Others

- Glipizide
- Sodium Cromoglycate
- Tolnaftate
- Tamsulosin HCl
- Hydroxychloroquine
- Formoterol
- Salmeterol

*) Fermion TOP 1 or 2 in the world

# Custom Development and Manufacturing Services – Key differentiators

- Capability to manufacture high potency APIs from gram to multi-ton scale
- Regulatory-compliant, fully automated best-in-class facilities
- Strong experience and leading talents in crystallization, particle size engineering and impurity control
- Dedicated lifecycle management engineers to ensure continuous improvements in cost-efficiency and product quality
- High quality, occupational health, safety and sustainanility standards


ORION

fermion

# Orion Diagnostica

Jaakko Rissanen
President

ORION DIAGNOSTICA

# Orion Diagnostica

**Figures in a nutshell**

- In 2014 net sales 56.4 m€ (-1%)*
- Over 80% from international sales
- Operating profit 6.4 m€ (+38%)
- Main market areas: Europe (especially northern), China, USA, Japan
- Own Sales Units in Finland, Sweden, Norway, Denmark, Czech Republic, Slovak Republic, Poland, Hungary and Germany
- Distributor network covering over 60 countries
- Personnel about 300 of which 50 outside Finland
- Compliance with high quality and regulatory requirements: ISO 9001, ISO 13485 and FDA

* comparison figures of 2013 include sales of products that were discontinued in 2013.

# Smart Solutions for Healthcare & Hygiene Monitoring

Orion Diagnostica is a mid-sized, reliable European IVD company with over 40 years experience.

We develop, manufacture and market diagnostic test systems for healthcare professionals especially in point-of-care.

# We operate in the IVD growth segments

| HUMAN IVD MARKET (Kalorama, 2013 figures) | USA | Europe | China | Japan | ROW | Global | CAGR |
|---|---|---|---|---|---|---|---|
| | USD billion | | | | | | % |
| **Global IVD market** | 24.4 | 15.2 | 1.7 | 4.8 | 8.5 | **54.6** | 4 |
| - Professional POC | | | | | | **6.0** | 4 |
| - POC for OTC and self-testing | | | | | | **8.9** | |
| - Core lab | | | | | | **39.7** | |
| **Global POC market (Prof & OTC)**<br>- Professional POC | 9.8<br>5.1 | 7.0<br>2.6 | | 0.9<br>5% | 1.2<br>6% | **18.8**<br>**7.8** | 5 |
| **Global infectious diseases** | | | | | | **13.4** | |
| - Professional POC<br>- POC as reference, (Alere estim) | | | | | | **0.9**<br>**1.5** | 4.4 |
| - Core lab | | | | | | **12.5** | 5 |
| **Global MDx market** | 3.2 | 1.2 | 0.2 | 0.6 | 0.5 | **5.7** | **8** |
| - POC MDx market | 1.9 | 0.3 | 3% | 10% | 8% | **2.2** | |
| **Global MDx inf diseases market**<br>- POC MDx market | | | | | | **3.0**<br>**0.7** | **8** |

# Our customers

| Point-of-Care | Small and mid-size laboratories | Infection control, industrial microbiology |
|---|---|---|

# Orion Diagnostica – Building well-being

A forerunner in point-of-care systems with immunological IVD POC products deployed already in the 1990s.

Our flagship product with ca 40.000 units installed globally, is the rapid, easy-to-use QuikRead go® CRP.

QuikRead go®

# QuikRead go®
# Your support in treatment decisions

Helps to target antibiotic treatment to those who really need it
Reduced risk for antibiotic resistance and cost savings in healthcare

# Orion Diagnostica – Building well-being

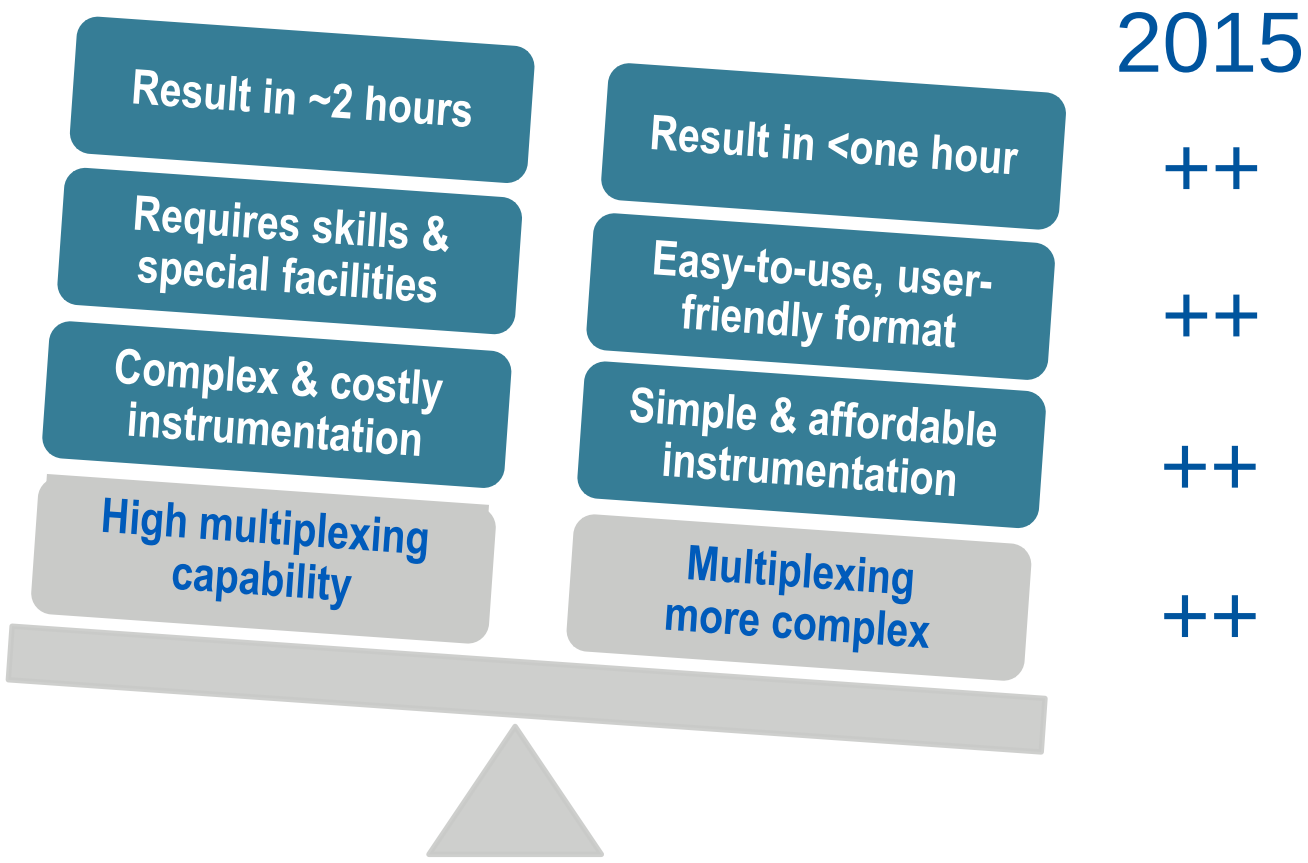
Our newest platform on the European markets is Orion GenRead®. It is based on SIBA®, a novel isothermal molecular diagnostics technology.

It brings flexible and easy detection of pathogens for laboratories of various settings and sizes. The first tests with low sample preparation requirements target gastrointestinal pathogens, e.g. *C. difficile* and *Salmonella*.

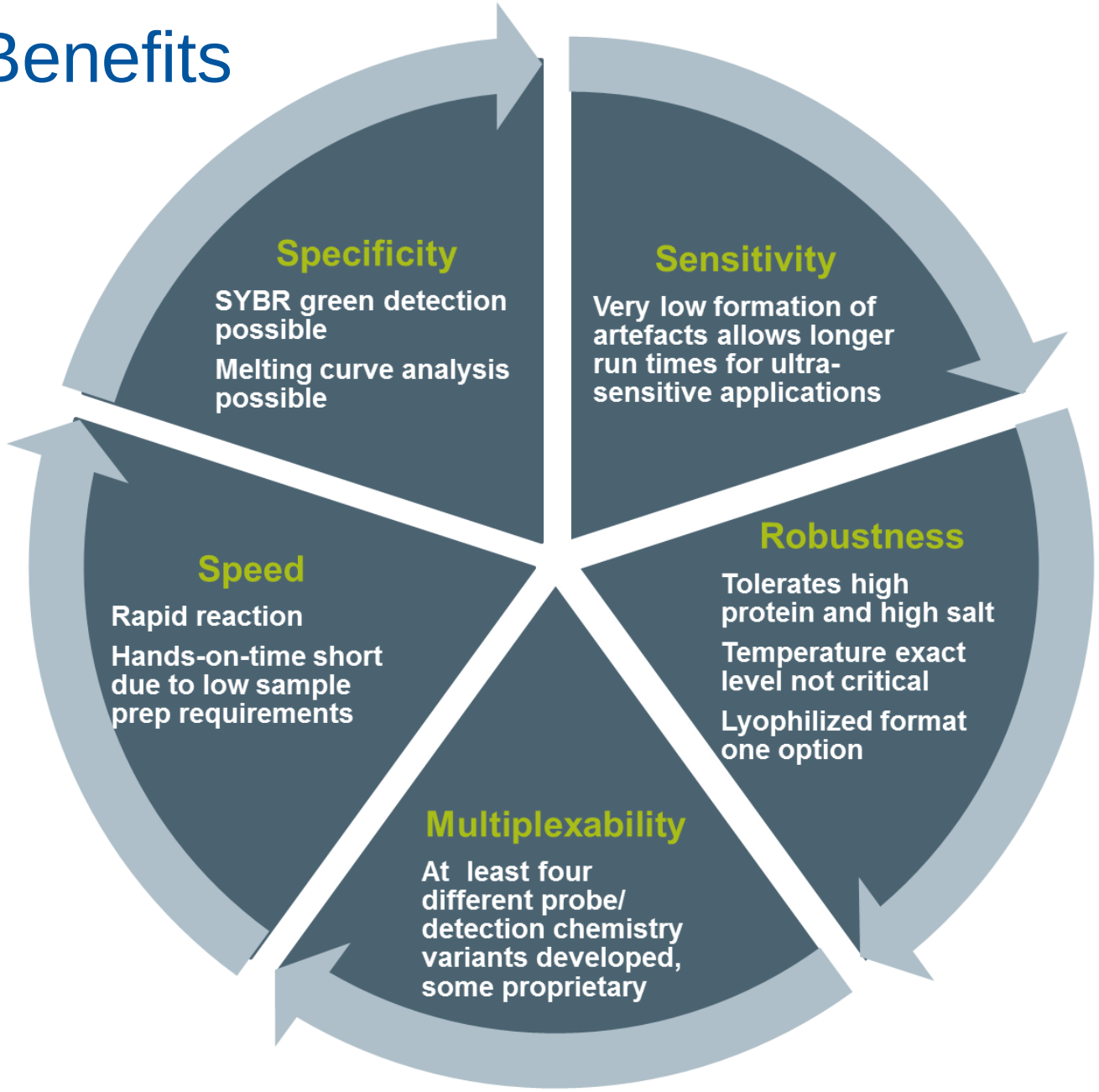
orion genread®

# Conventional PCR vs. Isothermal NAT

## Some features as presented in 2013



# SIBA® – Benefits



# Orion GenRead®
# Molecular testing for healthier life

Based on SIBA®, a novel isothermal molecular diagnostics technology
Flexible and easy pathogen detection for any laboratory

C. difficile
Salmonella
*More to follow…*

orion genread®

# Market Entry in In Vitro Diagnostics

## COUNTRY X

- ➔ Sales channel
  - ➔ Clinical acceptance
    - ➔ Laboratory acceptance
      - ➔ Payer exists
        - ➔ Trial(s) at end user
          - ➔ Procurement process
            - ➔ Purchase decision

➔ ROUTINE USE = **SALES CAN START!**

# Market Entry in In Vitro Diagnostics

| Country | Sales channel | Clinical acceptance | Laboratory acceptance | Payer exists | Trial use at end user | Procurement process | Purchase | Routine use |
|---|---|---|---|---|---|---|---|---|
| 1 | | | | | | | | |
| 2 | | | | | | | | |
| 3 | | | | | | | | SALES ! |
| 4 | | | | | | | | |
| 5 | | | | | | | | |
| 6 | | | | | | | | |
| 7 | | | | | | | | |
| . | | | | | | | | |
| . | | | | | | | | |
| n | | | | | | | | |

- All steps need to be covered in each country before sales can start
- Effective building of a distribution network can typically start only when the product is ready (~customer validation phase)

# Thank you!

# R&D pipeline review part II

Reijo Salonen
SVP, Research & Development

ORION
Building well-being

# Levosimendan for Low Cardiac Output Syndrome

Partner Tenax Therapeutics

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Building well-being

# Levosimendan development in US by Tenax Therapeutics

## Development of levosimendan for Low Cardiac Output Syndrome (LCOS)

- Phase 3 LEVO-CTS trial to evaluate the efficacy of levosimendan in reducing morbidity/ mortality in cardiac surgery patients with reduced ejection fraction
- Data read out early 2016*
- Fast track status granted by FDA and protocol approved under SPA

## Possibility to include sepsis shock as an additional indication?

- Collaboration with Imperial College London for LeoPARDS trial
- Data read out in 2016*
- More information: www.leopards-trial.org

*) www.tenaxthera.com

# LEVO-CTS & LeoPARDS trials

| | | | | |
|---|---|---|---|---|
| Levosimendan | Low Cardiac Output Syndrome | I | II | III |

## LEVO-CTS trial

- A Double-Blind, Randomized, Placebo-Controlled Study of Levosimendan in Patients with Left Ventricular Systolic Dysfunction Undergoing Cardiac Surgery Requiring Cardiopulmonary Bypass
- 760 patients, approximately 60 centers
- ClinicalTrials.gov identifier: NCT02025621

## LeoPARDS trial

- Double-blind randomized placebo controlled LeoPARDS trial to study the effect of levosimendan in septic shock
  - Levosimendan for the prevention of acute organ dysfunction in sepsis
  - Investigator initiated study performed in UK ICUs
  - Trial has enrolled over 300 of the estimated 516 patiens
  - Discussions ongoing with FDA about the possibility to include the data for US regulatory filing

# Dexmedetomidine for treatment of pain

Partner Recro Pharma

ORION
Building well-being

# Dexmedetomidine development for acute post-operative pain by Recro Pharma

| Dexmedetomidine (intranasal) | Treatment of pain | I | IIb |
|---|---|---|---|

- Phase II trial to study the effect and safety of intranasal formulation of dexmedetomidine in adult patients undergoing bunionectomy surgery in US
- Possibility to avoid many of the side-effects associated with opioids
- Primary efficacy endpoint is summed pain intensity difference SPID48, over 48 hours starting on post op day 1.
- As a result of interim analyses in April, the total enrollment was reduced to 170 patients (was 200-250 pts)
- Top-line results will be reported by mid-year 2015*

*) www.recropharma.com

ClinicalTrials.gov identifier: NCT02284243

# ORM-12741 for Alzheimer's disease

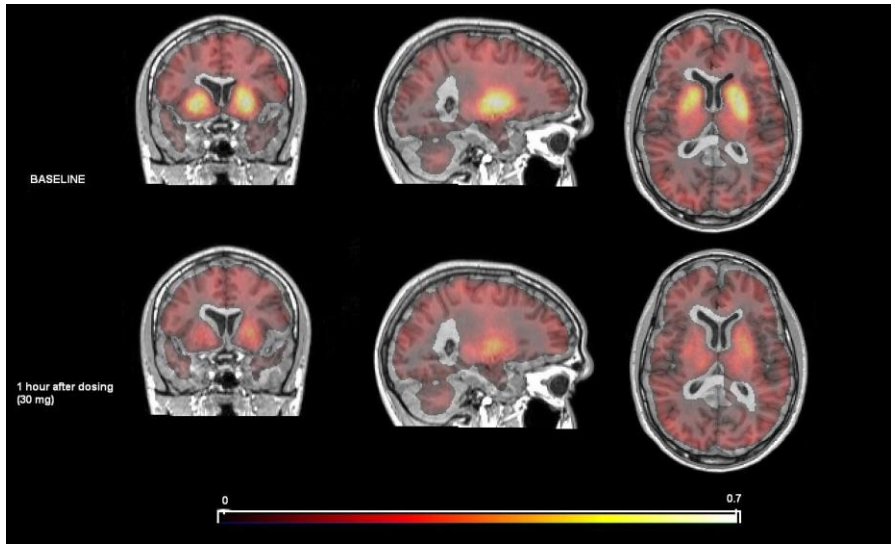
In collaboration with Janssen

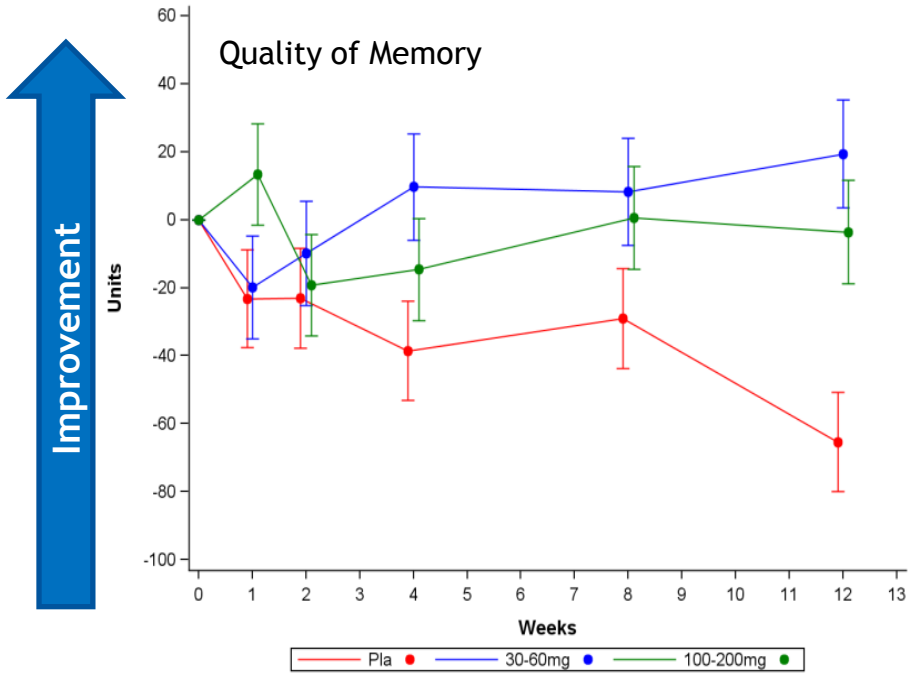
ORION
Building well-being

# 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 AD patients
  - Positive signals of efficacy in
  - Episodic and working memory
  - and
  - Neuropsychiatric symptoms

ClinicalTrials.gov identifier: NCT01324518



# Phase 2 study on efficacy of ORM-12741 in AD

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

## Improved formulation for the next Phase 2 study

- New formulation improving pharmacokinetic (PK) properties of ORM-12741 has been developed
- Phase 1 PK studies conducted to confirm qualities of the new formulation
- The improved formulation will be used in the next Phase 2 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


# ODM-104

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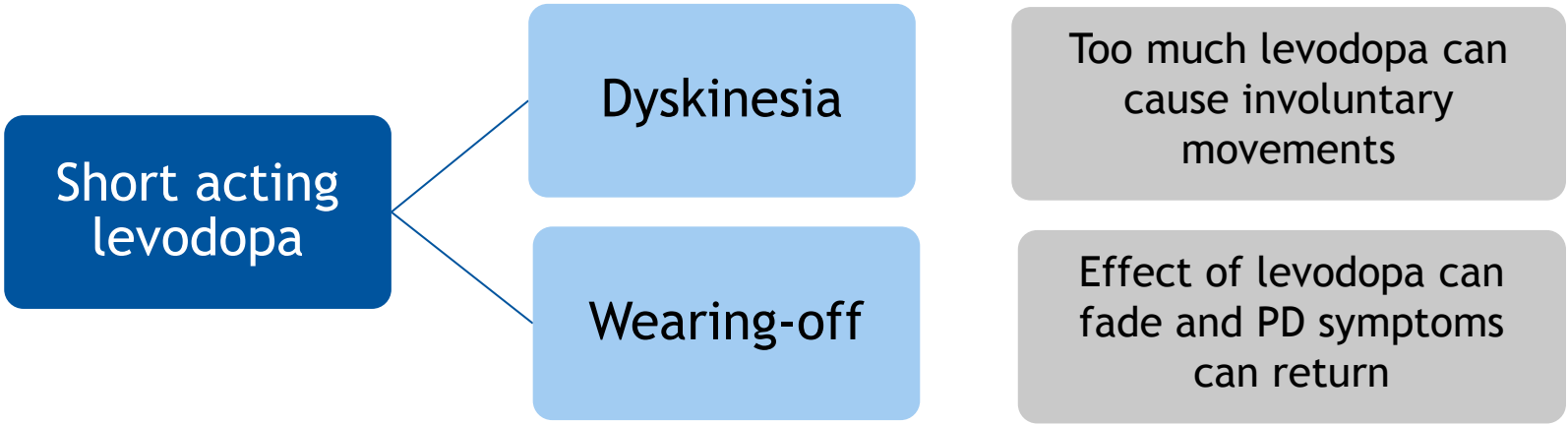
# Treatment of Parkinson's disease with levodopa

- Levodopa is the most effective medicine for treating 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






ORION Building well-being

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

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

- 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
- Orion Pharma is currently developing a next generation PD product enabling the optimization of levodopa/carbidopa together with ODM-104
- Preparations for a phase II Proof-of-Concept study are ongoing. ODM-104 product will be compared with Stalevo® (levodopa/carbidopa/entacapone combination) in 66 PD patients with end-of-dose wearing-off symptoms

*) ClinicalTrials.gov identifier: NCT01840423

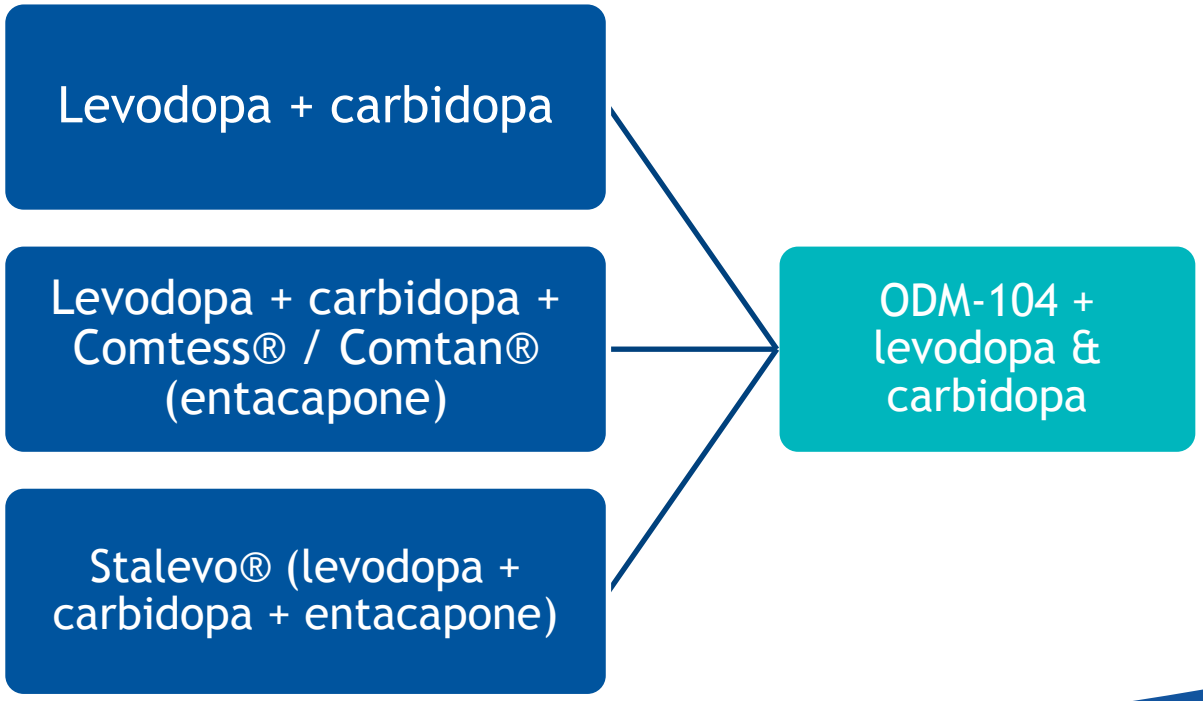
# Increased levodopa exposure[1] reduces OFF-time[2] in PD patients during different LD/AADCi ± COMTi[3] treatments q.i.d – A change from Stalevo[4]

| COMTi Dose mg | Sinemet[5] | | Stalevo | | Carbidopa+[6] | | ODM-104 | | ODM-104 with carbidopa+[7] | |
|---|---|---|---|---|---|---|---|---|---|---|
| | AUC[1] | OFF[2] | AUC | OFF | AUC | OFF | AUC | OFF[11] | AUC | OFF[12] |
| - | 0.74[8] | 0.8[9] | | | | | | | | |
| **100** | | | | | 1.26 | | 1.20 | - | **1.32** | In PoC study |
| **200** | | | 1.0 | 1.0 | 1.27 | -0.6[10] | 1.26 | - | **1.33** | - |

[1] Levodopa AUC 0-16 h*ng/ml in healthy subjects
[2] Reduction of daily OFF- time, hours by patient diary PD patients with end-of-dose wearing off
[3] Levodopa/aminoacid decarboxylase inhibitor ± cathecol-omethyltransferase inhibitor
[4] Levodopa/carbidopa + entacapone in combination or in separate tablets
[5] Levodopa/AADCi (standard levodopa branded or generics)
[6] Carbidopa optimized + entacapone 200 mg (ODM-101)
[7] ODM-104 + optimized carbidopa
[8] Kuoppamäki et al 2014
[9] Kuoppamäki 2009
[10] Trenkwalder et al 2013
[11] ODM-104 not studied alone
[12] To be studied

# 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®



# ODM-106

Target: First/Best-in-class GABA B PAM molecule for the treatment of Essential tremor

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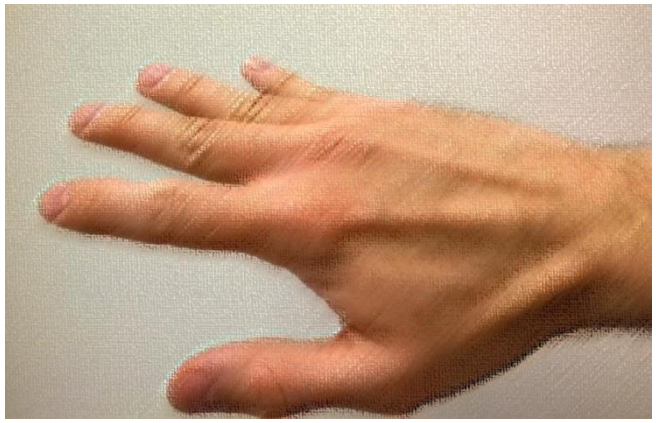
# Essential Tremor

- Chronic, slowly progressive postural and/or kinetic tremor, usually affecting both upper extremities
  - May initially be intermittent and then becomes persistent
  - May also affect the head, voice, jaw, lips and face
  - Tremor amplitude is highly variable, worsened by emotion, hunger, fatigue and temperature
- Affects patients quality of life, social and employment prospects
- Most common movement disorder
  - 8 times more common than Parkinson's Disease
  - Prevalence 0.5-1.5%, >40 yr 4%
  - Usually starts in middle age or later, but possible also earlier in life



# Unmet needs in Essential Tremor

**Approximately 50% fail on current treatments due to efficacy or side-effects**

- Mainly treated with generic beta-adrenergic blockers (propranolol) and anticonvulsants (primidone)

**Deep Brain Stimulation (DBS) used for last option for the treatment of severe patients**

**Current R&D activity is low**

- SAGE-547, a GABA-A PAM, in clinical phase as an infusion
- Some non-drug therapies in development for more severe cases

# GABAB PAM (gamma-aminobutyric acid B positive allosteric modulator)

Positive allosteric modulator: a ligand that binds to a distinct (allosteric) site on the receptor and hereby increases the activity of the endogenous agonist

Decrease of GABA activity in several brain areas in essential tremor which could be ameliorated by a GABAB PAM

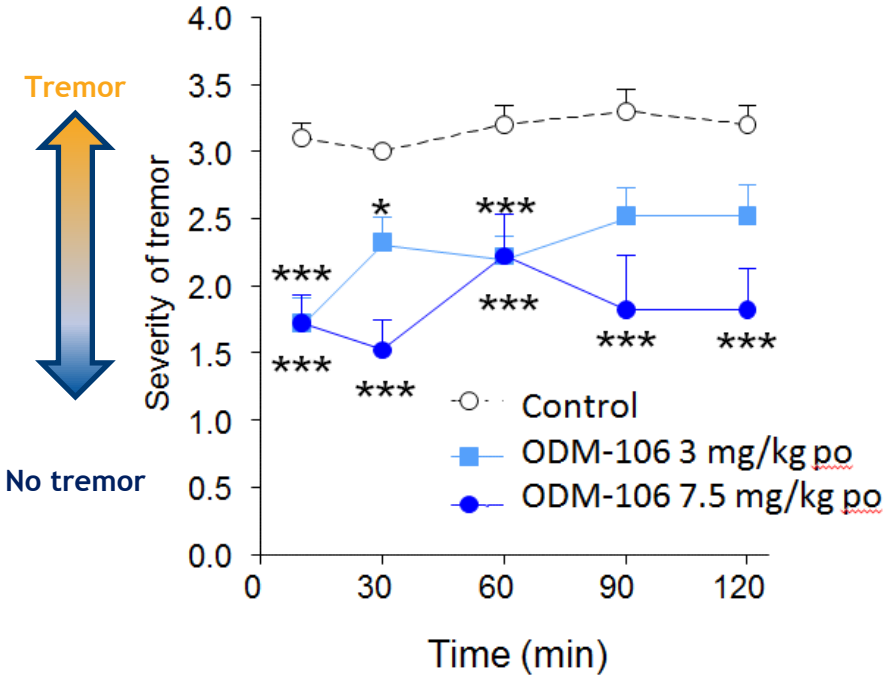
Advantages of a PAM

- A more physiological approach
- Better safety and selectivity
- Less side-effects
- Avoiding development of tolerance through receptor desensitization

# ODM-106 shows efficacy and safety in Essential tremor

| ODM-106 (GABA-B receptor positive allosteric modulator) | Essential tremor | I |
|---|---|---|

- Alleviates tremor in essential tremor animal model (harmaline –induced tremor)
- No signs of development of tolerance after repeated doses
- No sedative or other CNS side-effects in preclinical models
- Well tolerated in the preclinical safety studies
- Efficacy also shown in parkinsonian tremor, levodopa-induced dyskinesia and pain models
- Phase I FIMPAM trial ongoing




ClinicalTrials.gov identifier: NCT02393950



Building well-being

# ODM-108

Target:
Best-in-class TRPA1 antagonist molecule for the treatment of Neuropathic pain

ORION
Building well-being

# Neuropathic Pain

**Caused by a lesion or disease affecting the somatosensory nervous system**

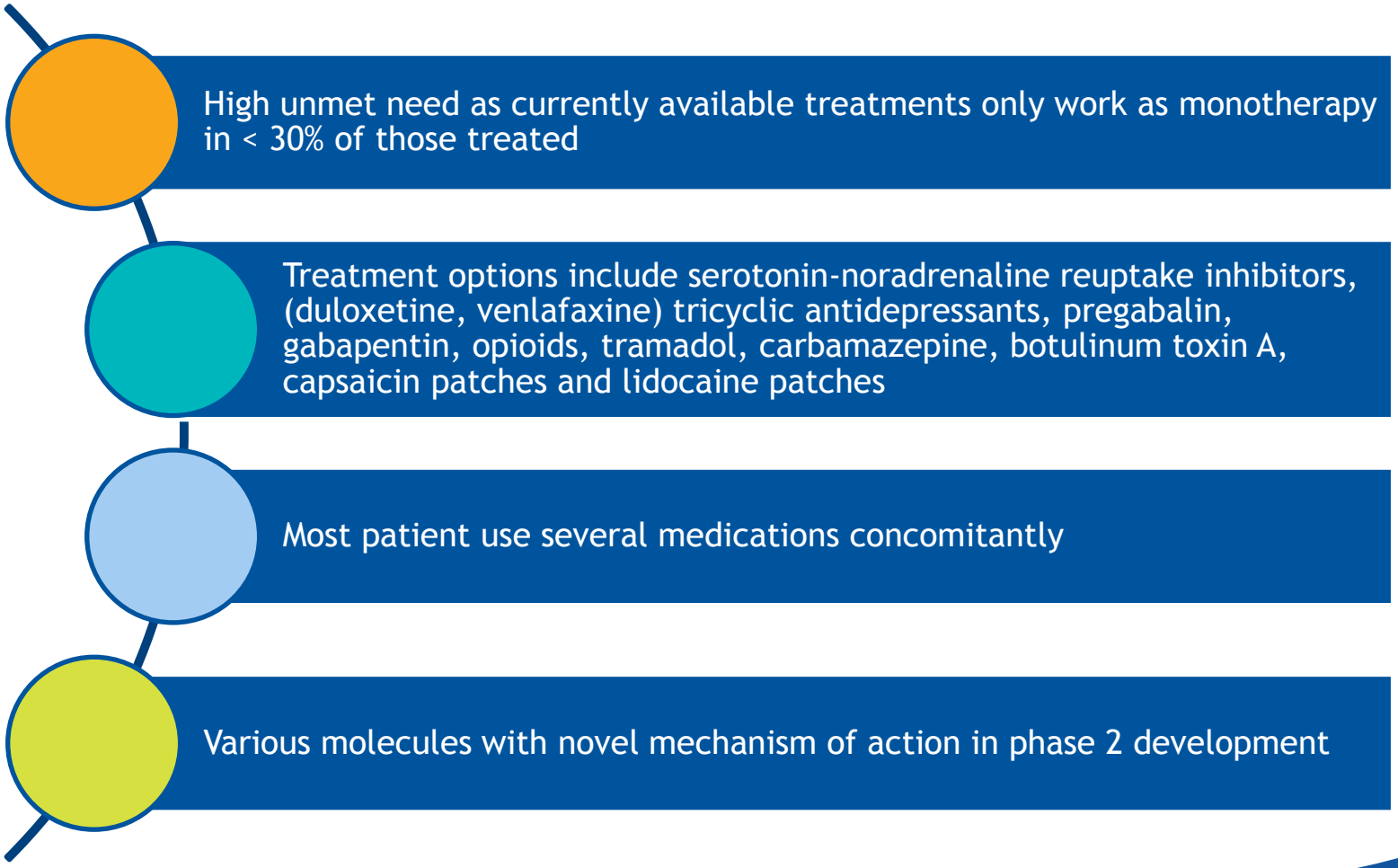
- Trauma, infection, cancer, anti-cancer treatments, etc.

**Causes distress and suffering**

- Very high impact on quality of life
- Sleep, enjoyment of life, work and earning are all affected

**Prevalence 3.3-8.2%**

# Unmet needs in Neuropathic Pain






ORION Building well-being

# TRPA1 antagonist (Transient Receptor Potential Ankyrin 1)

TRPA1 receptors are expressed on pain neurons and when activated sends signals of pain in humans

Highly competitive target with very difficult chemistry

Advantages of TRPA1 antagonist

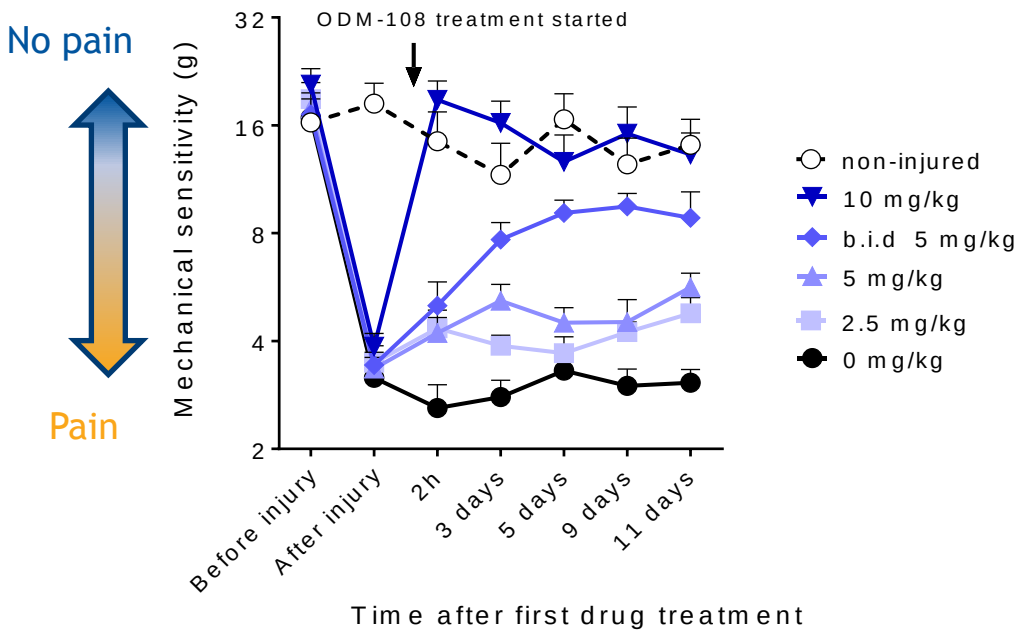
- Robust functional antagonism
- High selectivity
- Less side-effects
- No tolerance to repeated dosing

# ODM-108 shows efficacy and safety in Neuropathic pain

| ODM-108 (negative allosteric modulator of TRPA1 ion channel) | Neuropathic pain | I |
|---|---|---|

- ODM-108 blocks pain in several animal models of pain (STZ in figure, SNI, CFA)
- No CNS side-effects seen in preclinical models
- Well tolerated in the preclinical safety studies
- Phase I FIMTRIP trial ongoing

ClinicalTrials.gov identifier: NCT02432664






ORION Building well-being

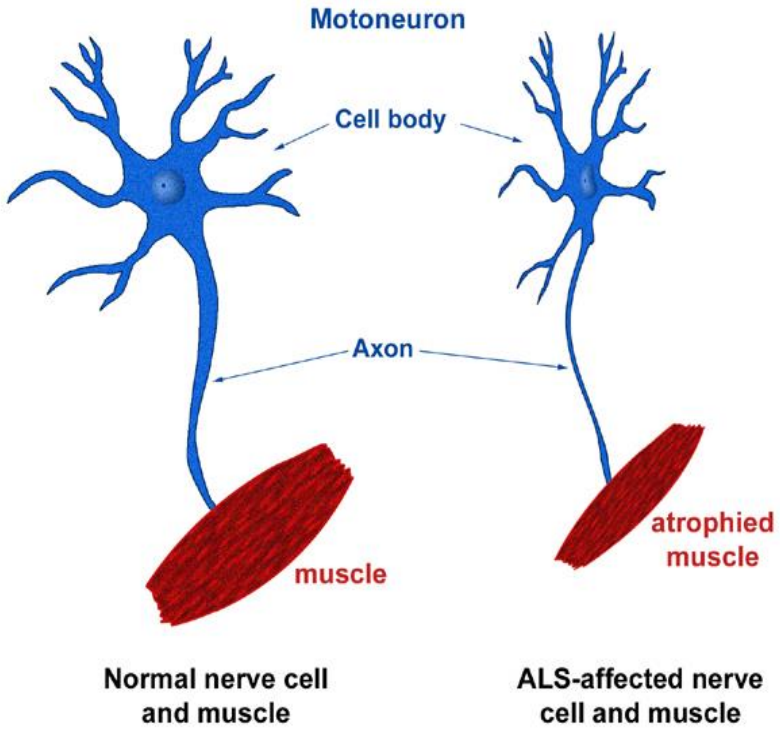
Target:
Best symptomatic treatment for Amyotrophic Lateral Sclerosis (ALS)

# ODM-109

ORION
Building well-being

# Amyotrophic lateral sclerosis - ALS

- Orphan disease with prevalence of
- ~0.4 patients/10,000
- Degeneration of motoneurons leads to skeletal muscle weakness and diaphragm failure
- 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 weakness available




A clear unmet need in ALS for a drug that improves endurance and function at the level of diaphragm /skeletal muscle force



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# 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 and its long-acting metabolite OR-1896 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

# Levosimendan increases calcium sensitivity by binding selectively to troponin C in cardiac and skeletal muscles

| Effect/parameter | Levosimendan |
|---|---|
| Calcium sensitization (troponin C) | + |
| Affects fast muscle fibers | + |
| Affects slow muscle fibers | + |
| ATP/oxygen sparing effect | + |
| Long-acting metabolite | + |
| Crossing BBB | - |
| PK interaction with riluzole | - |

# LEVALS study - levosimendan in ALS patients

| | | |
|---|---|---|
| ODM-109 (oral levosimendan) | ALS | I II |

- The first phase II study aims 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 study will recruit approx. 50-60 patients in Europe

**Levosimendan potentially delays the need for respiratory support and improves QoL in ALS patients by increasing skeletal muscle force**

## Regulatory considerations for ODM-109

- Possibility to seek parallel orphan designation in EU and US
- Several options for fast track designation

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# Q&A


PRODUCT
SALES
DEVELOPMENT
PROFIT
OPERATING
EASYHALER
GENERIC
CLINICAL
ORION
BUFOMIX
MARKETING
NET
PHASE
PRECEDEX
COLLABORATION
GROWTH
PARTNERS
SIMILAR
INTENSIVE
DRUGS
BAYER
ORM
HIGHER
CANCER
INHIBITOR
SIMDAX
DEVELOPMENT
DELIVERIES
INVESTMENT
QUARTER
CLEARLY
PERIOD
GREW
MILLION
SIGNIFICANT
PROGRESSED
CONTINUED
NOVARTIS
ROYALTIES
REVIEW
ADDITION
DECLINING
INCREASE
CARE
FUTURE
REGARDS
DEXDOR
ESPECIALLY STRONGLY
OUTLOOK
PROPRIETARY
STEADILY
PLANNED
FAMILY
LEVEL
MILESTONE
CURRENT
GERMANY
REMAINS
NETWORK
RECEPTOR
COMPOUND
PLEASED
EXPECTED
LEVOSIMENDAN
ENTACAPONE
ORGANISATION
CERTAIN
DISEASE
ANDROGEN
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FOLLOWING
SYMPTOMS
STRONG
BEGINNING
GOOD
MODULATOR
HOSPIRA
REORGANISATION
ANNOUNCED
EXTENSION
GRANTED
PROSTATE
ANTAGONIST
CHANGES
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