# Orion Capital Markets Day 2013

20 November 2013 Helsinki

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# Agenda

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|---|---|
| Orion today | Timo Lappalainen, President & CEO |
| Key elements of financial targets | Jari Karlson, CFO |
| Orion production strategy | Virve Laitinen, SVP, Supply Chain |
| Break | |
| R&D pipeline review | Reijo Salonen, SVP, Research & Development |
| Proprietary Products update | Liisa Hurme, SVP, Proprietary Products |
| Break | |
| How Specialty Products is succeeding in Generics? | Markku Huhta-Koivisto, SVP, Specialty Products |
| Orion Diagnostica | Jaakko Rissanen, President, Orion Diagnostica |
| Closing remarks and Q&A | |
| Lunch | |

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

# Forward-looking statements

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.

# Orion today

Timo Lappalainen
President & CEO

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# Key market development parameters

- Proprietary markets continue to drive the value IF you have a differentiated product
  - Market access will be the key
  - Developed 0-1%(1)
    - Developed markets are still 74% of the global branded markets in 2016(2)
  - Pharmaemerging 7-9%(1)
- Generics markets have enjoyed the patent cliff over the past years
  - Competitive supply chain will be the key
  - Developed markets 6-7%(1)
- Animal Health markets growth 5%(3)
- In-vivo diagnostics markets growth 5%(4)

*(1) Source: IMS Health Market Prognosis, June 2013, 2012 - 2016*

*(2) Source: IMS Market Prognosis, May 2012*

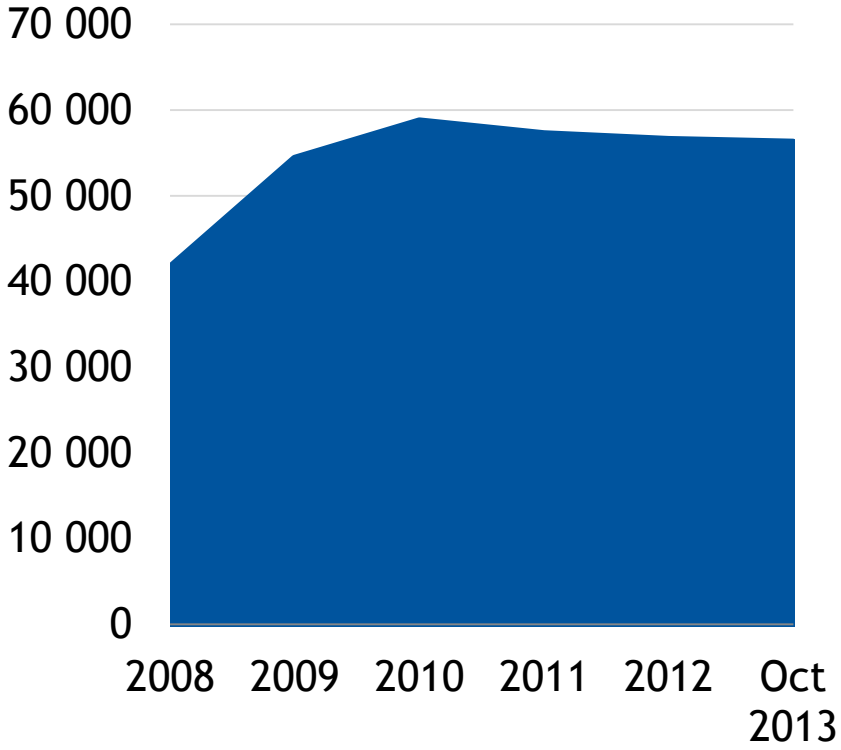
*(3) Source: Vetnosis, Outlook 2013 Report*

*(4) Kalorama Information: The Worldwide Market for In Vitro Diagnostic Tests, 8th Edition, July 2012*

# Ownership base 2008-2013

## Ownership structure by number of shares


## Number of shareholders



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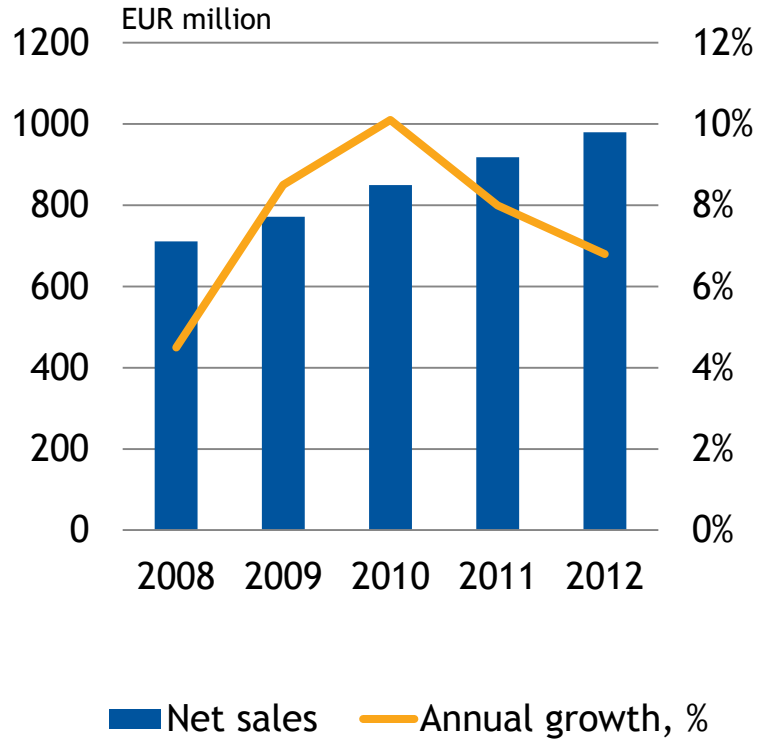
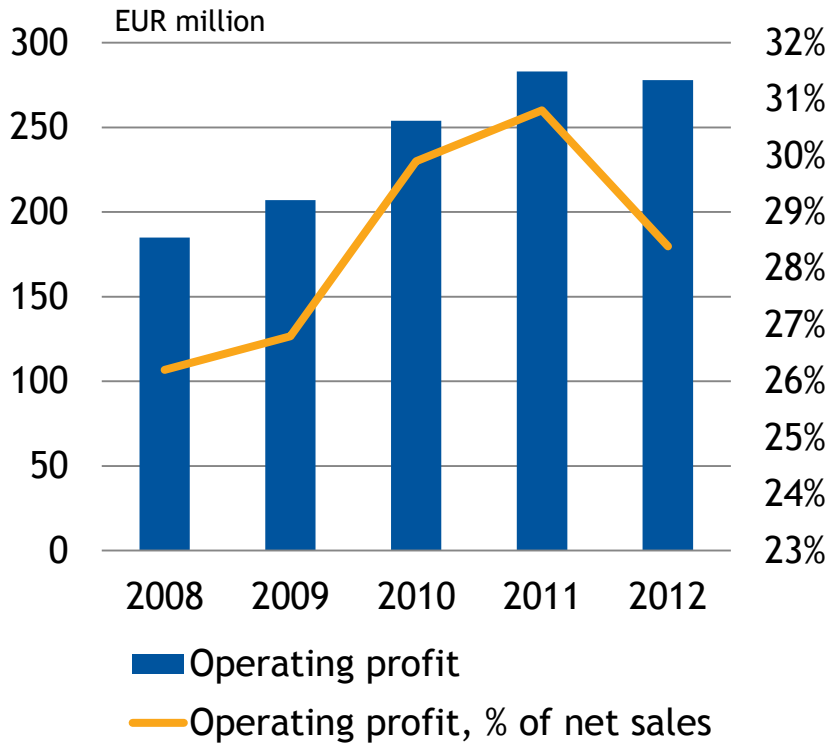
# Financial performance in 2008-2012

## Net Sales 2008-2012




CAGR 8.35%

## Operating Profit 2008-2012




CAGR 10.72%



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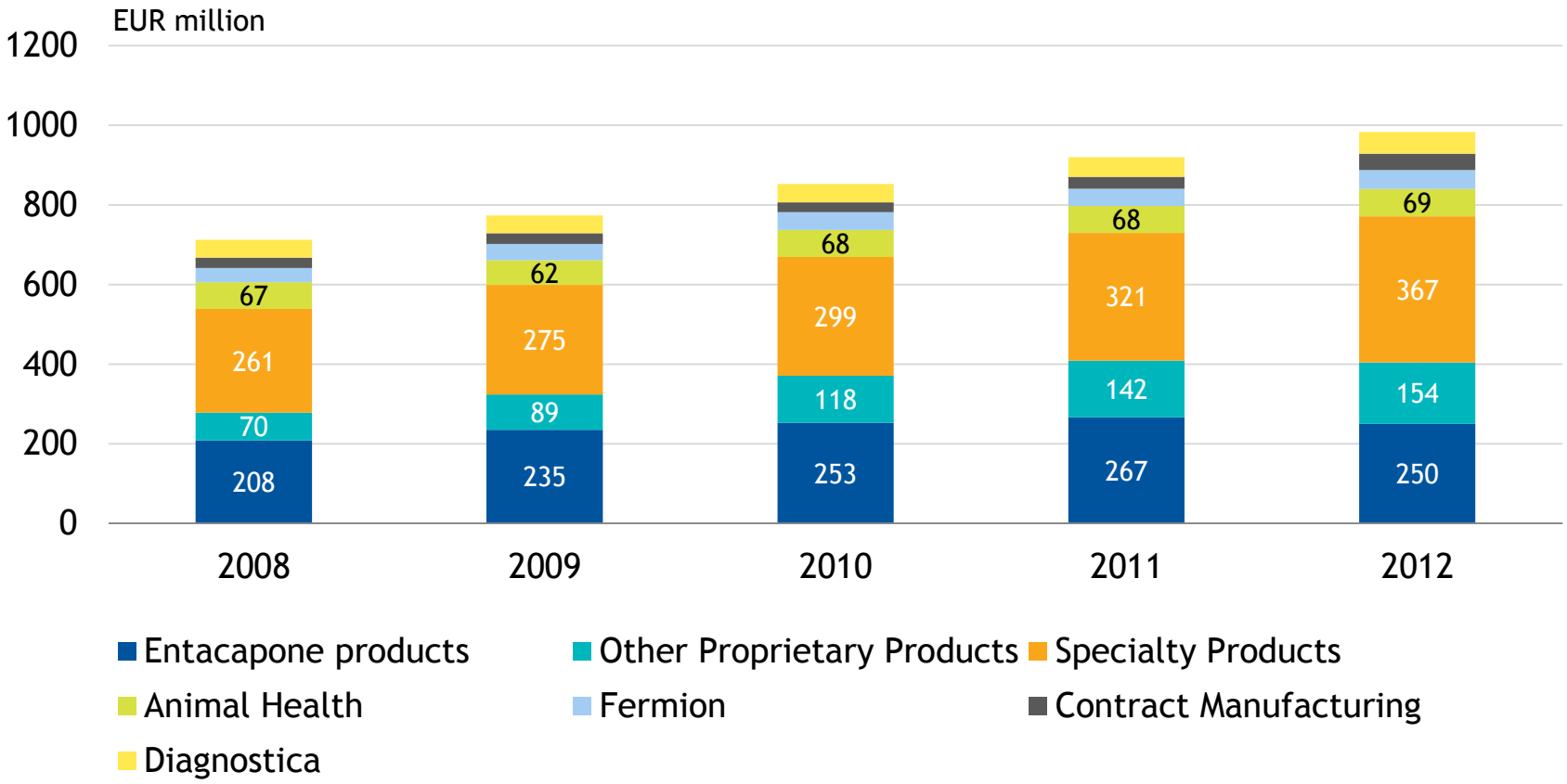
# Net sales by business divisions 2008-2012




Proprietary Products CAGR 9.77%
Specialty Products CAGR 8.96%



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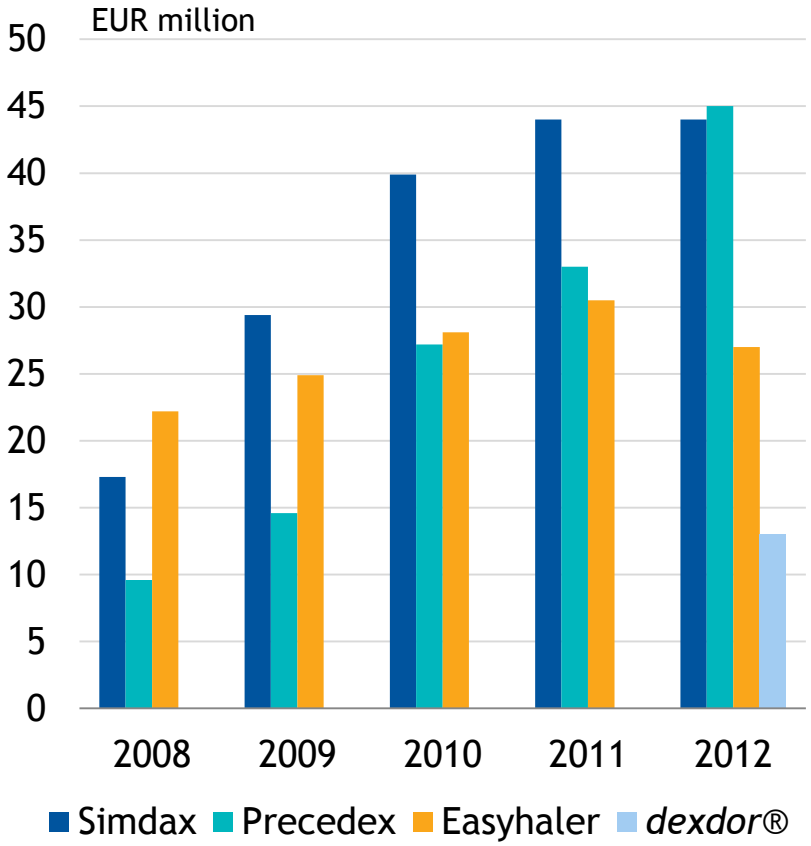
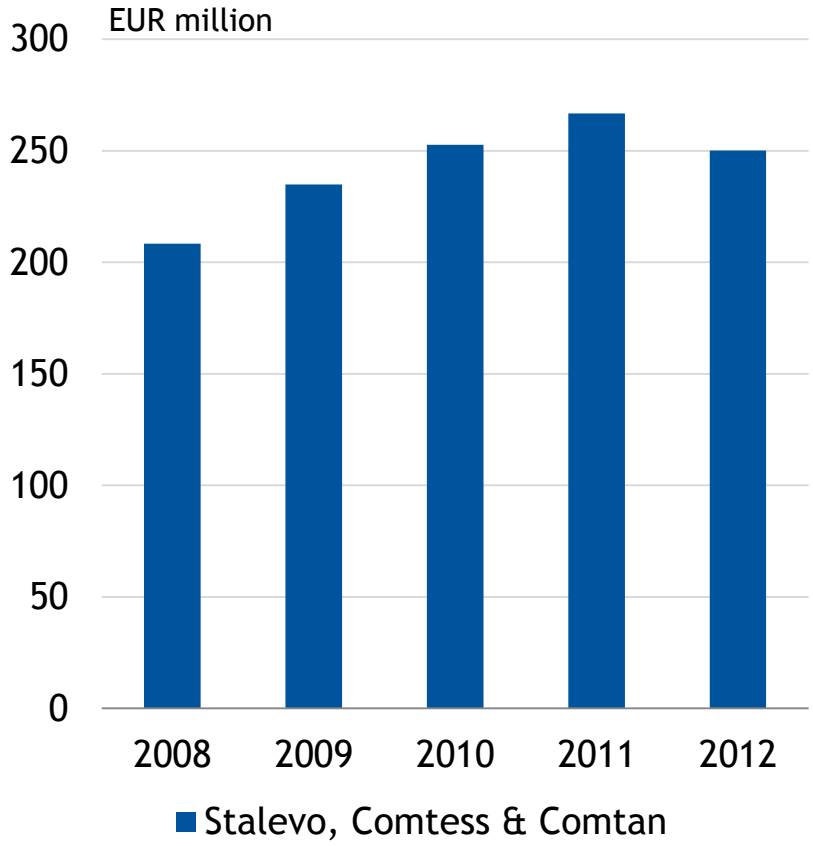
# Development of key PP products



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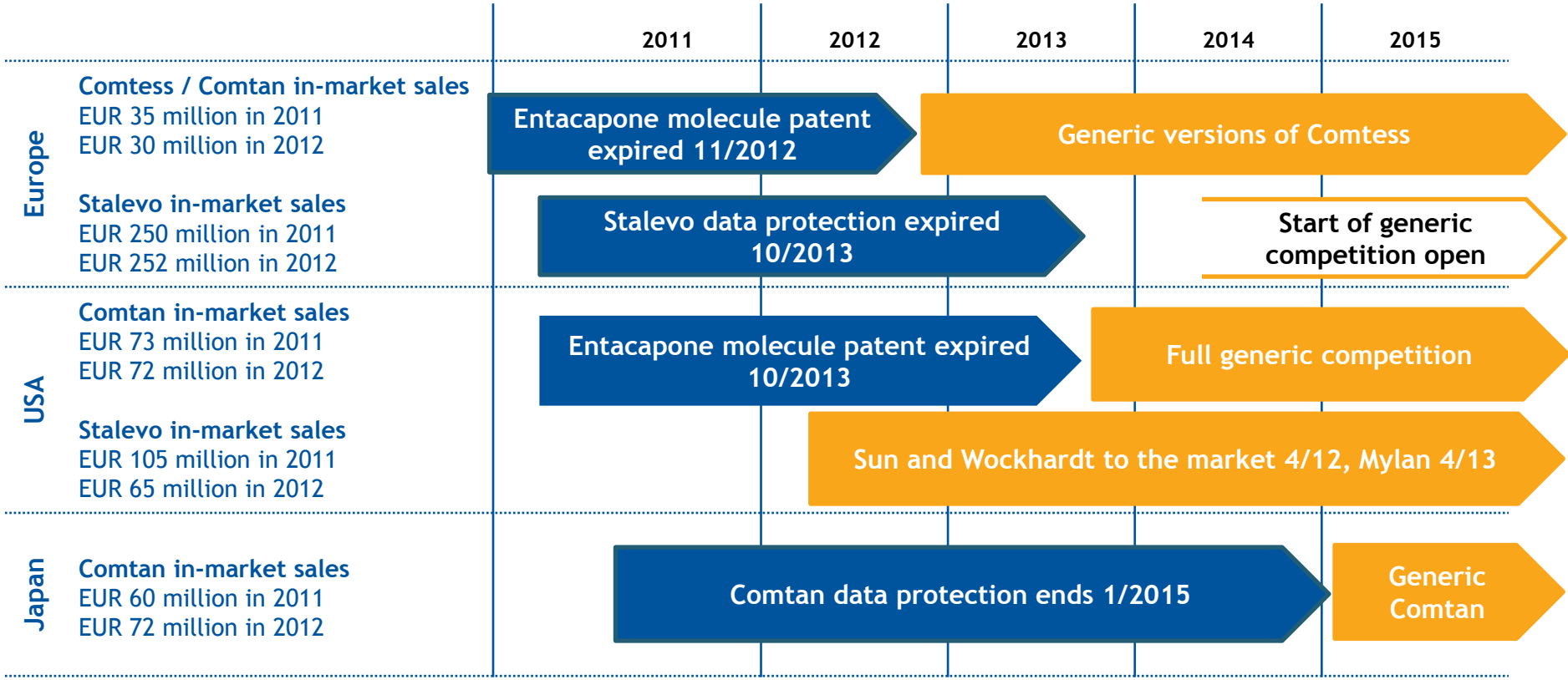
# Product protection situation of key products

| | | | Key patents or data protection expire | | |
|---|---|---|---|---|---|
| Molecule | Product | Indication | Europe | USA | Japan |
| Entacapone | Stalevo®, Comtess® and Comtan® | Parkinson's disease | November 2012<br>October 2013 [1)] | October 2013 [2)] | 2015 [3)] |
| Levosimendan | Simdax® | Acute decompensated heart failure | September 2015 | Not marketed | Not marketed |
| Dexmedetomidine | Precedex®<br>*dexdor*® | Intensive care sedative | July 2013<br>September 2021 [4)] | January 2014 [5)] | June 2012 |

[1)] Stalevo data protection expired
[2)] Wockhardt and Sun on markets since April 2012, Mylan since April 2013
[3)] Data protection expires; currently only Comtan available, Stalevo in registration
[4)] *dexdor*® data protection expires
[5)] Pediatric Exclusivity granted by FDA ends in January 2014

# Turning points of Parkinsons's franchise




ROW

**Comtan in-market sales** EUR 22 million in 2011, EUR 23 million in 2012
**Stalevo in-market sales** EUR 71 million in 2011, EUR 78 million in 2012

Source: IMS Health 2012



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# Orion’s strategy

## Orion’s values



Management of complexity in cost efficient way



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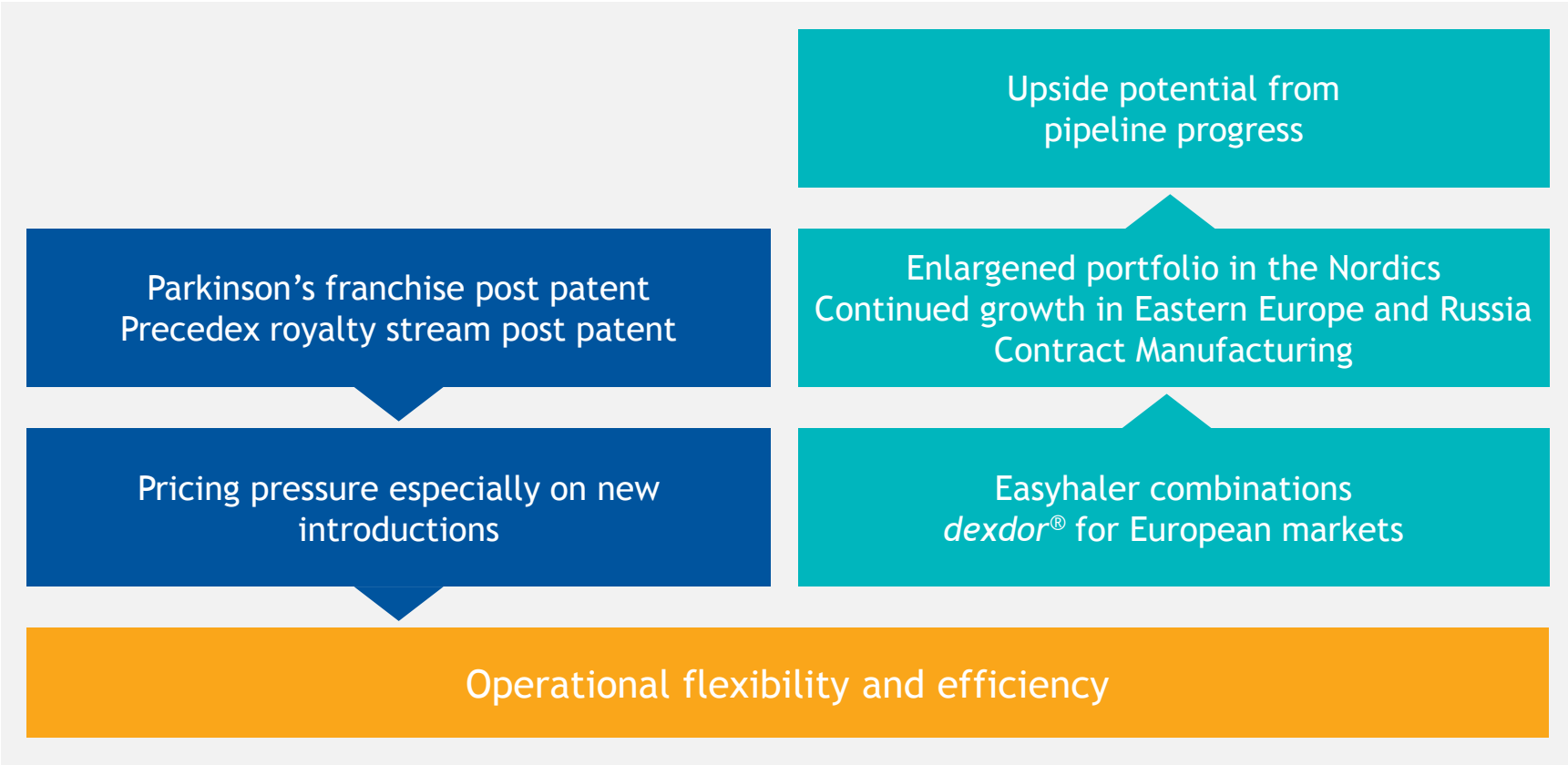
# Orion's partnering framework

- Part of Orion's strategy is to share risks and rewards of phase III trials with partners
  - However, each case merits its individual considerations
- Partnering is a long and winding road due to its long-term and substantial financial commitment
- Orion's key considerations for partnering
  1. Partner's development and commercial capabilities for the therapy area especially in the US
  2. Orion to have access to European markets
  3. Cost sharing of the development phase
  4. Partnership compatibility to both companies

# Balancing mid-term – building long-term



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# Today's presentations

## Proprietary Products

- Patented prescription drugs
- CTAs: CNS, oncology & critical care, Easyhaler pulmonary drugs
- Net sales in 2012 EUR 404 million

## Fermion

- Active pharmaceutical ingredients (API's) for Orion and other companies
- Net sales in 2012 EUR 48 million (excluding supplies for own use)

## Specialty Products

- Generic prescription drugs
- Self-care products
- Net sales in 2012 EUR 367 million

## Contract Manufacturing & Other[1)]

- Pharmaceutical manufacturing for other companies
- Net sales in 2012 EUR 41 million

## Animal Health

- Veterinary medicines and care products for pets and production animals
- Net sales in 2012 EUR 69 million

## Orion Diagnostica

- Diagnostic test systems for point-of-care testing in healthcare and hygiene testing for industry
- Net sales in 2012 EUR 54 million

1) Contract manufacturing and other is included in the Pharmaceuticals business segment but is not a separate business division. It is part of the Group's Supply Chain organisation.



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# Key elements of financial targets

Jari Karlson
CFO

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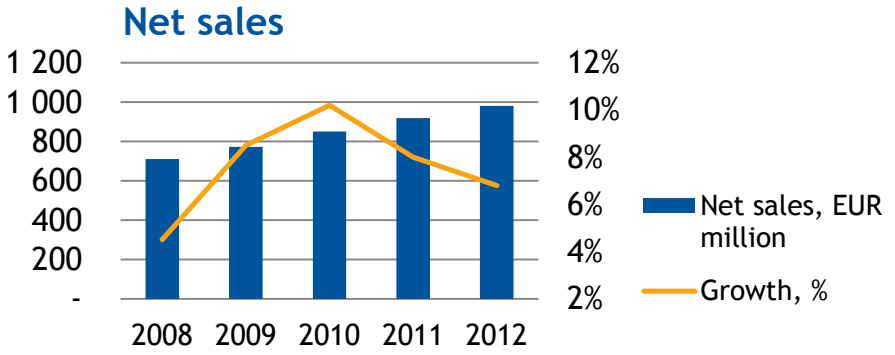
# Orion’s financial objectives

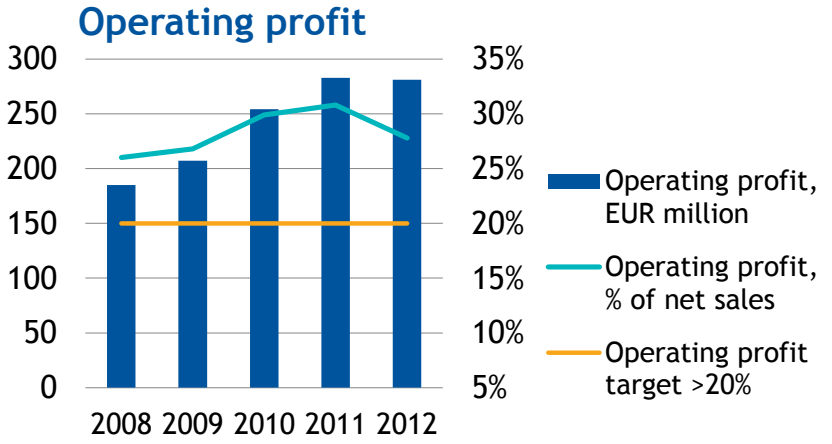
**Orion’s financial objectives are:**

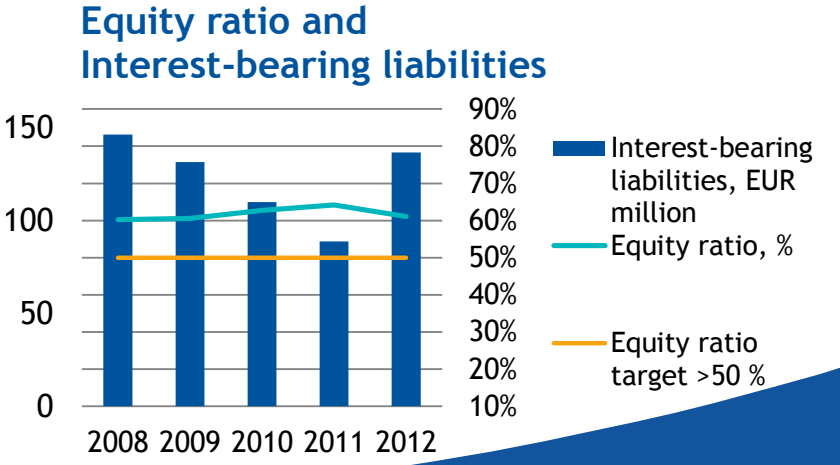
- Ensuring financial stability
- Profitable growth

**The objectives are achieved through:**

- Increasing net sales. Achievement of this objective requires continuous investment in development of the product portfolio.
- Maintaining profitability at a good level, the aim being operating profit that exceeds 20% of net sales.
- Keeping the equity ratio at least 50%.



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# Where we are (and have been)

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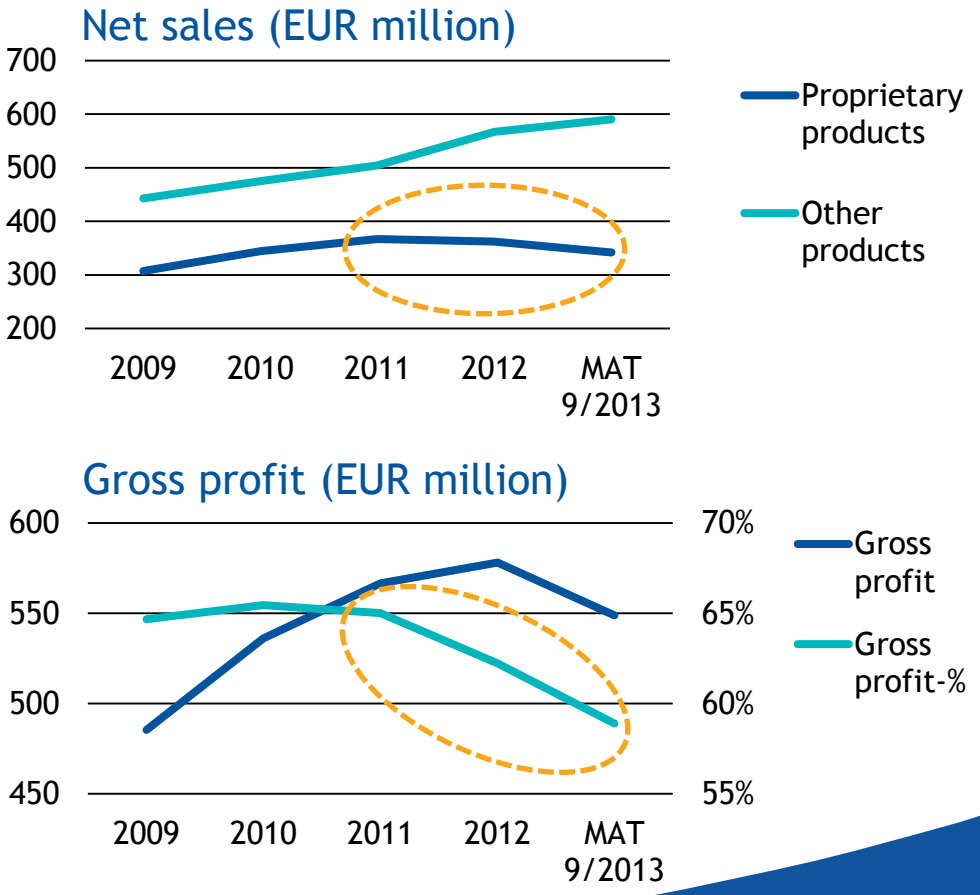
# Product sales and gross profit
## - clear decline in margins over last few years

- Orion had for many years a stabile 65% gross profit from products sales
- Over the last two years the gross profit has however declined to less than 60%
  - Share and also total sales of proprietary products started to decline in 2011
  - Quite rapid growth in some lower margin business areas like Fermion
  - Increase in manufacturing costs (partly temporary)
  - Price erosion



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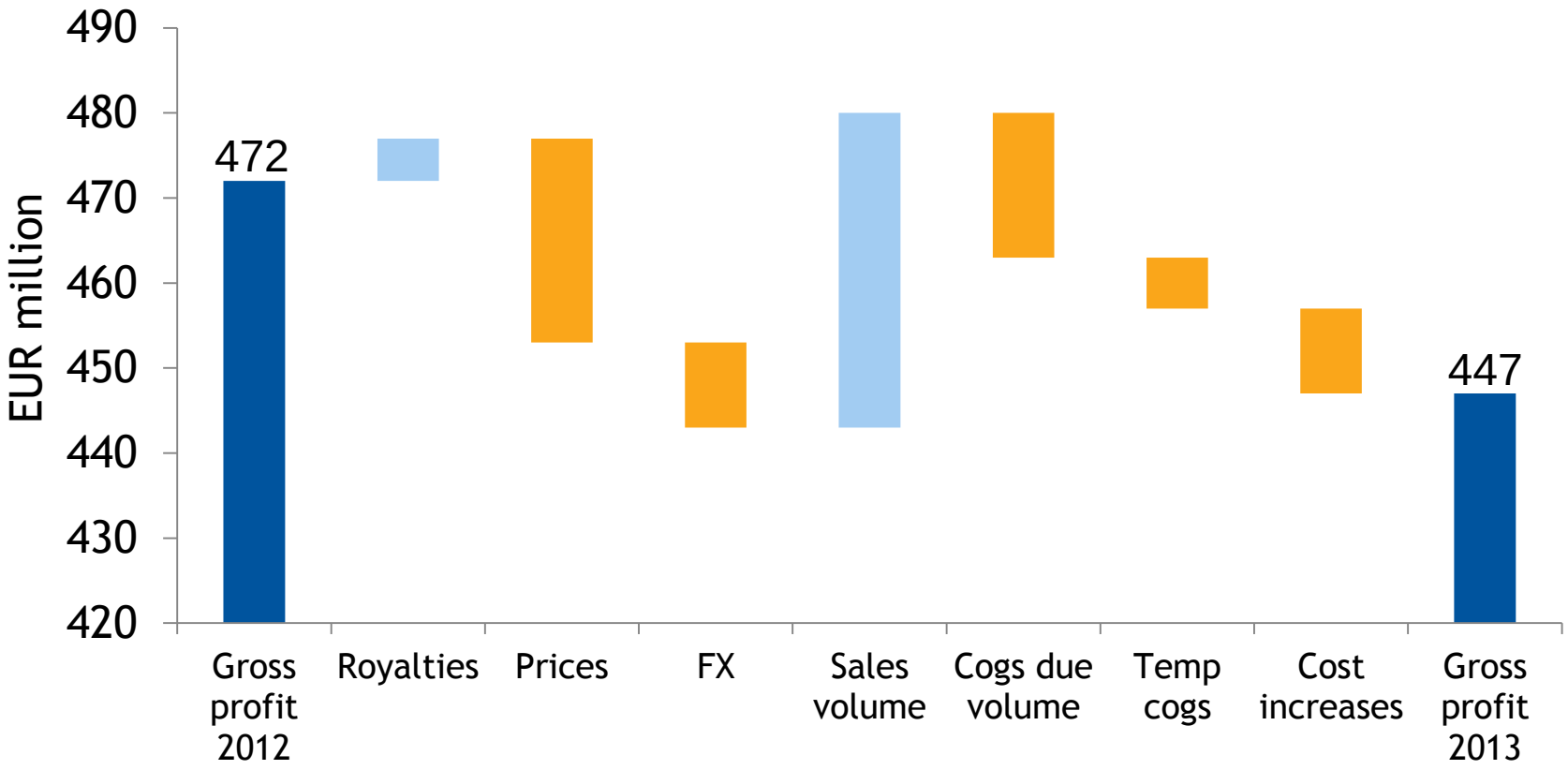
# Key components of gross profit change
## - from 1-9/2012 to 1-9/2013



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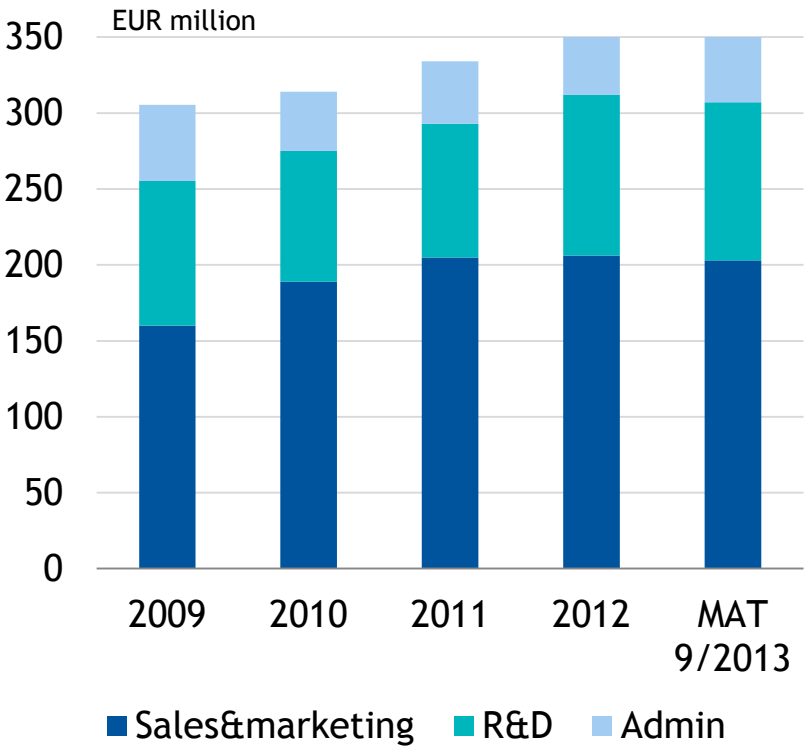
# Key components of gross profit change

- Price and currency changes have had negative impact
- Volumes have increased
  - Higher sales, higher cost of goods
- Product mix impact has also been negative
  - Increased share of sales generated by lower margin business units
- Manufacturing costs have increased
  - Short term impact mainly due to capital expenditure programs
    - Costs related to capex but not activated
    - Overtime and additional work to maintain service level
    - Orion Diagnostica rationalisation
  - Long term challenges
    - Increased headcount and other longer term impacts e.g. related to changes done because of increasing regulatory requirements
    - Depreciation related to high capex
- Some losses of sales due to limitations in manufacturing capacity
  - Mainly timing issues

# Consistent management of the cost structure

## Costs by function




- Sales have increased 28% from 2009 to MAT 9/2013 (to EUR 988 million)
- Fixed costs have increased 15% over the same period (GS&A costs by 18%)
  - Establishment of presence in several countries after Simdax acquisition in mid 2009
  - Sales resources constantly reallocated and/or reduced based on need
  - R&D headcount lower than in 2009. Increasing volume of programs possible by networking.
  - Administration costs have not increased with sales



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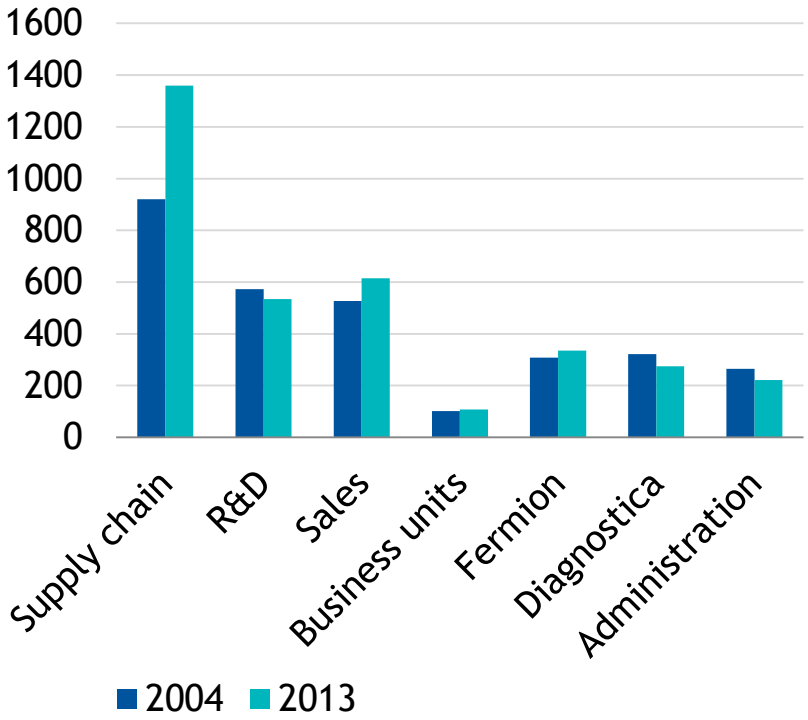
# Consistent management of the cost structure

## Employees by function




- Headcount has increased by 16% over the last 10 years from 3 000 to 3 500 while sales have increased by 80%
- In several functions there are now less people than 10 years ago
- Areas with increase
  - Large growth in supply chain is due to increase in volumes, product portfolio and regulatory requirements
  - In most sales regions there are now less people than at the peak during the last decade. Overall growth is due to:
    - establishment of presence in several countries after Simdax acquisition in mid 2009 and
    - growth in Eastern Europe



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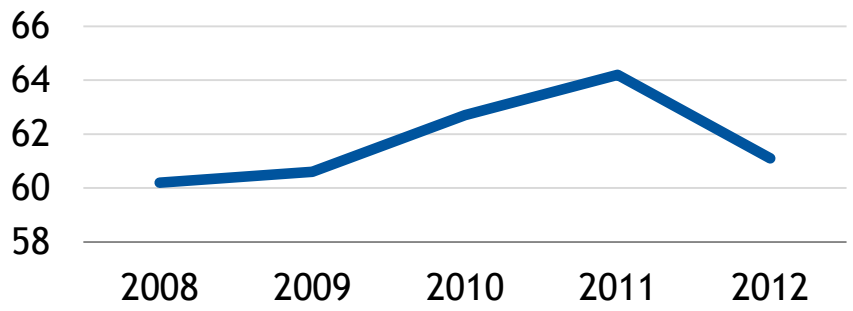
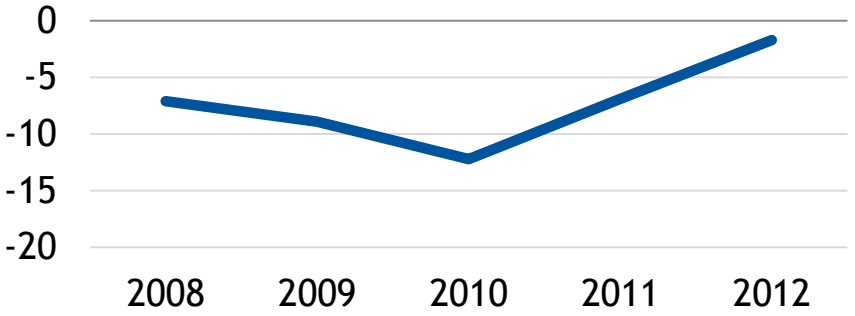
# Orion has maintained a solid financial position

- Orion has solid financial position which provides good basis for future development of the company
- Maintaining financial strength is an important goal for Orion
  - Capacity to take required R&D risks
  - Capacity to act when good opportunities are identified (organic growth, licensing, M&A)
  - Capability to continue long term development of the company also during volatile periods
  - Maintaining high dividend level

Equity ratio




Gearing



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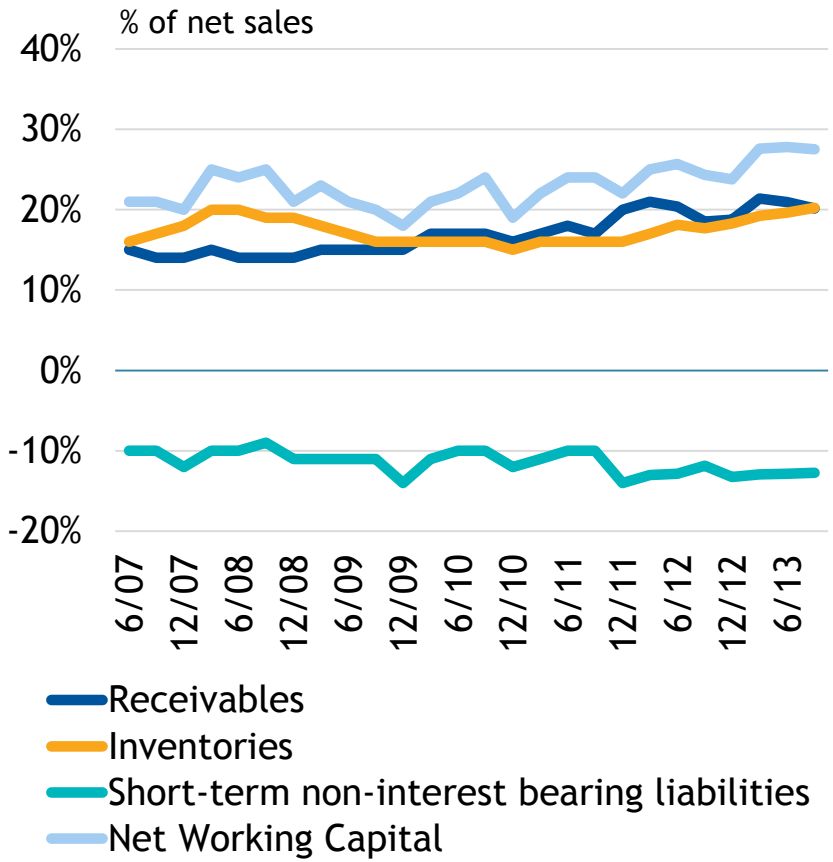
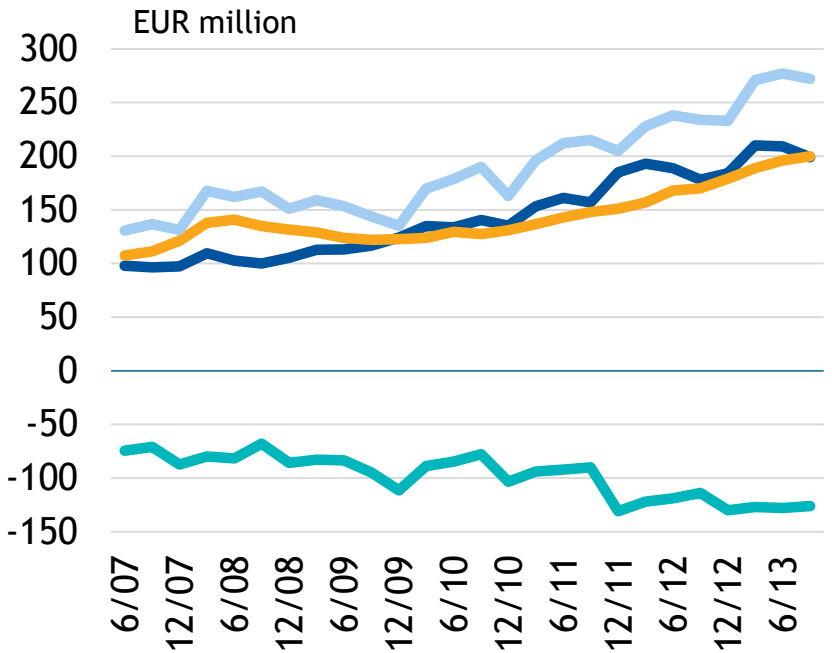
# Development of net working capital
## - Growth a little faster than sales growth




Receivables
Inventories
Short-term non-interest bearing liabilities
Net Working Capital



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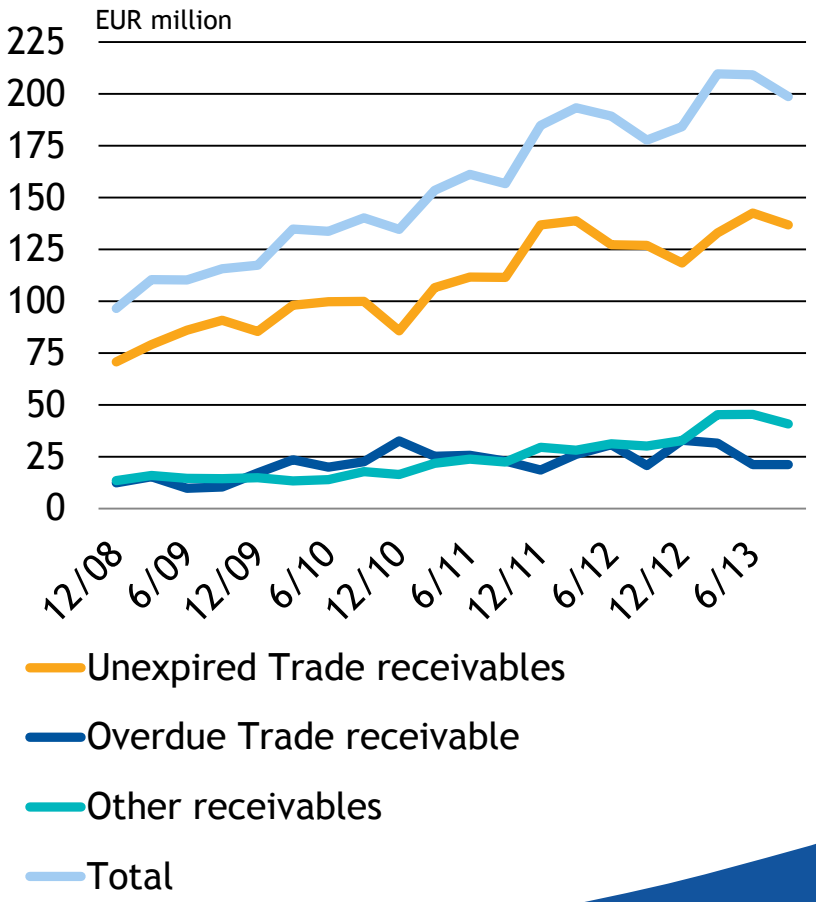
# Development of receivables
## - Overdue and bad debt under control

- Main part of growth from unexpired trade receivables which have increased clearly faster than sales
  - 25 million of the growth is due to a change in one distribution agreement
  - Growth in sales in regions with significantly longer payments terms than in Northern Europe
- Establishment of South Europe region in 2009 increased overdue trade receivable amount
  - Successful management efforts -> Amount has started to decrease
- In 2013 major growth in other receivables (accruals and advance payments)



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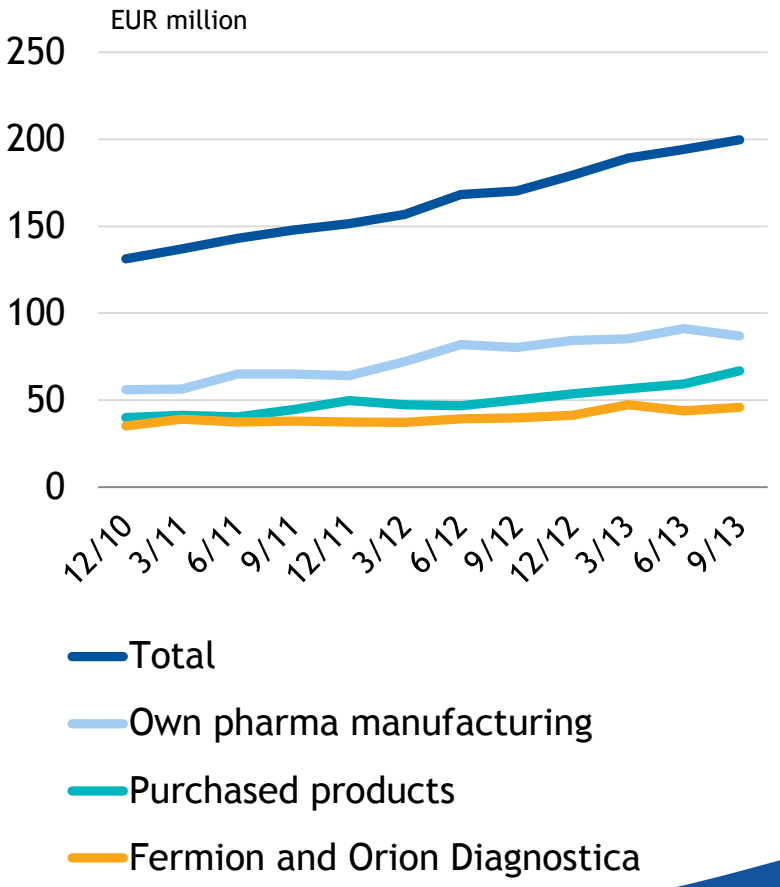
# Development of inventories
## - Increase in value of purchased products

- Inventory values started to increase faster than sales in 2011 after a relatively stabile period
- Inventories of internally manufactured goods increased fast until mid 2012
- Inventories of purchased products have increased steadily since 2010
  - Purchased volumes have increased
  - Difference in service levels between Orion and the suppliers
  - Long delivery times
- Fermion inventory development in line with growth of business and Orion Diagnostica very stabile for several years



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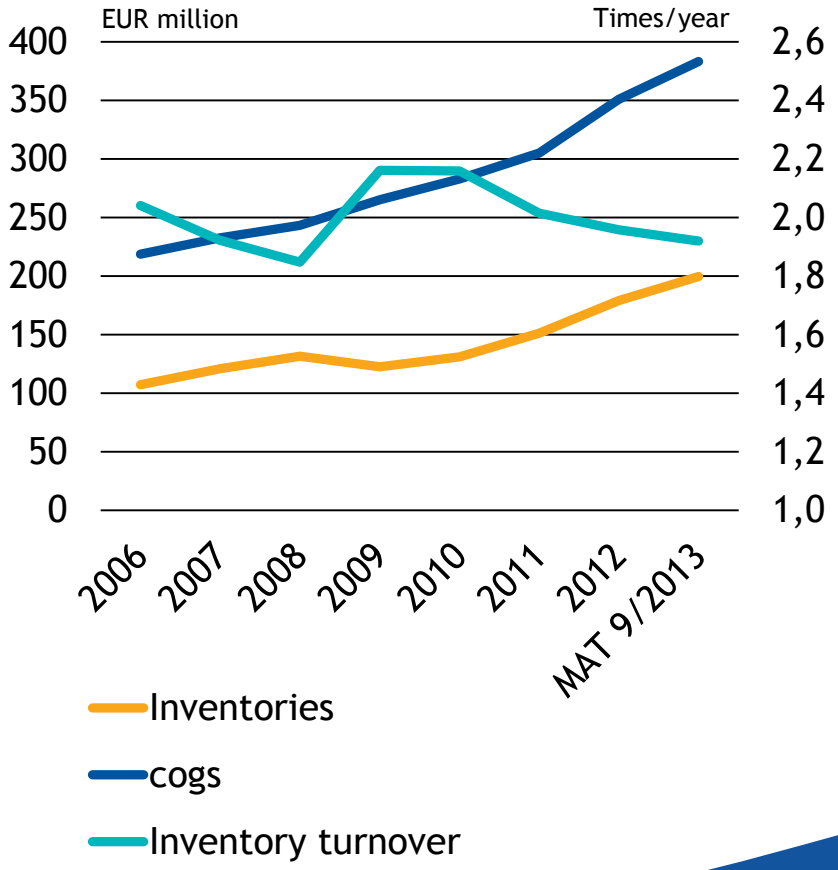
# Development of inventories
## - Inventory turnover has remained quite stabile

- Over a longer period the inventory turnover has remained quite stabile
- Main driver of the increase in inventory values have been growth of cost of goods sold
  - Ongoing change in product mix
  - Decreasing margins due to both change in product mix and overall pressure on market prices
- Also complexity of the business mix has increased
  - Larger number of products and stock keeping units (SKU)
  - Growth of sales in new regions and countries



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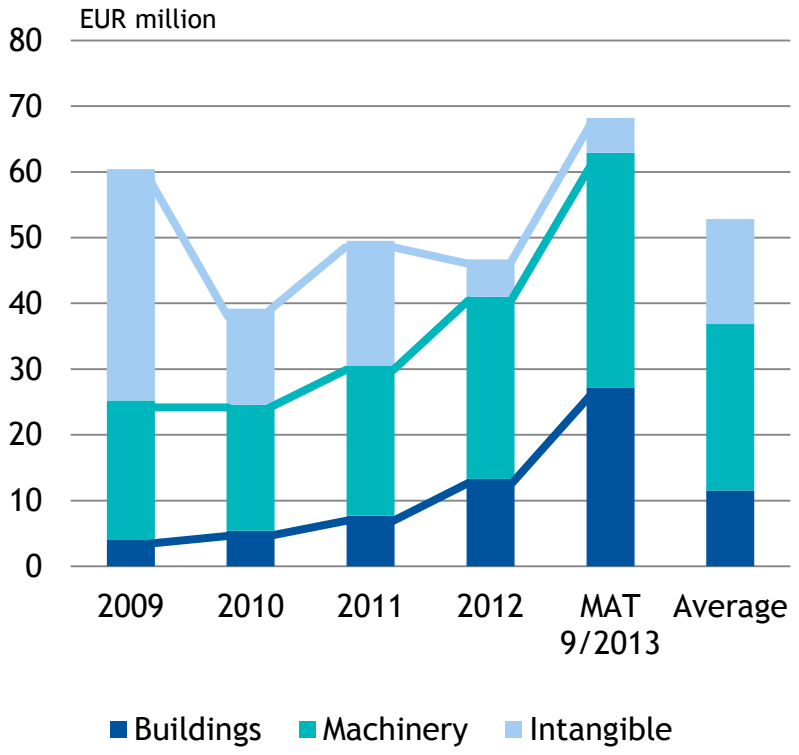
# Currently a peak in capital expenditure
## - Unusually large building investments

- Major on-going maintenance capacity increased investments have increased especially the building capex
- Also machinery capex has increased but less than investments on buildings
- Significantly lower intangible investments than in previous years
  - In-licensing capex has always been volatile and dependent on small number of larger deals
  - Recently most in-licensing type of deals have been done w/o upfront payments



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# The way forward

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# Some challenges

- Share of lower margin business areas in Orion continues to increase over the next few years
- Pricing pressures continue
  - Competition in generics, API and diagnostic products
  - Market access and reimbursement of new proprietary products
  - Global pressure on costs of health care systems
- Continuously increasing regulatory requirements
  - Increasing complexity on supply chain processes
  - Costs of developing new products

Just waiting for “new Stalevo” is not a solution

# Continuous improvement

- Orion tradition has been to improve operations and manage the cost structure all the time
  - Orion is almost a hundred year old company with long term focus
  - Need to earn dividends every year since there is no retained earnings buffer
  - Important driver behind high profitability during a long period of time

# Continuous improvement

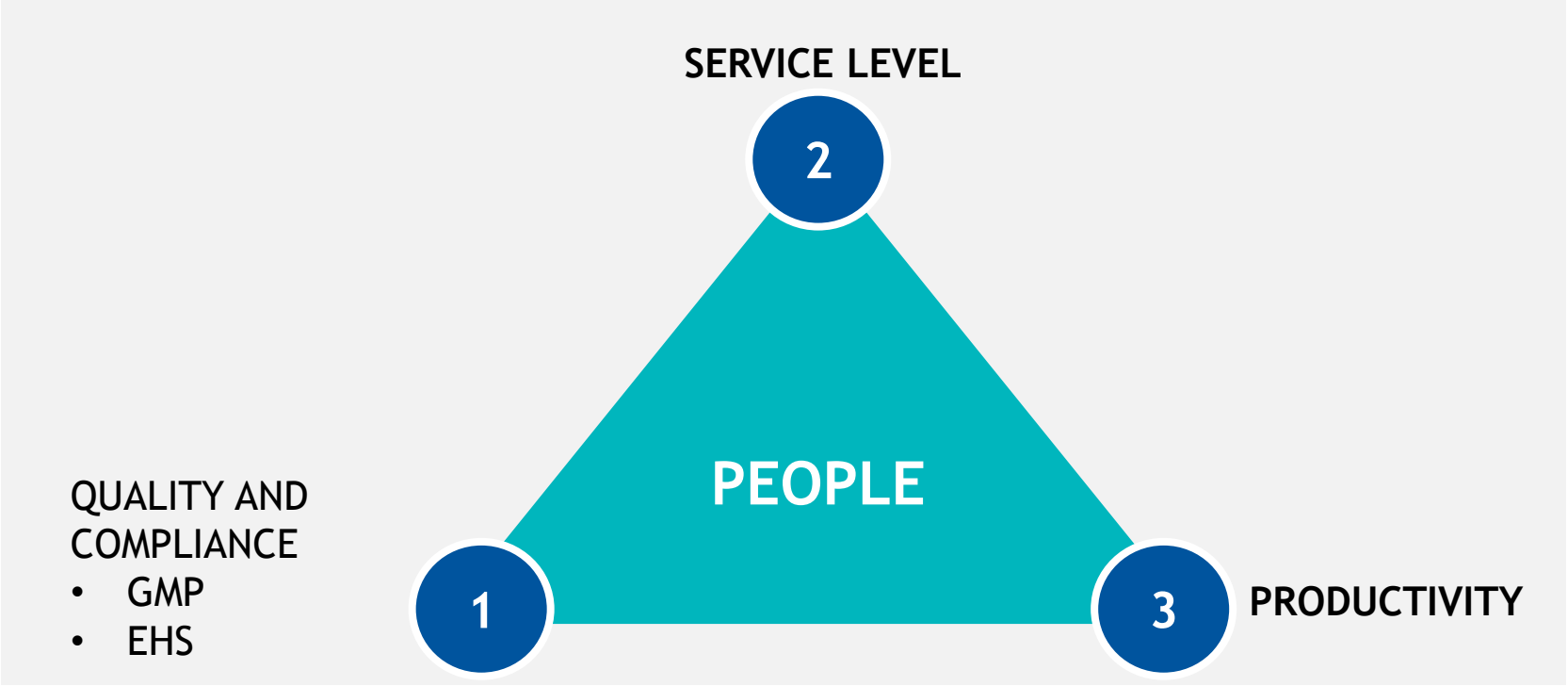
- Orion tradition has been to improve operations and manage the cost structure all the time
  - Orion is almost a hundred year old company with long term focus
  - Need to earn dividends every year since there is no retained earnings buffer
  - Important driver behind high profitability during a long period of time
- Some examples:
  - Sales operations have been adjusted consistently over the years to match resources and needs
    - Both product portfolio and geographic focus
  - Growth in R&D programs has been done by increasing networking and improving processes
    - Less people than 10 years ago
  - Realignment of Orion Diagnostica operations and product portfolio to allow growth of the future products
  - Process improvements in administrative functions
    - Less people while company has been constantly growing

# Key development programs

1. Improvement of productivity of the supply chain operations
   - To get value out of the heavy capital expenditure program
2. Improved turnover of net working capital
   - All components important but main focus on inventory management
   - Continuous process improvement taking place in purchasing where e.g. centralized in-direct purchasing function has been established
   - Collection and credit management processes have been improved
3. Reduction and management of complexity of the product portfolio
   - Systematic and regular analysis of product/brand profitability and elimination of products not generating required profitability
   - Improvement of capabilities to manage complexity to make required growth of especially generic portfolio possible
     - Generic business is by definition quite complex with large number of relatively small products

# Improvement of supply chain productivity

- Quality and compliance is essential
- Service level needs to remain high



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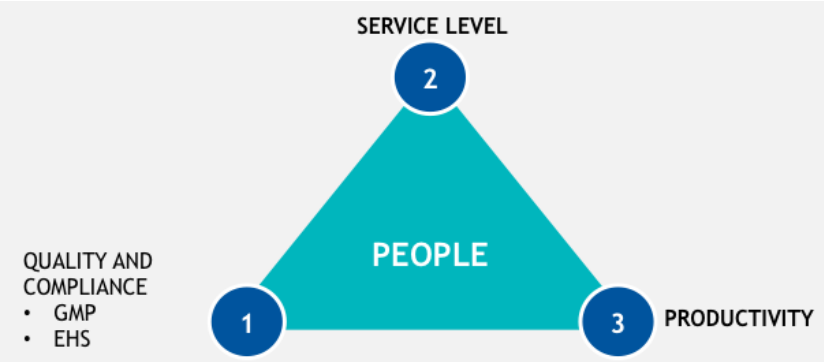
# Improvement of supply chain productivity
## - Challenging mix of goals

Service level to stay high

- Demand management
- Forecast accuracy
- Lead time reduction
- Supplier network management and optimization
- Complexity management skills




Productivity to be improved

- Product portfolio management and optimization
- Productivity improvement
- Improved capacity utilization
- Working capital optimization
- Make or buy decisions
- Investment programs optimization
- Various cost reduction initiatives



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# Faster inventory turnover

- Faster turnover without lowering service level
  - Service level needs to remain high, but it need not to be the same for all type of products and customers -> ABC classification
- Key targets
  - Reduction of inventory value of internally manufactured products and materials in production
  - Faster turnover of purchased product inventories

# Faster inventory turnover

- Faster turnover without lowering service level
  - Service level needs to remain high, but it need not to be the same for all type of products and customers -> ABC classification
- Key targets
  - Reduction of inventory value of internally manufactured products and materials in production
  - Faster turnover of purchased product inventories
- Actions going-on
  - Detailed analysis of the inventory movements
  - Action plan covering e.g. sales forecasting, safety stock levels, packaging operations, lead times in supply chain, cooperation with suppliers
  - Improved reporting and analysis
  - Continuous improvement of the processes

# Summary

## - Actions are driven by financial objectives

| Increasing net sales | Profitability at good level (EBIT > 20% of net sales) | Equity ratio at least 50% |
|---|---|---|
| - Compliance and Service level<br>- Cost competitiveness (importance increasing all the time)<br>- Active resource management (right resources in right places) | - Management of cost structure<br>- Management of complexity<br>- Product portfolio<br>- Resource management | - Good profitability<br>- Management of working capital<br>- Optimisation of capex |


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# Orion production strategy

Virve Laitinen
Senior Vice President
Supply Chain

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# Orion Pharma Supply Chain network

## Suppliers

- 2 own API plants by Fermion
- Suppliers for API +excipients
- Suppliers for packaging materials

## Production Sites

- 4 own final product manufacturing sites by Orion Pharma
- External manufacturers
- In-licensed products partners and suppliers

## Partners & own sales

- Orion subsidiaries
- European wide wholesalers and distributors network
- Strategic partners
- Key customers

## Customers

- Human products
- Veterinary products
- app. 400 products in portfolio
- app. 150 new launches annually

**EU, US and Japan GMP**



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# Orion Manufacturing Operations in Finland

**Oulu Fermion plant | ~90 employees**

- API production

**Kuopio Plant | ~50 SC employees**

Production types

- Liquids
- Suppositories

**Turku Plant | ~500 SC employees**

Production types

- Tablet & capsule production
- Hormone tablet production
- Cancer tablet production
- Hormone gel production
- Basic & medic cream production

**Espoo Plant | ~730 SC employees**

Production types

- Tablet production
- Inhalation production
- Injection production

**Salo Plant | ~30 SC employees**

- Centralised warehouse
- Tablet packaging

**Hanko Fermion plant | ~160 employees**

- API production



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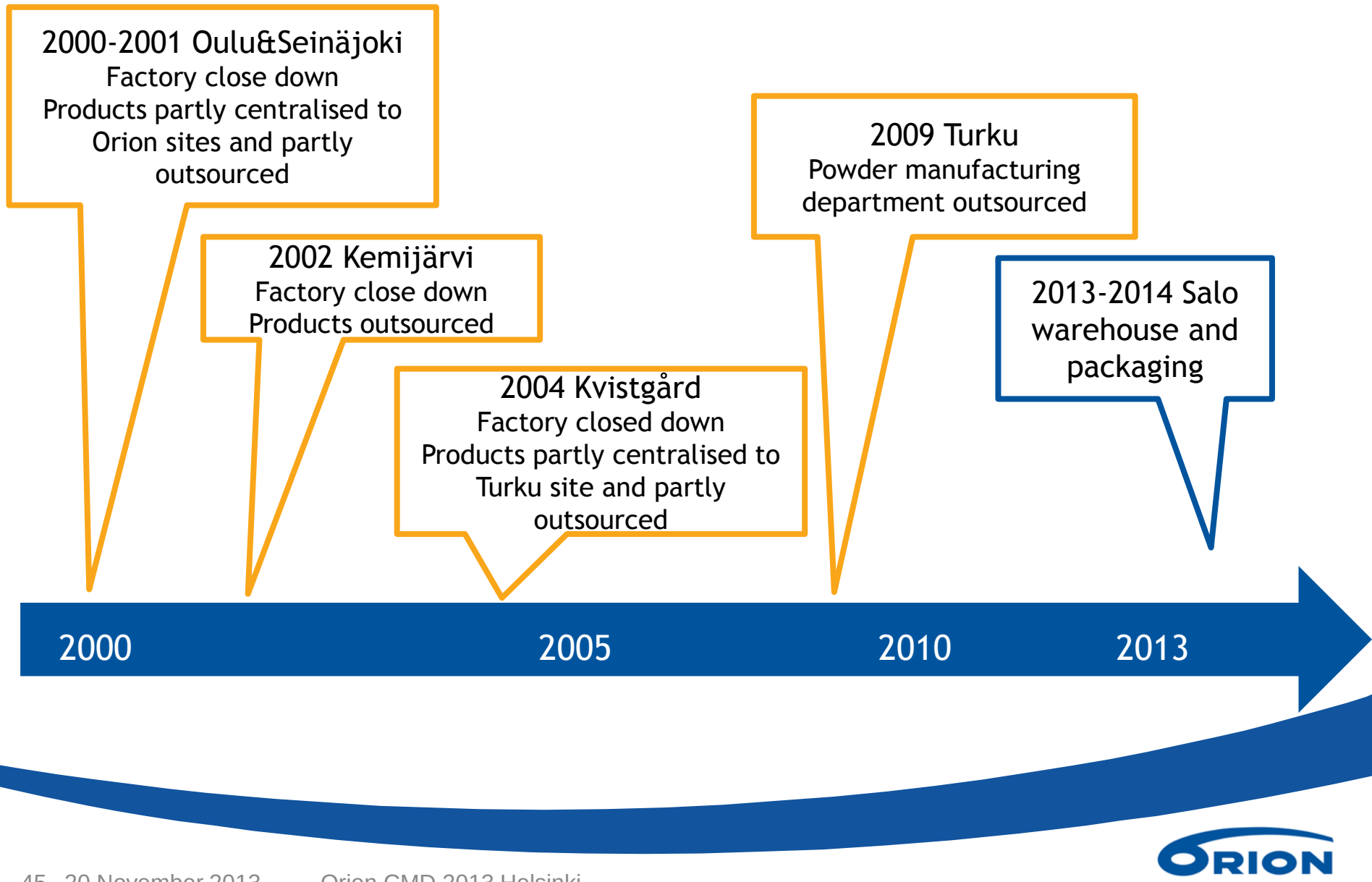
# Production footprint development



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# Production strategy evaluations – focus areas

| | | Strategic position |
|---|---|---|
|  | **Tablet manufacturing and packaging** | • Strategic products:entacapone, key RX and generic products<br>• Espoo and Turku:tablet manufacturing capacity<br>• Salo:centralised packaging operations and warehousing<br><br>• Close down one tablet department during 2014 |
|  | **Small volume parenterals Injections and ampouls** | • Strategic products:Simdax and *dexdor*®<br>• Close down some production technologies during 2015 |
|  | **Easyhaler inhalation technology** | • EH specific manufacturing and analytic technology in-house<br>• Investment program on-going to increase capacity according to business needs |
|  | **Hormone gel production and packaging** | • Hormone gel manufacturing capacity expansion on-going<br>• Focus area for growth opportunities by contract manufacturing services |

# Orion's production focus areas

Salo Plant

Packaging and warehouse operations by end of 2014

Espoo Plant

Easyhaler inhalation production capacity expansion

Espoo Plant

Tablet production rationalisation

Turku Plant

Hormone gel production expansion

| EUR million | 2010 | 2011 | 2012 | Estimate 2013 |
|---|---|---|---|---|
| CAPEX | 38 | 49 | 50 | 80 |



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# How do we develop our competitiveness?

## Quality and Compliance

- Ensure robust compliance level with justified Orion approach
- Culture:quality on the shop floor
- Right first time execution

## Service Level

- Implement customer centric approach
- Change from supply to demand driven
- Optimise end to end processes
- One joint Orion supply chain approach

## Productivity

- Lower costs to improve margins
- Optimise procurement
- Improve plant efficiency
- Simplify operations
- Optimise CAPEX

Lean process driven operating models



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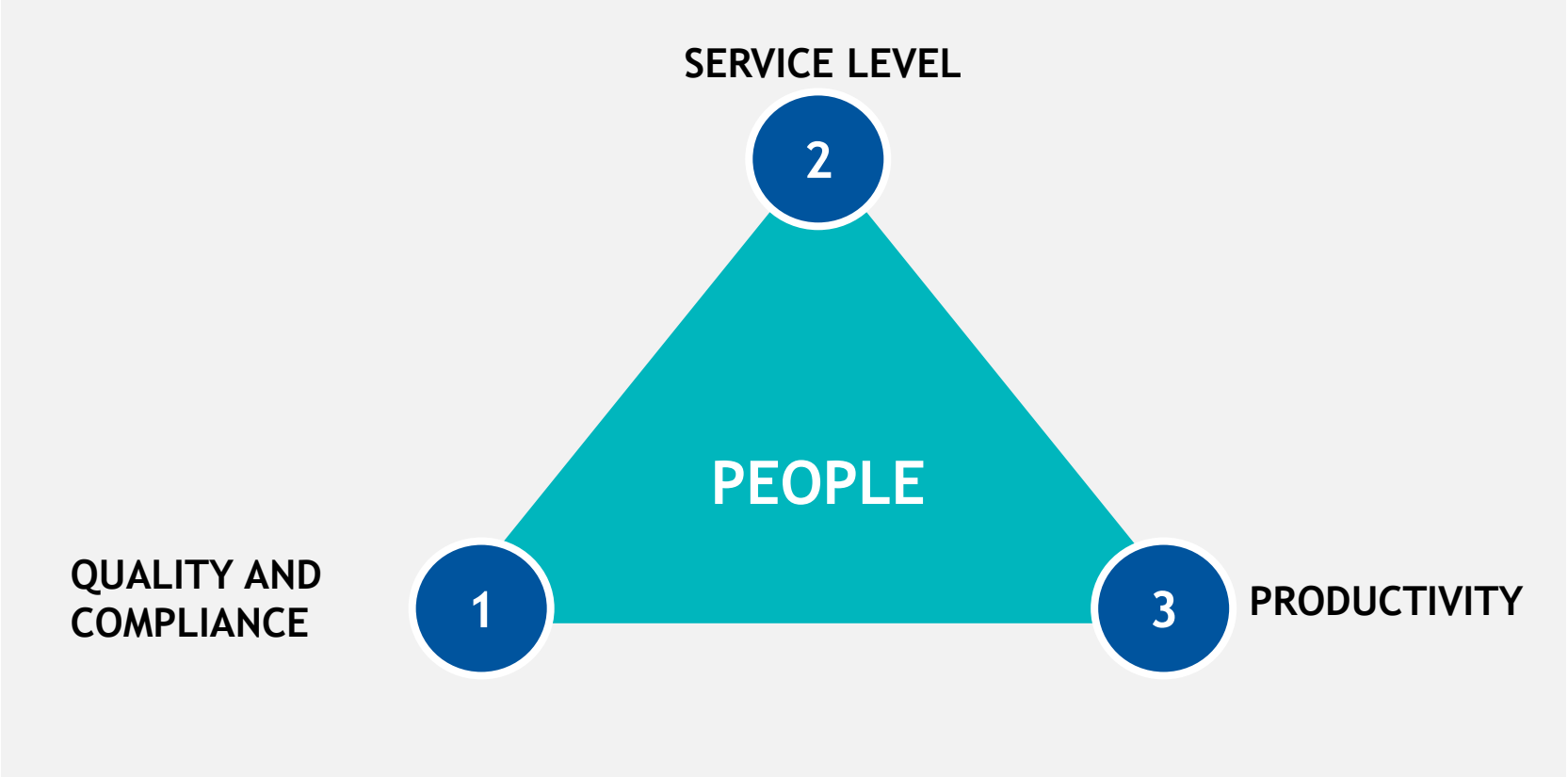
# Orion Supply Chain focus areas: Quality & compliance, service level and productivity



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# R&D pipeline review

Reijo Salonen
Senior Vice President
R&D

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# Key clinical pharmaceutical development projects

| Project | Indication | Clinical phases | | | Registration |
|---|---|---|---|---|---|
| | | I | II | III | |
| Easyhaler® budesonide-formoterol | Asthma, COPD | ● | ● | ● | ○ |
| Stalevo® for Japanese markets [1)] | Parkinson's disease | ● | ● | ● | ○ |
| Easyhaler® salmeterol-fluticasone | Asthma, COPD | ● | ● | ○ | |
| ODM-101 (more effective levodopa product) | Parkinson's disease | ● | ● | | |
| ORM-12741 (alpha-2c adrenoceptor antagonist) | Alzheimer's disease | ● | IIa | | |
| ODM-201 (androgen receptor inhibitor) | Advanced prostate cancer | ● | ● | | |
| ODM-103 (more effective COMT inhibitor) | Parkinson's disease | ○ | | | |
| ODM-104 (more effective COMT inhibitor) | Parkinson's disease | ○ | | | |
| ODM-102 (alpha-2c adrenoceptor antagonist) | Alzheimer's disease | ○ | | | |

[1)] Conducted by partner Novartis

● Phase completed ○ = Phase ongoing



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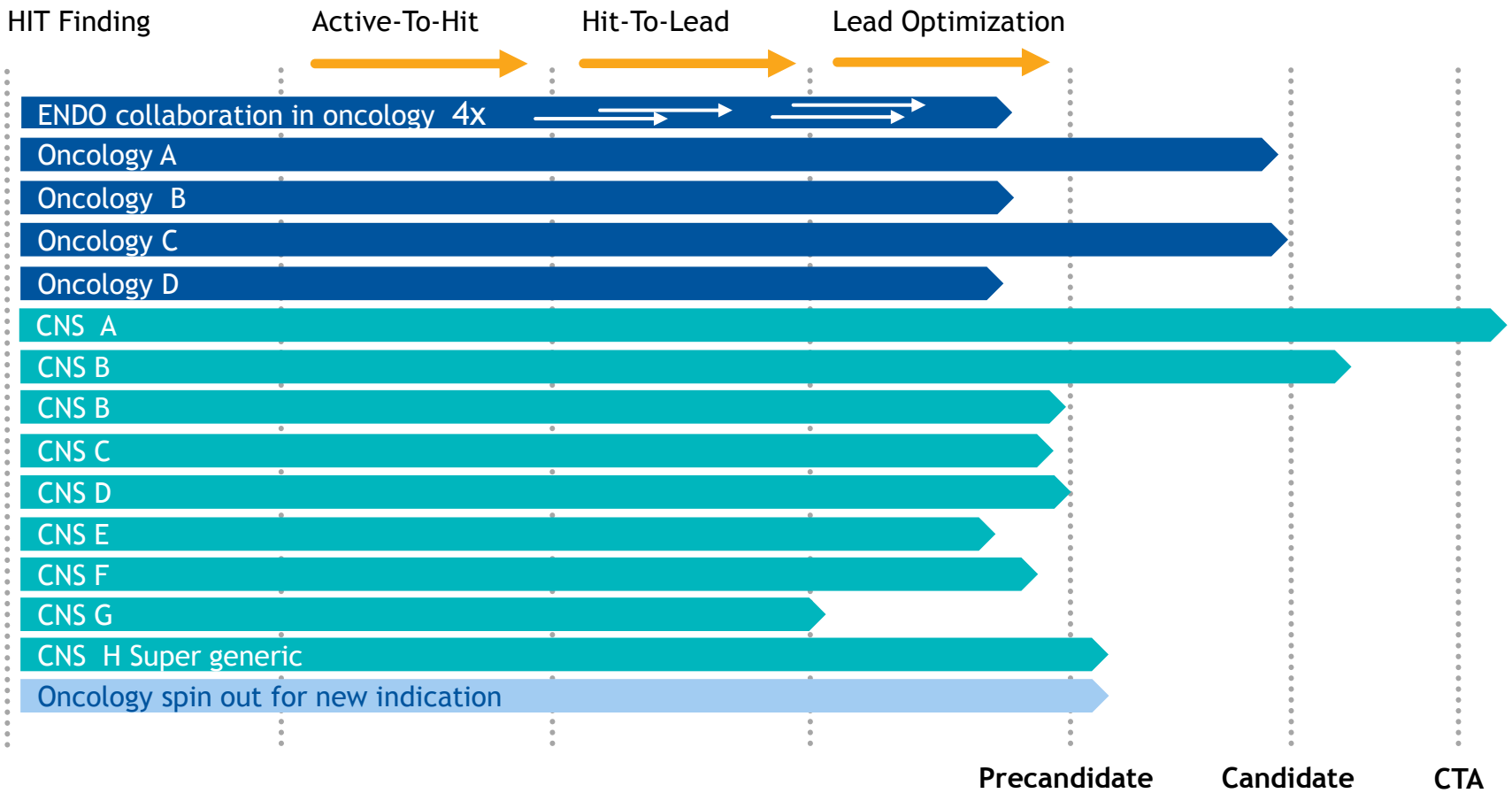
# Research projects 2012 (18)



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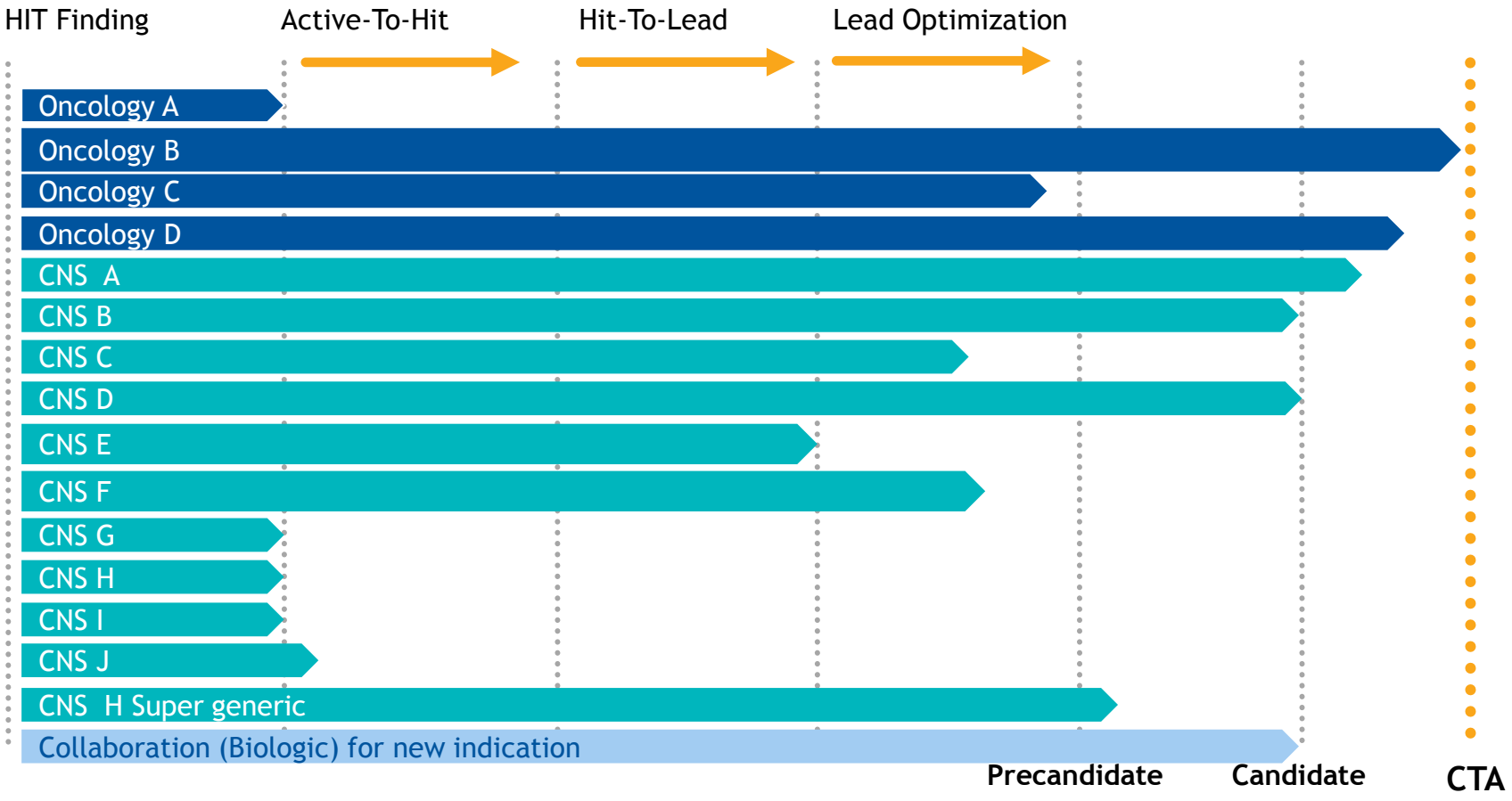
# Research projects 2013 (16)



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# ODM-201 – a new generation androgen receptor (AR) inhibitor for prostate cancer

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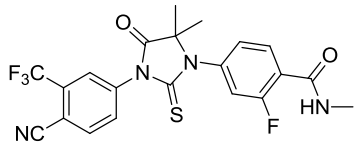
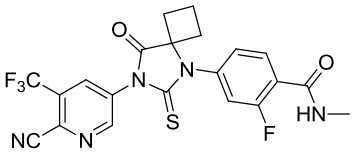
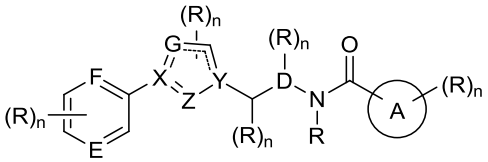
# ODM-201 has a unique profile



Enzalutamide
(MDV-3100)

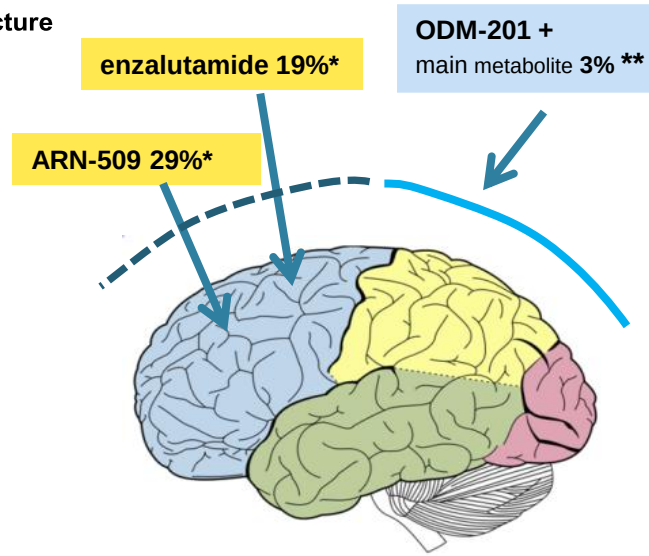


ARN-509



General chemical structure
for ODM-201

| Compound | AR affinity Ki (nM) | Antagonism WT AR IC50 (nM) | Proliferation VCaP IC50 (nM) |
|---|---|---|---|
| enzalutamide | 78 | 155 | 400 |
| ARN-509 | 53 | 168 | 300 |
| ODM-201 | 9 | 65 | 500 |
| ORM-15341 (main metabolite) | 8 | 25 | 600 |




*Refs. Clegg et al, Cancer Research 2012; Forster at al, Prostate 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

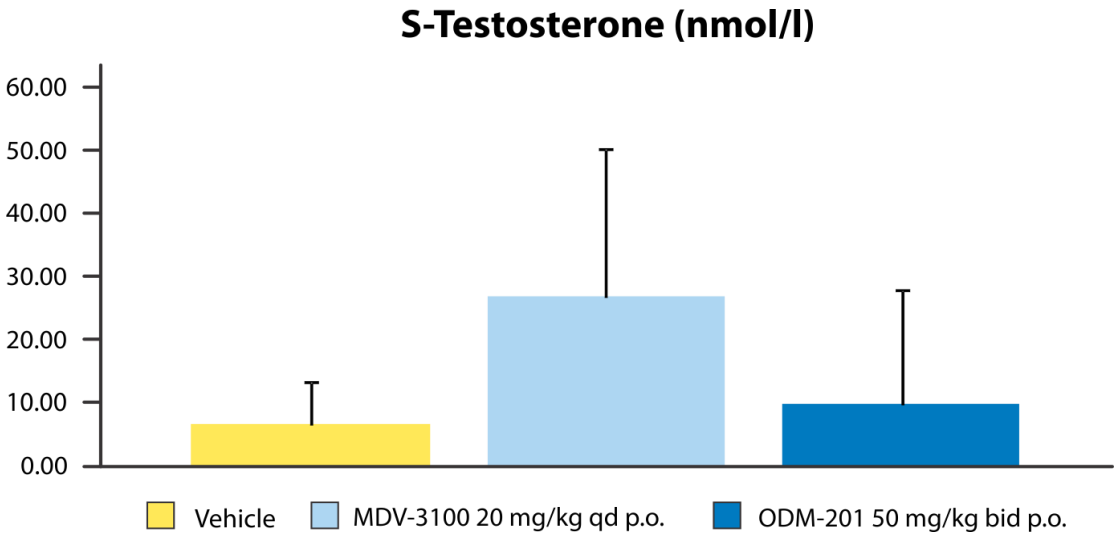
- No brain entry
- No CYP inhibition or induction expected with therapeutic doses



Source: ECC2013 poster E17-2119

# ODM-201 does not increase serum testosterone levels in vivo

Serum testosterone levels in xenograft after 3-wk dosing in mouse

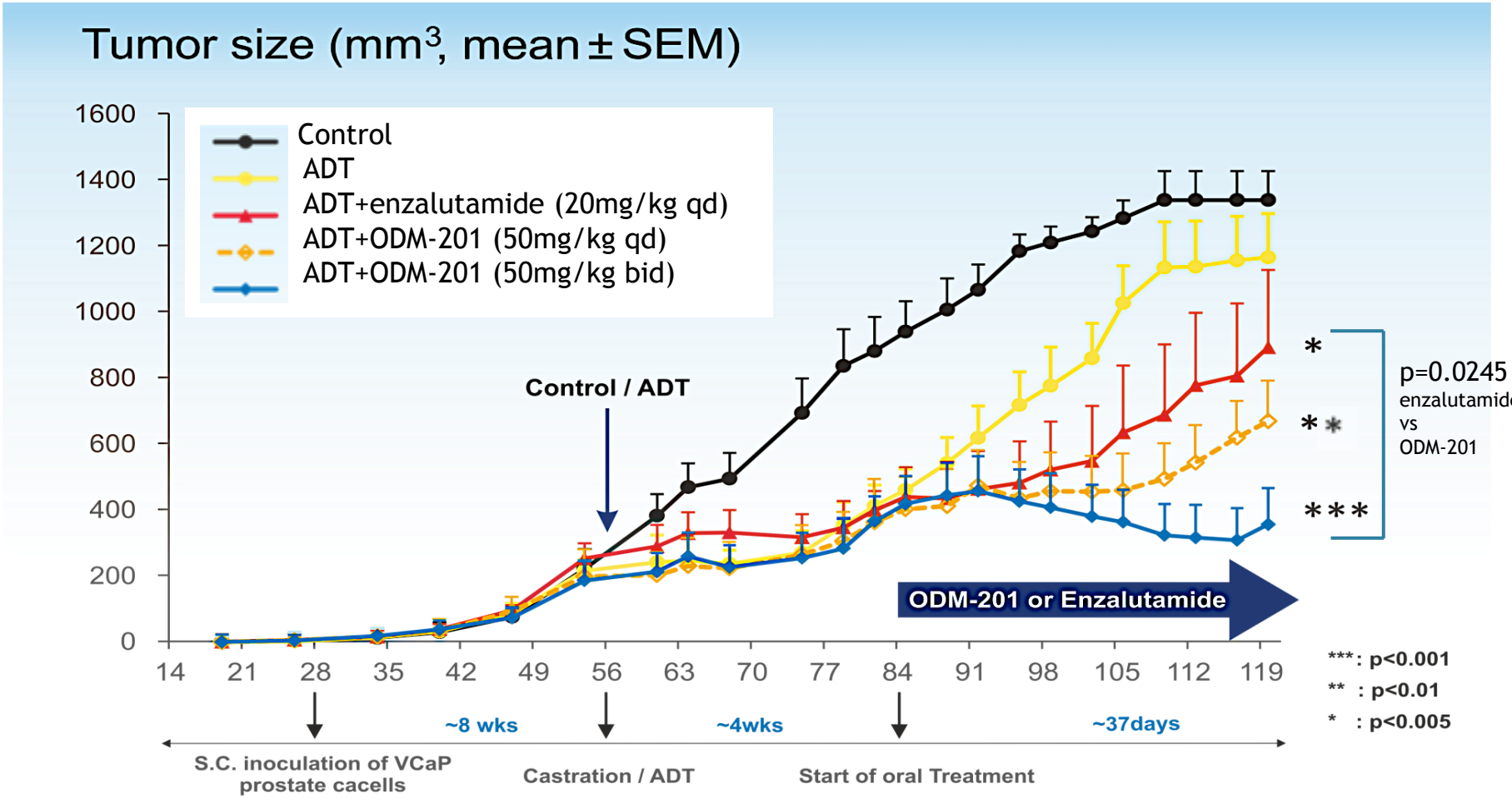



- ODM-201 does not increase serum testosterone levels like enzalutamide in mouse
- In CRPC patients, enzalutamide reported to increase bone marrow testosterone**

**Ref. Efstathiou et al., 2011 J Clin Oncol abstract

# Superior inhibition of tumor growth by ODM-201 in castration-resistant mouse VCaP xenograft model

- Derived from a bone metastasis of a patient with CRPC
- Contains endogenous (wild type, non-mutated) AR gene amplification and AR overexpression




Presented at 2013 ASCO GU
Fizazi et al. ASCO GU 2013

# ODM-201 ARADES Phase I/II Study Design

| STUDY PHASES: | P1 Dose escalation | P2 Dose expansion |
|---|---|---|
| GOAL: | Tolerability - MTD | Define dose for further clinical trials |
| OBJECTIVES: | Safety, PK, Efficacy | Safety, Efficacy |

| P1 Dose escalation | P2 Dose expansion | |
|---|---|---|
| 900 mg bid | 700 mg bid | CYP17i-naïve, chemo-naïve |
| 700 mg bid | 200 mg bid | CYP17i-naïve, post-chemo |
| 500 mg bid | 100 mg bid | Post-CYP17i |
| 300 mg bid | | |
| 200 mg bid | | |
| 100 mg bid | | |

Progressive mCRPC
Post/naïve chemo/CYP17i
n=24

Progressive mCRPC
Stratification by dose and treatment history
Planned 35 patients in each dose level

# ARADES Phase I/II inclusion/exclusion criteria

## Key inclusion criteria

- Progressive mCRPC
- Chemotherapy-naïve or ≤ 2 prior chemotherapy regimens
- Prior CYP17-inhibitor therapy allowed
- **Obligatory prior use of an AR inhibitor (bicalutamide, etc)**

## Key exclusion criteria

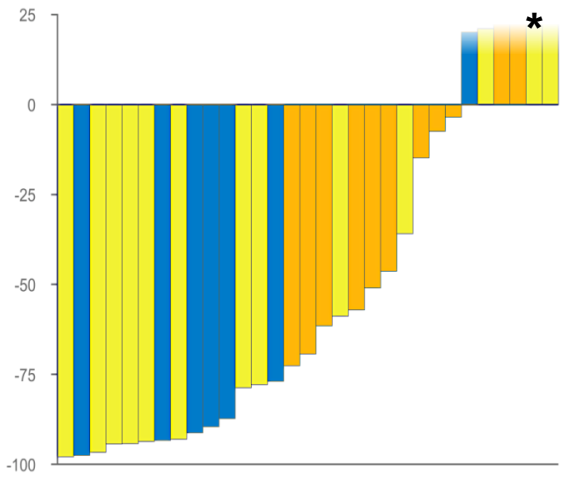
- Prior therapy with enzalutamide or any investigational AR antagonist
- **Patients with history of seizures or at risk of seizures were not excluded**

# Demography for ARADES phase I/II
## (doses 100mg bid / 200mg bid / 700mg bid)

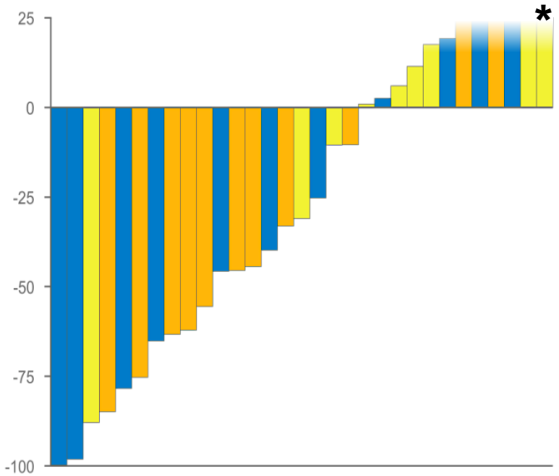
| ITT population | Chemo-/ CYP 17i-naïve (n = 37) | Post-chemo/ CYP 17i-naïve (n = 32) | Post-CYP17i (n = 55) |
|---|---|---|---|
| Age (median years, range) | 73 (55-83) | 67 (53-82) | 69 (55-89) |
| Baseline PSA (median ng/mL, range) | 101 (2.7-1294) | 94 (8.4-663) | 139 (8.9-5000) |
| Baseline CTC count ≥ 5 | 47% | 45% | 49% |
| Disease localization | | | |
| Bone | 86% | 84% | 87% |
| Lymph nodes | 51% | 44% | 44% |
| Visceral | 27% | 26% | 31% |

# In ARADES I/II study 12 wk PSA response was most pronounced in Chemo-/CYP17i naive patients

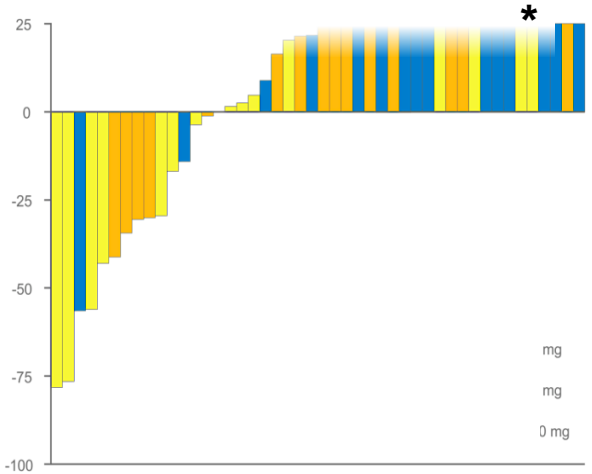
**Chemo-/CYP17i-naïve**




**Post-chemo/CYP17i naïve**




**Post-CYP17i**




**≥ 50% PSA response rate 86% at 700mg bid**

100 mg bid 200 mg bid 700 mg bid

*Data truncated at +25%



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# Most common (>10%) adverse events in ARADES study by grade

| Follow-up until week 12 | N of patients (%) (N=124) | | |
|---|---|---|---|
| | Grade 1-2 | Grade 3 | Grade 4 |
| Fatigue /Asthenia | 30 (24%) | 1 (1%) | - |
| Back pain | 17 (14%) | 1 (1%) | - |
| Constipation | 16 (13%) | - | - |
| Nausea | 13 (10%) | 1 (1%) | - |
| Pain | 13 (10% ) | 1 (1%) | - |
| Decreased appetite | 12 (10%) | - | - |

- No clear evidence that any observed toxicity is drug related
- No related seizures - one case of convulsion was reported 27 days after stopping treatment
- Safety profile after longer treatment period remains similar

# Conclusions from clinical studies

**ODM-201 is a safe and well tolerated treatment**

- Adverse events were mostly mild, and seemed to be related to prostate cancer or concomitant diseases

**High response rate in chemo/CYP17i-naïve patients**

- 700 mg bid has the best responses in chemo-/CYP17i-naïve patients. High dose further supported by efficacy data of the formulation bridging study (data to be presented in 2014)

**Pharmocokinetic data from ARAFOR formulation bridging study suggest that the new tablet formulations can be used in future confirmatory trials**

# Future studies with ODM-201

**A Phase 3 study in nmCRPC patients is scheduled to start recruitment in Q2/2014**

- Patients at high risk for developing metastasis as assessed by PSA doubling time
- To demonstrate the efficacy of ODM-201 for delaying progression to metastatic disease
- Over 300 sites in more than 20 countries
- The study was discussed with EMA and FDA as part of end of phase 2 advice process

**Discussions ongoing with partner candidates about other studies (phase 2 and 3)**

# Alpha2C ORM-12741 for Alzheimer's disease

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# Introduction -Alpha-2 adrenoceptor (AR) subtypes

**alpha$_{2A}$ AR**

- the "major subtype"
- universally expressed
- mediates most of the prominent effects of subtype-nonselective alpha-2 agonists

**alpha$_{2B}$ AR**

- expressed mainly in the periphery, but also in the thalamus
- role in peripheral vasoconstriction

alpha$_{2C}$ AR

- physiological fine tuner of synaptic neurotransmission
- expressed mainly in the CNS (striatum, not in locus coeruleus) in the rat, monkey and human
- no significant contribution to the alpha-2 agonist -mediated sedation or cardiovascular effects

# Introduction – ORM-12741

- ORM-12741 is a highly potent and selective alpha-2C adrenoceptor antagonist
- Rodent models predict beneficial effects on cognition and neuropsychiatric symptoms
- Safe and well tolerated in Phase 1 studies

# ORM-12741 Phase 2a Study in Alzheimer's Disease

## Objective

- To evaluate safety and efficacy of ORM-12741 in treatment of cognitive and behavioral symptoms of Alzheimer's disease

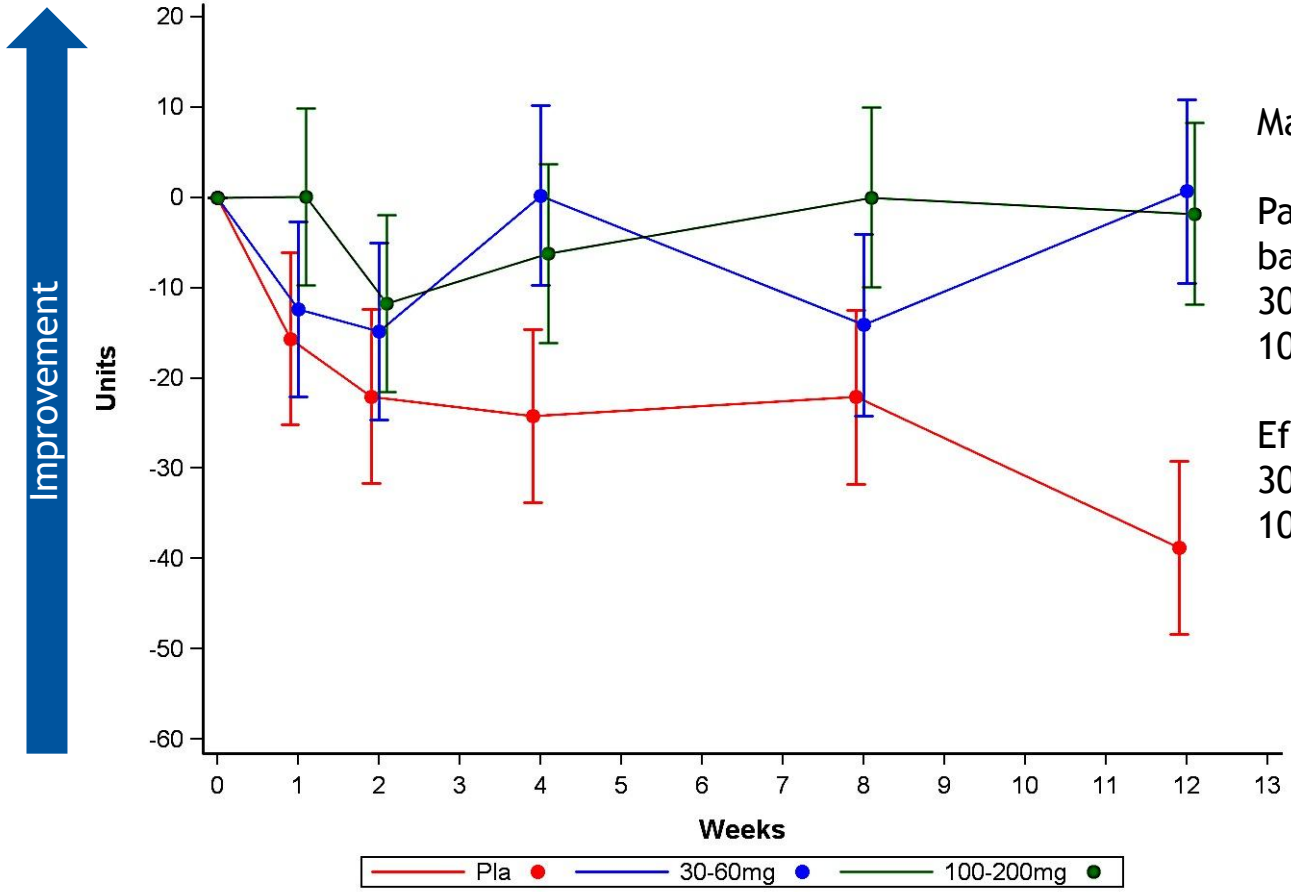
## Design and Methodology

- Randomised, double-blind, placebo-controlled, parallel-group Phase 2a study in 100 pts
- Patients with moderately severe Alzheimer's disease (MMSE 12 - 21)
- Behavioural and psychological symptoms present (NPI ≥ 15)
- All on stable dose of donepezil, rivastigmine or galantamine for at least 3 mo
- 2 dose levels of ORM-12741 and placebo for 12 weeks as an add-on therapy

## Main Endpoints

- A battery of computerized neurocognitive tests (CDR System)
  - Pre-specified primary emphasis on composite scores for Quality of Episodic Memory, Quality of Working Memory, Speed of Memory and Power of Attention
- Neuropsychiatric inventory (NPI)
- Safety: AEs, vital signs, safety lab, ECG

# Clear and statistically significant positive treatment effect on Quality of Episodic Memory (ITT population, changes from baseline)




Main treatment effect p=0.03

Pairwise comparisons from baseline up to week 12:
30-60 mg vs. placebo, p=0.046
100-200 mg vs. placebo, p=0.012

Effect size at week 12:
30-60 mg vs. plac 1.09
100-200 mg vs. plac 1.02



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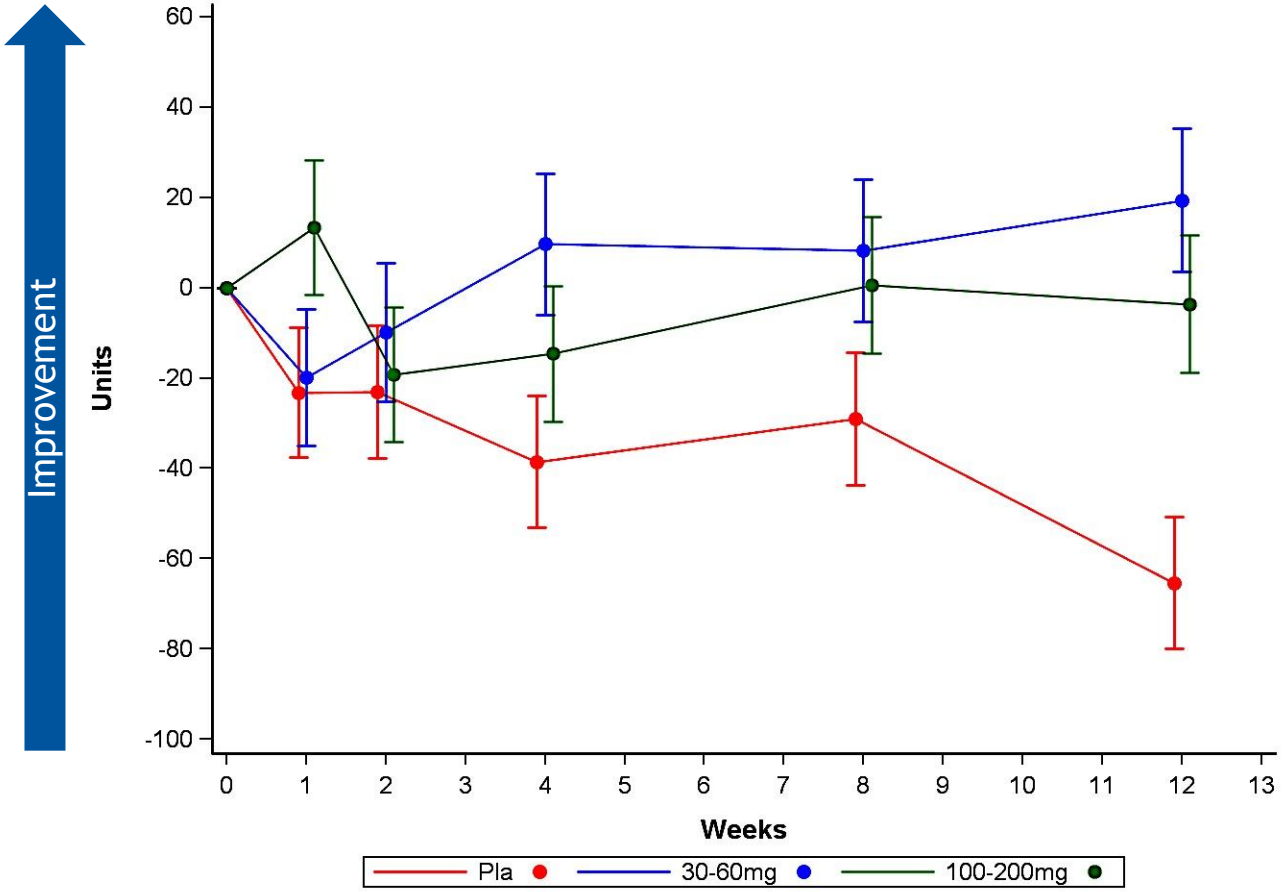
# Clear and statistically significant positive treatment effect on Quality of Memory (ITT population, changes from baseline)




Values are LSMeans (SEM)

Main treatment effect p=0.013

Pairwise comparisons from baseline up to week 12:
30-60 mg vs. placebo p=0.006
100-200 mg vs. p=0.019



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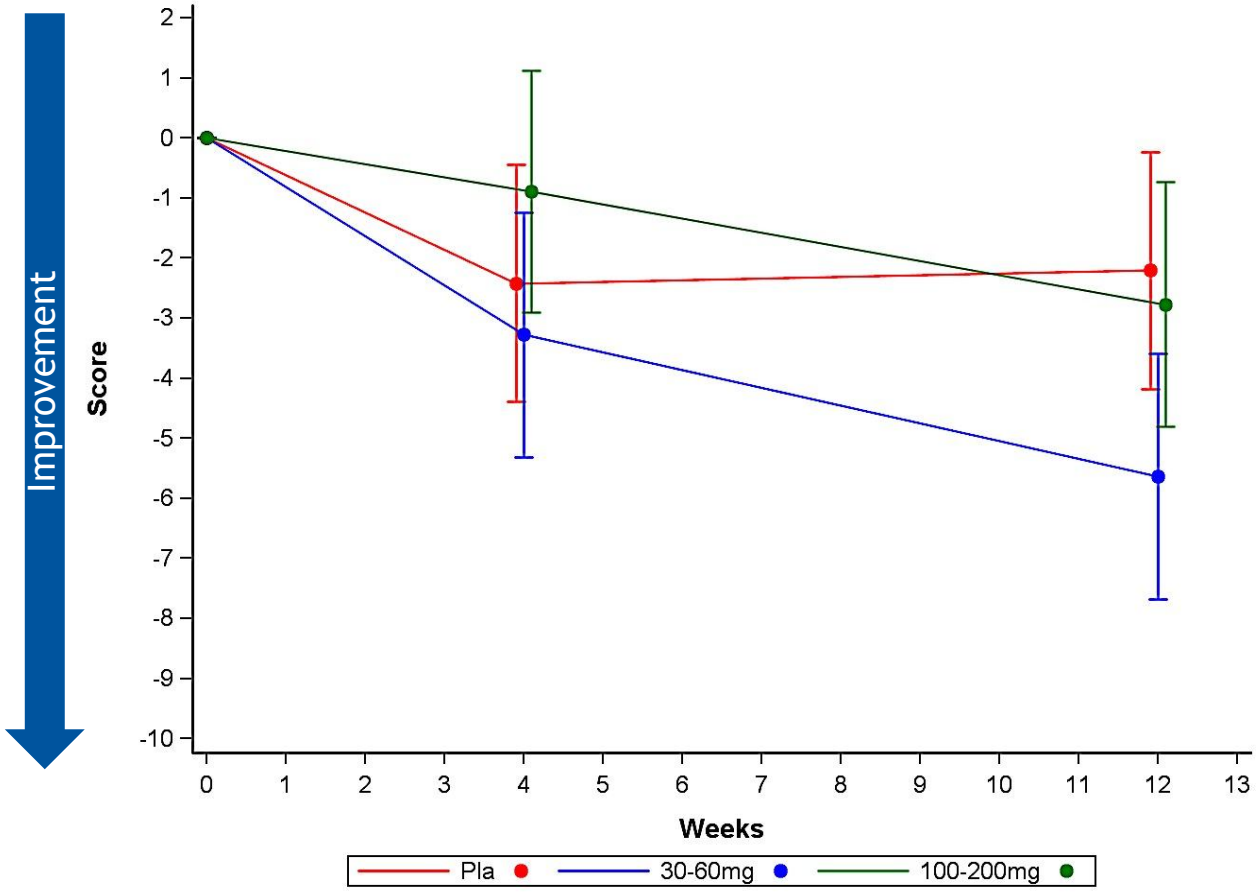
# Trend for positive treatment effect in Neuropsychiatric Inventory (NPI) total score for the low dose group (ITT population, changes from baseline)




Values are LSMeans (SEM)

Main treatment effect p=0.12

Pairwise comparisons from baseline up to week 12:
30-60 mg vs. placebo p=0.11
100-200 mg vs. placebo p=0.72

**NPI domains**
Delusions
Hallucinations
Agitation/Aggression
Depression/Dysphoria
Anxiety
Elation/Euphoria
Apathy/Indifference
Disinhibition
Irritability/Lability
Aberrant motor behaviour



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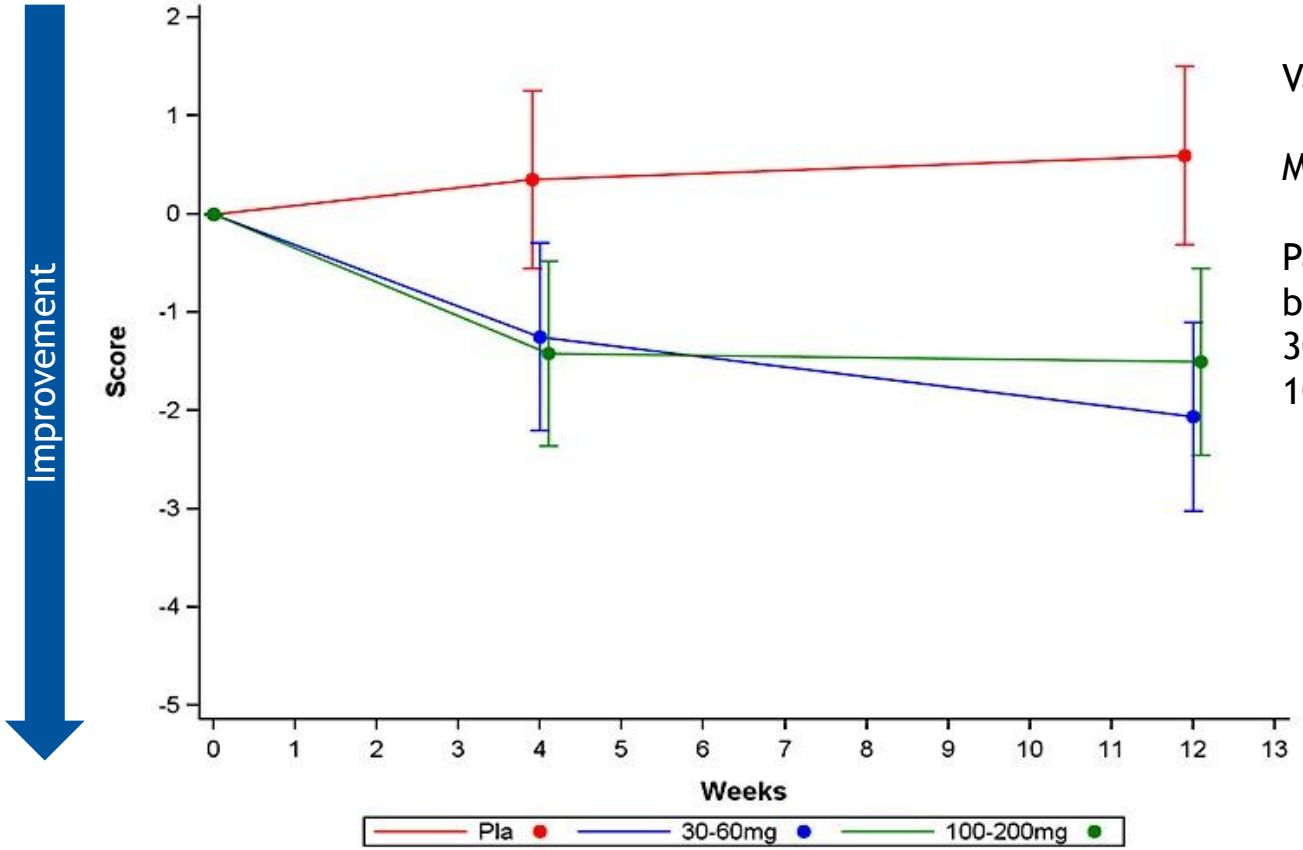
# Clear and statistically significant positive treatment effect on Neuropsychiatric Inventory (NPI) Caregiver Distress score
## (ITT population, changes from baseline)




Values are LSMeans (SEM)

Main treatment effect p=0.034

Pairwise comparisons from baseline up to week 12:
30-60 mg vs. placebo p=0.020
100-200 mg vs. placebo p=0.031



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# ORM-12741 Phase 2a Study - Conclusions

- Clear positive effects on memory measures on active treatment groups as compared to placebo
  - No clear differences in efficacy between the active dose groups
- A clear positive treatment effect in NPI Caregiver Distress score for both doses and a positive trend in NPI total score for low dose
- ORM-12741 was generally well tolerated

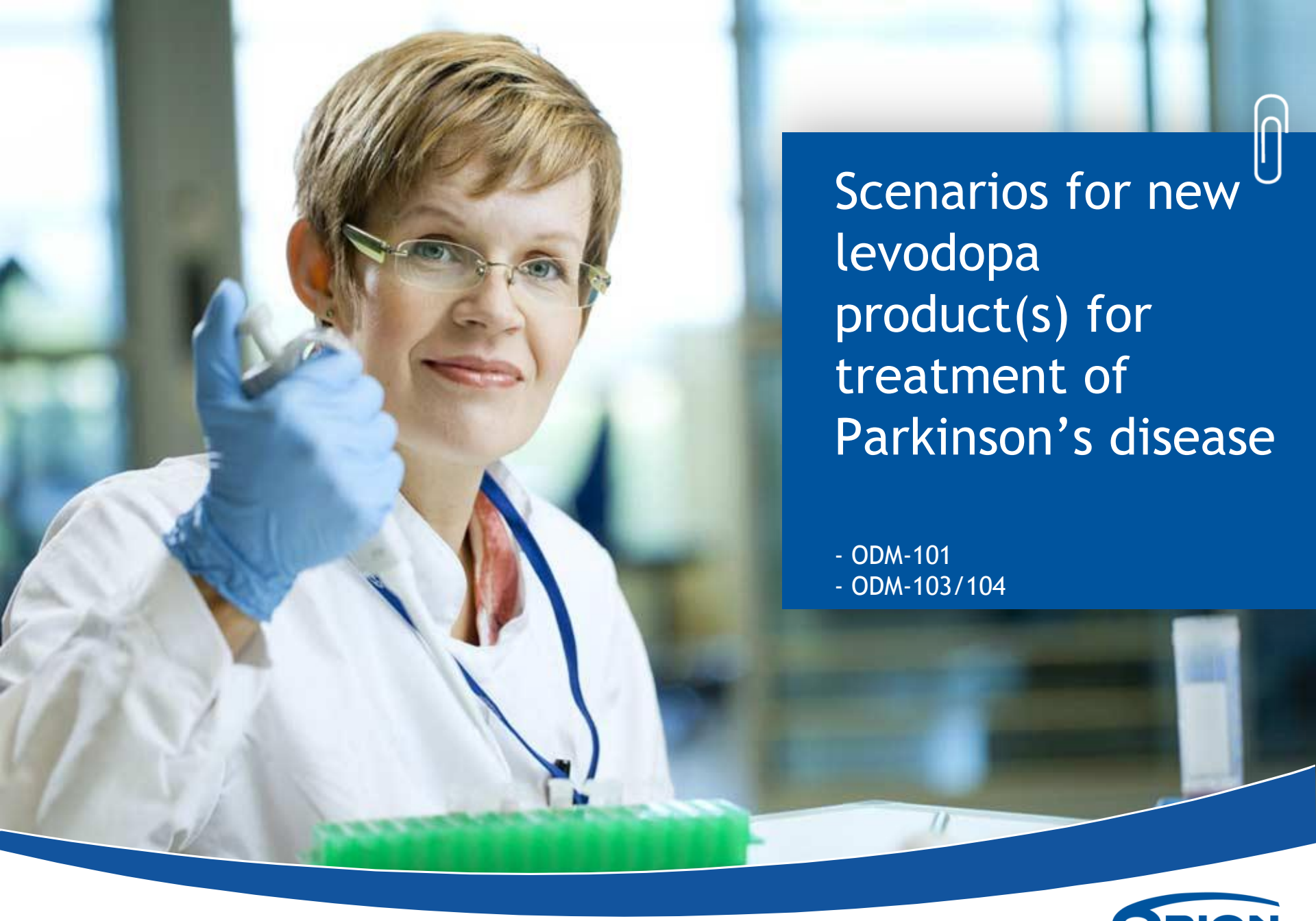
The results merit further exploring efficacy and safety of ORM-12741 in AD patients.

# ORM-12741 Drug development for treatment of AD
# Next Steps

- Phase 2b in AD patients focusing on
  - Confirmation of Phase 2a results in larger population
  - Additional endpoints
  - Dosing
- Development options for Phase 3

  Cognition
  - ✓ Pros': Several compound shown to work, clear study designs, endpoints & regulatory path
  - ✓ Cons': Old generic drugs on market, new competitors in pipeline, lower prize expectation than for the latter

  Neuropsychiatric symptoms
  - ✓ Pros': Huge unmet need, less competition, high value
  - ✓ Cons': Endpoints & regulatory path less clear – need clarification before Phase 3
- Emphasis of the study and designs currently discussed with partner candidates



# Scenarios for new levodopa product(s) for treatment of Parkinson's disease

- ODM-101
- ODM-103/104

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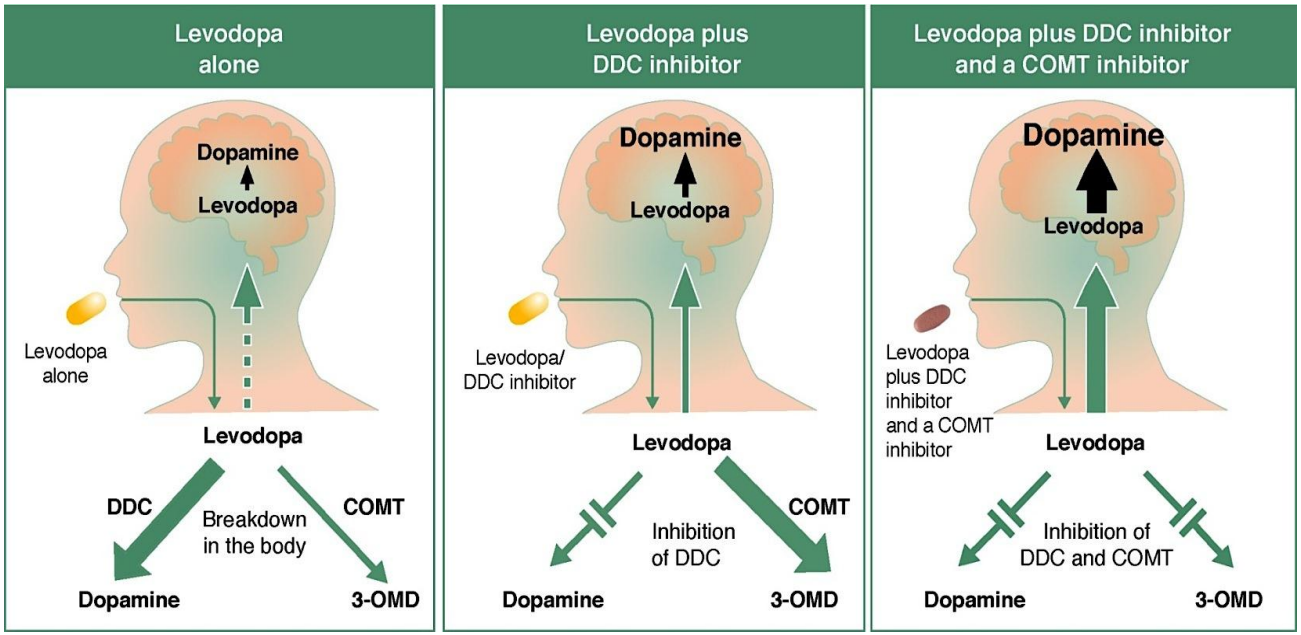
# Main assumptions for new Orion levodopa product(s)

There is a continuing unmet need for peroral levodopa products with improved efficacy which could be achieved by:

- Increasing COMT-inhibition (ODM-103/104)
- Improving levodopa formulation
- Increasing AADC-inhibition (ODM-101)
- Any combination of the 1, 2 and 3 (potentially synergistic)



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# ODM-101

- Fixed combination tablet for peroral administration of levodopa, carbidopa and entacapone
- The ratios, strengths and pharmaceutical formulations of levodopa, carbidopa and entacapone have been improved
- The target indication of ODM-101 is Parkinson´s disease and end-of-dose motor fluctuations - the same as currently Comtess®/Comtan® and Stalevo®.

# ODM-101 PoC study

- Efficacy and safety of ODM-101 compared to a standard combination (Stalevo®); a randomized, double-blind, crossover, proof of concept (PoC) study in patients with Parkinson's disease and end-of-dose motor fluctuations
- Randomized, three 4 week period cross-over comparison of ODM-101 (105 and 65 mg of carbidopa) with Stalevo
- Total of 117 PD patients with wearing off
  - 101 in the Cross-over(all 3 periods) and
  - 111 in the parallel group populations (1st period)
- Change from baseline in OFF-time primary variable. Change in ON-time and UPDRS I-IV other variables.

# Summary of ODM-101 PoC study key results

**ODM-101 was more effective than Stalevo**

- ODM-101 65 and 105 mg reduced mean daily OFF-time by **0.6 (p = 0.021)** and **0.7 (p = 0.015) hours***.
- ODM-101 65 and 105 mg increased mean daily ON-time without troublesome dyskinesia by **0.6 hours (p=0.053 and 0.033)***
- No differences in ON-time with troublesome dyskinesia
- No statistically significant differences in UPDRS II or III scores
- No new safety concerns observed

*from statistical model and as compared to Stalevo and with carry over adjustment

# Status of development ODM-101

## Phase I

- Pharmacokinetics studies completed.

## Phase II

- PoC study completed in Q4 2012.

## Phase III

- FDA and EMA advise for further development available
- FDA's Special Protocol Assessment (SPA) completed and the agreement on pivotal phase III studies available
- Partnering ongoing

# Current status with ODM-103 and ODM-104 in Phase I

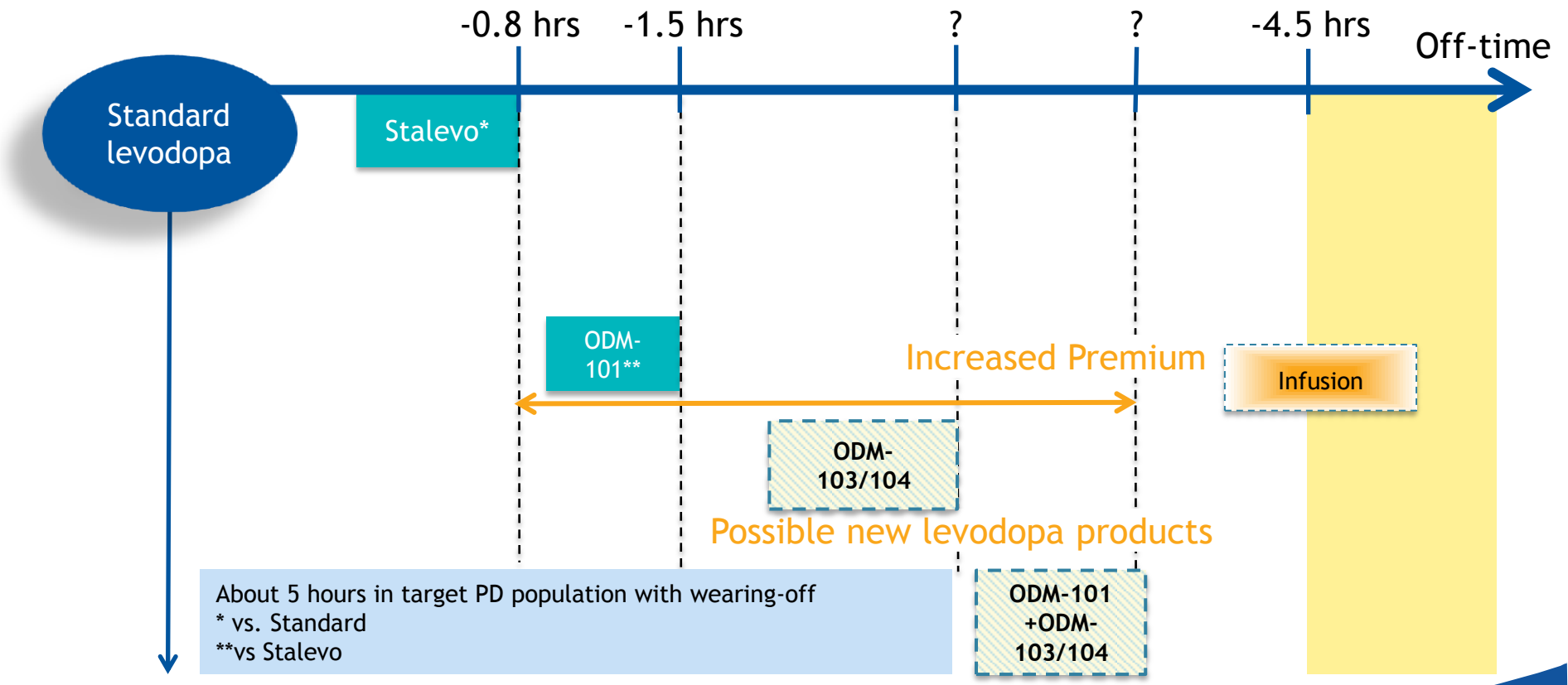
ODM-103 Phase I study:

- Single dose part completed; dosing up to 400 mg
- Repeated dose part ongoing; dosing currently up to 200 mg
- Well tolerated and effective COMT-inhibitor
- ODM-103 dose escalation put on hold to wait ODM-104 to catch up for comparison

ODM-104 Phase I study:

- Single dose part ongoing; dosing currently up to 200 mg
- Repeated dose part with 10 mg to be initiated in November
- Well tolerated

# Target is to develop the best possible peroral levodopa product to increase premium for market access - improved efficacy / reduced OFF-time



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# Proprietary Products update

Liisa Hurme
Senior Vice President
Proprietary Products

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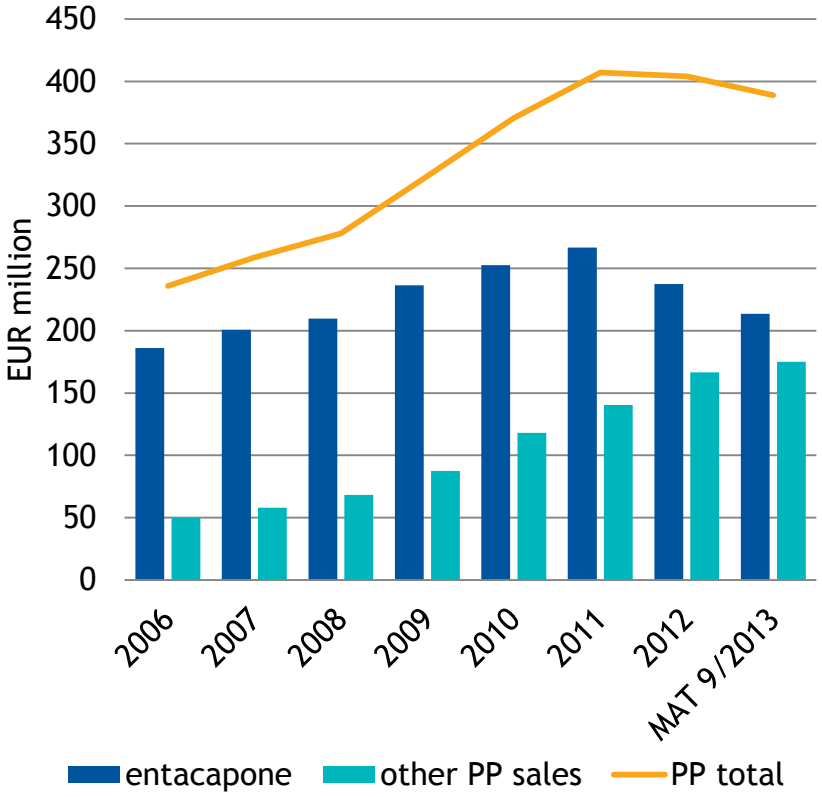
# Proprietary Products business transition is successful

- Robust entacapone sales have been successfully supplemented with new sales
- Product portfolio has expanded as planned:
  - Simdax +15 countries
  - *dexdor*® +27 countries
  - Easyhaler products +18 countries

Steady growth of PP portfolio with new products and robust entacapone sales



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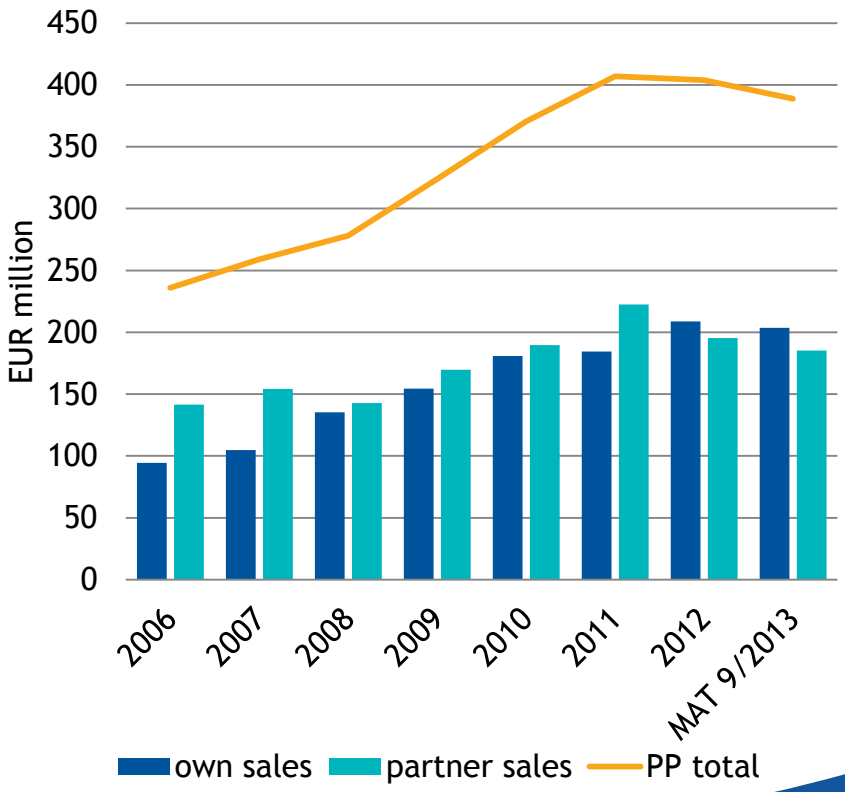
# Proprietary Products business transition is successful

- Proprietary product sales have been quite stable for the past few years
- Strengthening the European market position:
  - Orion sales organisation expansion from 13 countries to 27 countries

Equation between owns sales and royalties from partners has changed



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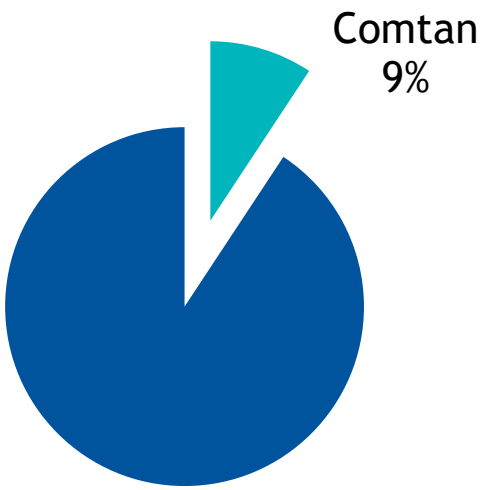
# Entacapone franchise status and prognosis in USA and Europe

**Comtan TRx value share - USA**




**Stalevo TRx value share - USA**


Source: IMS Health,
TRx sales in USA, 9/2013

**In Europe Stalevo data exclusivity expired on Oct 23, 2013**

- No marketing authorisations granted thus far
- To date, several MAAs submitted in various European countries
- Orion prepared to enter the generic market in Europe
- Sandoz has rights for generic Stalevo in Novartis territory



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# Stalevo has untapped potential in Rest of the World

**Japan**
- Stalevo regulatory process ongoing

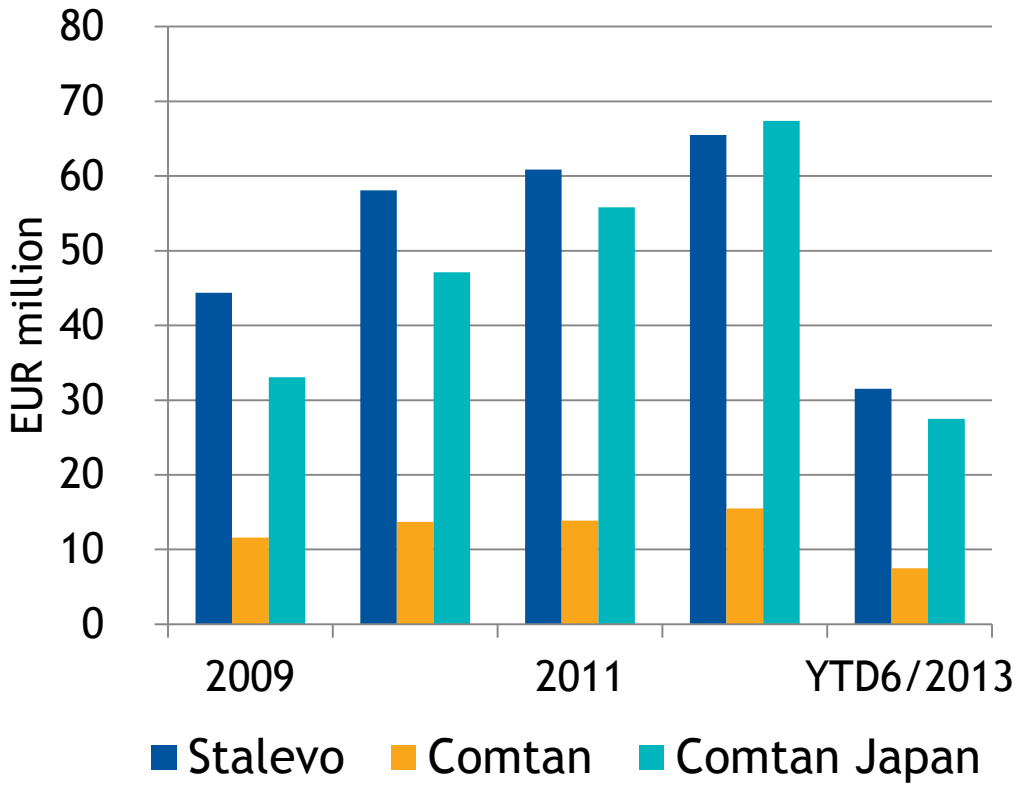
**China**
- Stalevo market access process ongoing

**Other RoW markets growing***
- China Comtan +52%
- Mexico Comtan & Stalevo +13%
- Argentina Stalevo +15%

*Source: IMS Health

MAT6/2012 vs. MAT6/2013

**Entacapone franchise sales development in RoW**




Source: IMS Health



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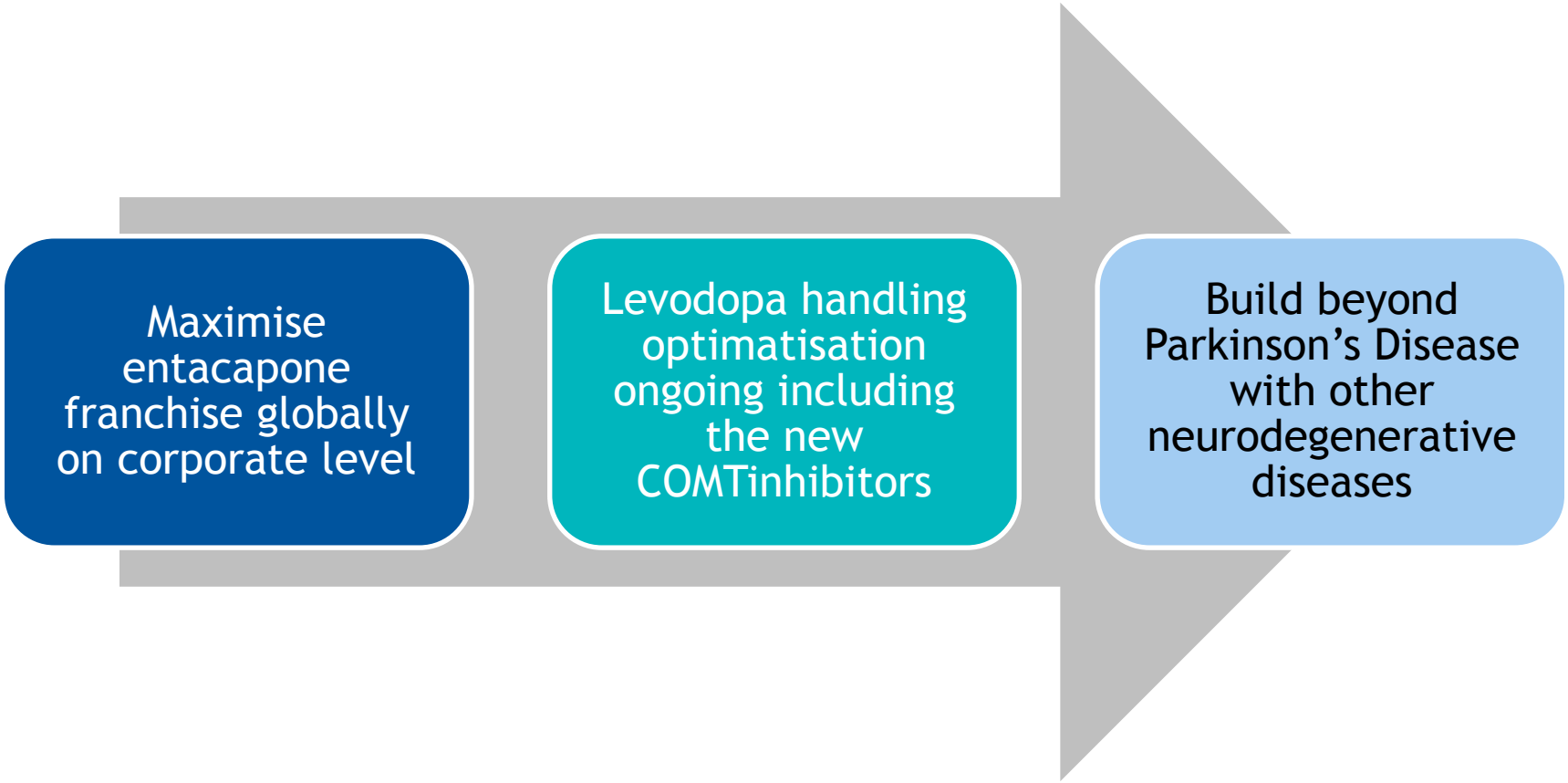
# CNS Business to be continued with wider scope



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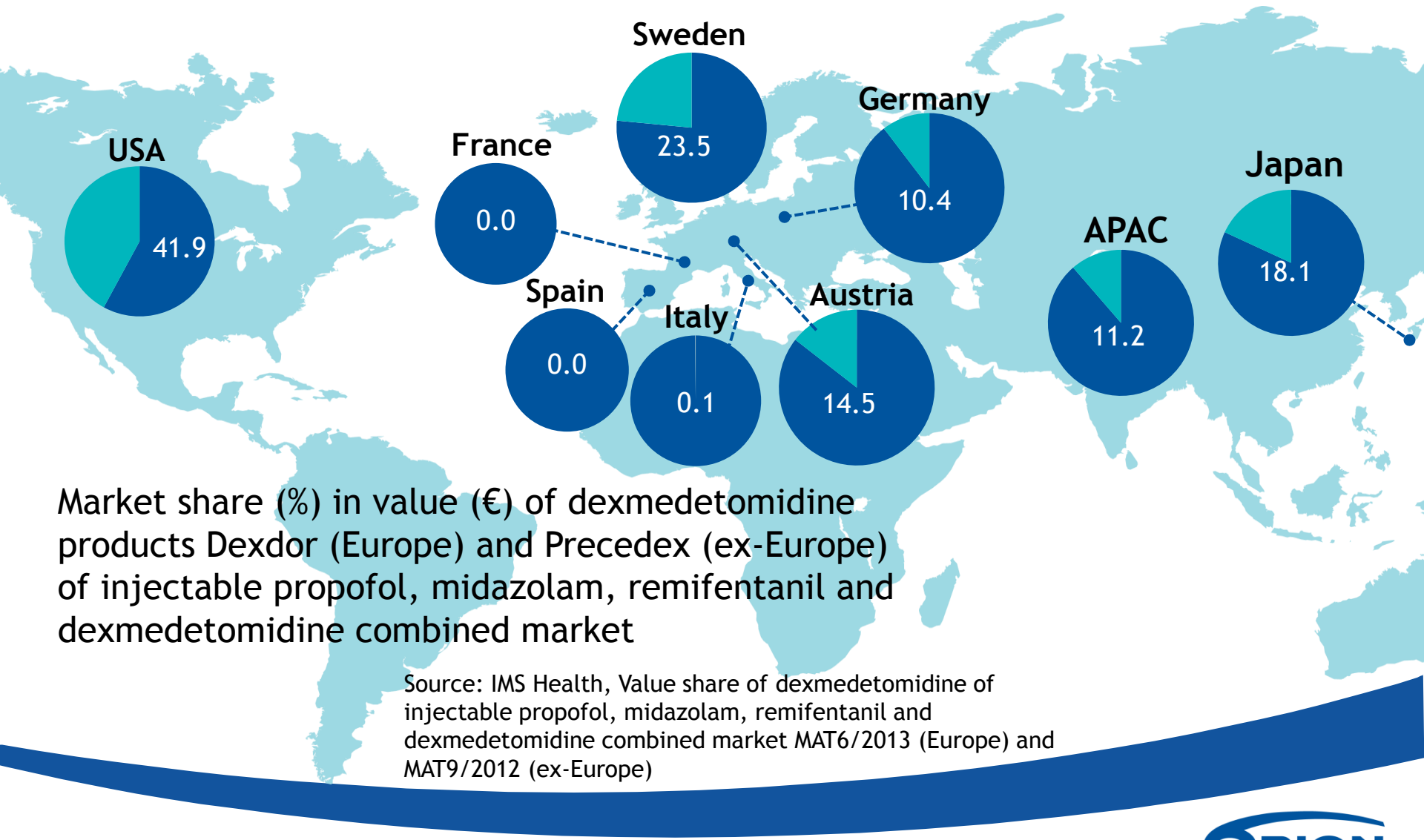
# Dexmedetomidine franchise going strong globally




Market share (%) in value (€) of dexmedetomidine products Dexdor (Europe) and Precedex (ex-Europe) of injectable propofol, midazolam, remifentanil and dexmedetomidine combined market

Source: IMS Health, Value share of dexmedetomidine of injectable propofol, midazolam, remifentanil and dexmedetomidine combined market MAT6/2013 (Europe) and MAT9/2012 (ex-Europe)



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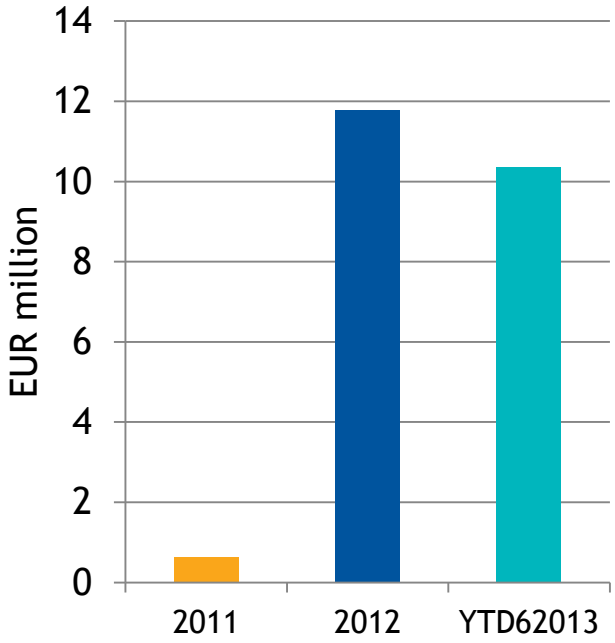
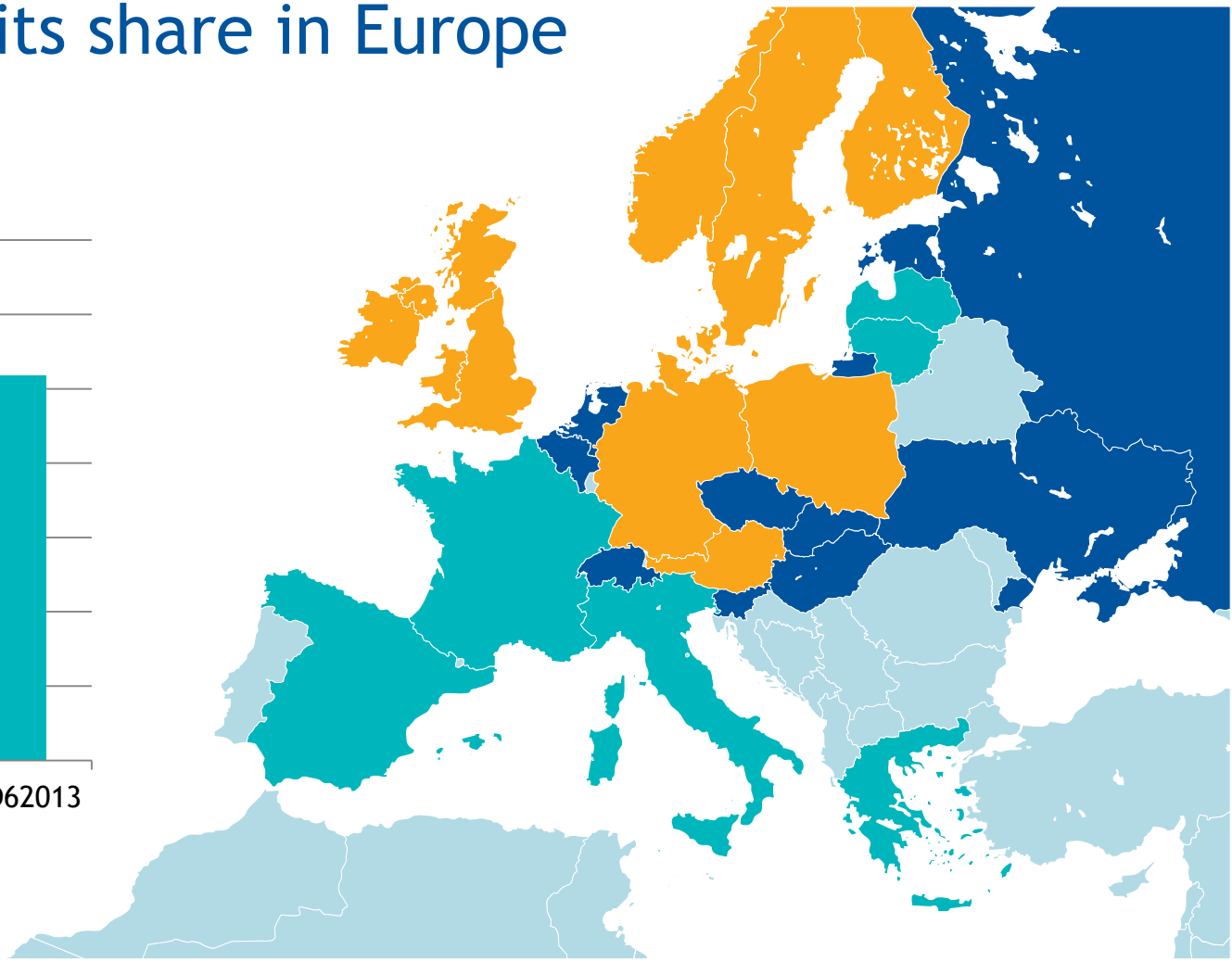
# *dexdor*® takes its share in Europe

**_dexdor_® sales in Europe**




Source: IMS Health





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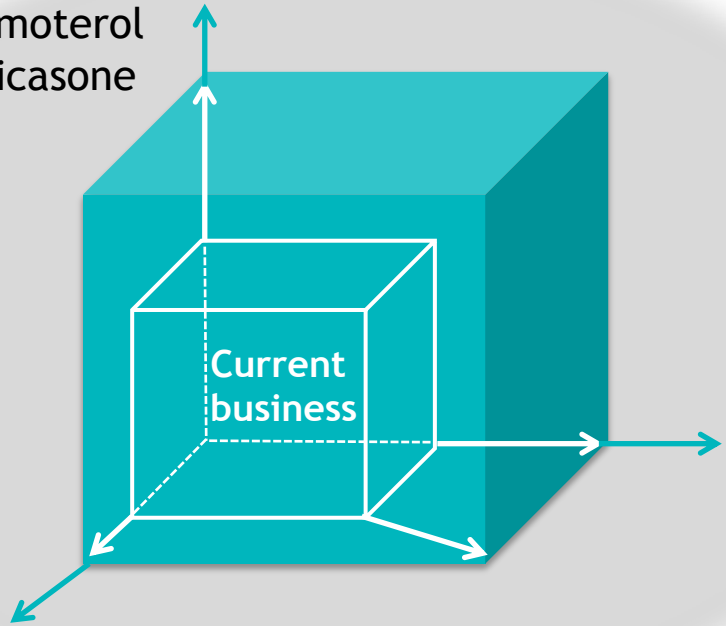
# Drivers for Proprietary Products Growth

**New product opportunities**
- Easyhaler budesonide-formoterol
- Easyhaler salmeterol-fluticasone
- ODM-201
- ORM-12741




**New customers**
- Insurance companies
- Pharmacies
- Oncologists

**New territories for existing products**
- Simdax for USA
- Easyhaler mono products in ex-Europe and ex-USA
- Stalevo China and Japan

**New business segments**
- Oncology
- Neurodegenerative diseases outside PD



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# How Specialty Products is succeeding in Generics?

Markku Huhta-Koivisto
Senior Vice President
Specialty Products

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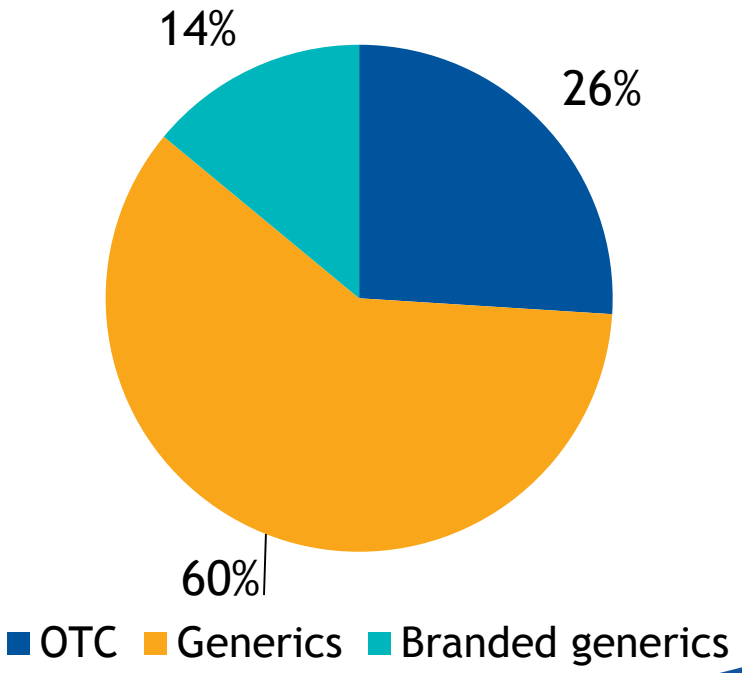
# Large portfolio of Off-patent prescription products and self-care products for GPs, specialists, pharmacists, hospitals and consumers

- Branded generics market value and potential is growing
  - products with added value
  - some Eastern European markets are changing towards substitution Gx markets
  - securing availability is crucial
- Generic markets are expanding
  - price competition tough, but volumes and value increasing
  - securing of availability is also important
- Self-care products (SC), over-the-counter products (OTC) and non-medical products distribution through pharmacies
  - Orion is the market leader in Finland
  - some products are available in Scandinavia and Russia

Breakdown of SpP net sales by product type 2012



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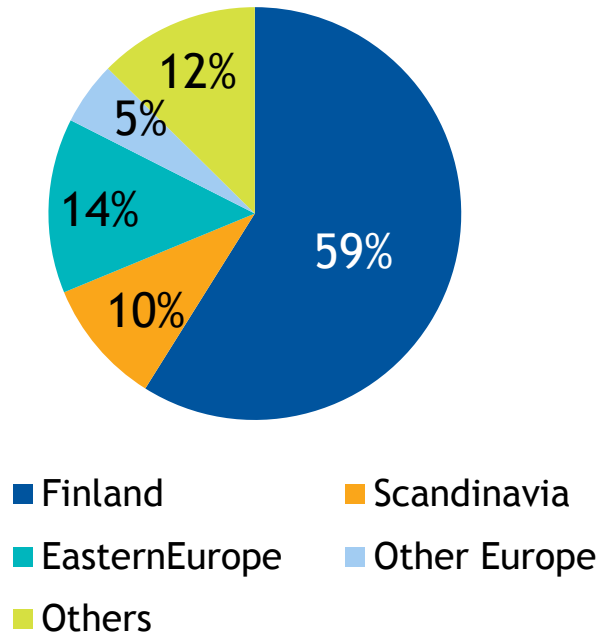
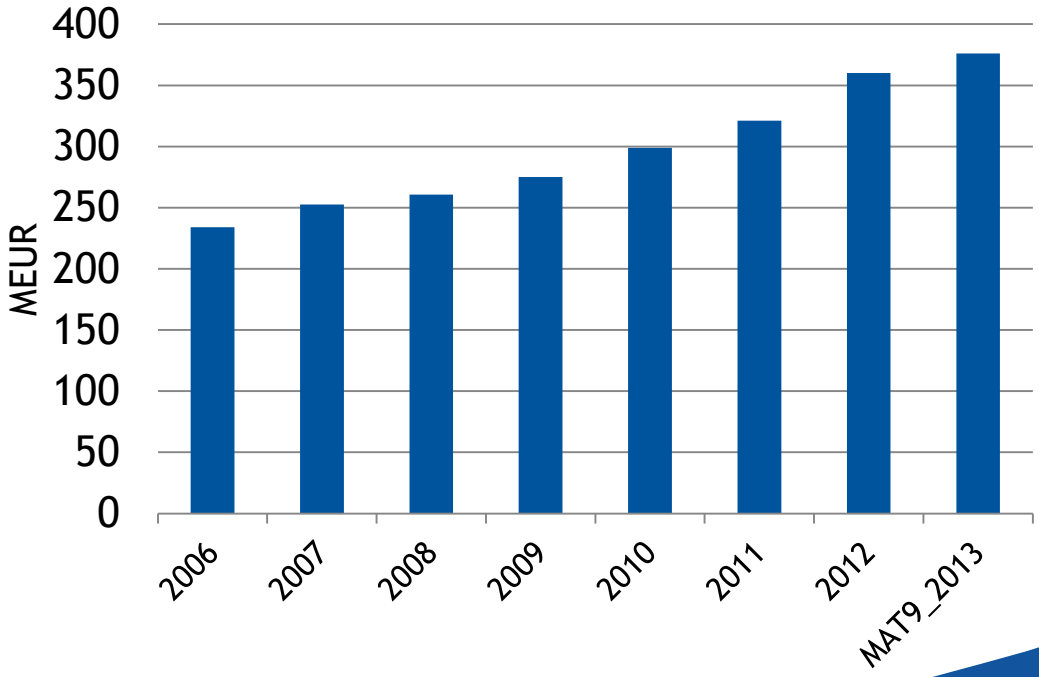
# SpP steady sales growth during last years

- Finland dominates, Scandinavia growing
- Orion's second largest business with sales in over 100 countries

Breakdown of SpP net sales by geographic area 2012




Development of SpP net sales from 2006 to MAT9/2013



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# Orion's strategy

## Orion's values



Management of complexity in cost efficient way



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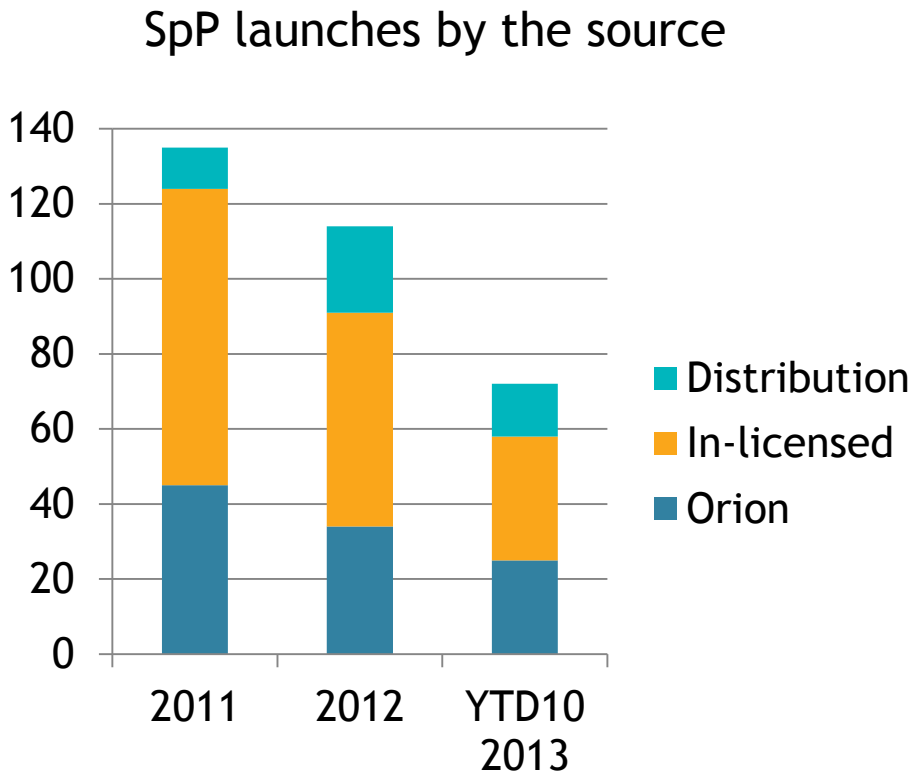
# How are we getting our products

- Develop ourselves to Orion's own production
- Use CROs to develop to Orion's own production
- Utilize the patent opportunity for expiring own PP products
- Use CRO/CMO for development and manufacturing
- Do co-development
- In-license from third party
- Make distribution agreement



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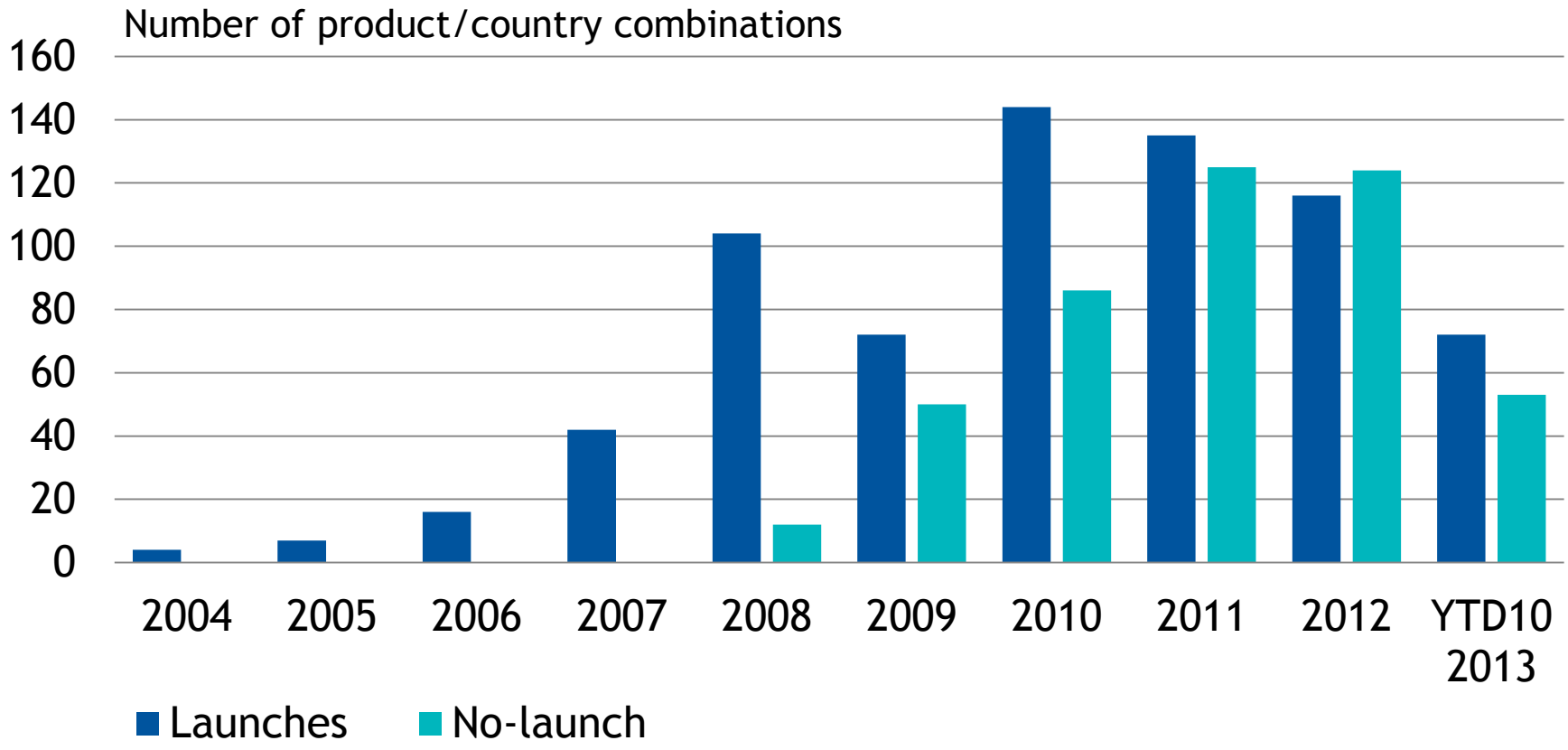
# SpP launches 2007 – YTD10/2013



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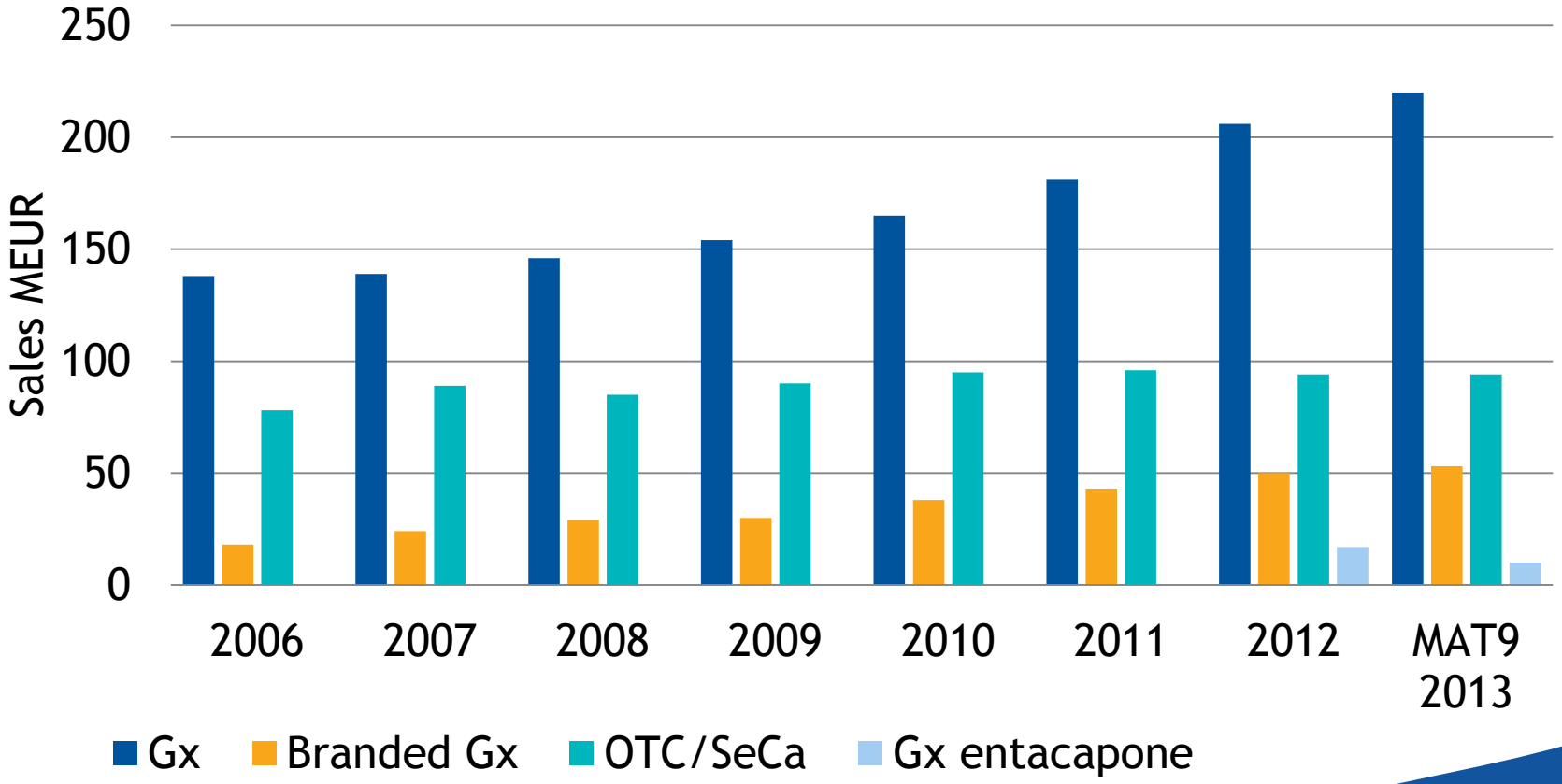
# Where is our growth coming?
## Product types



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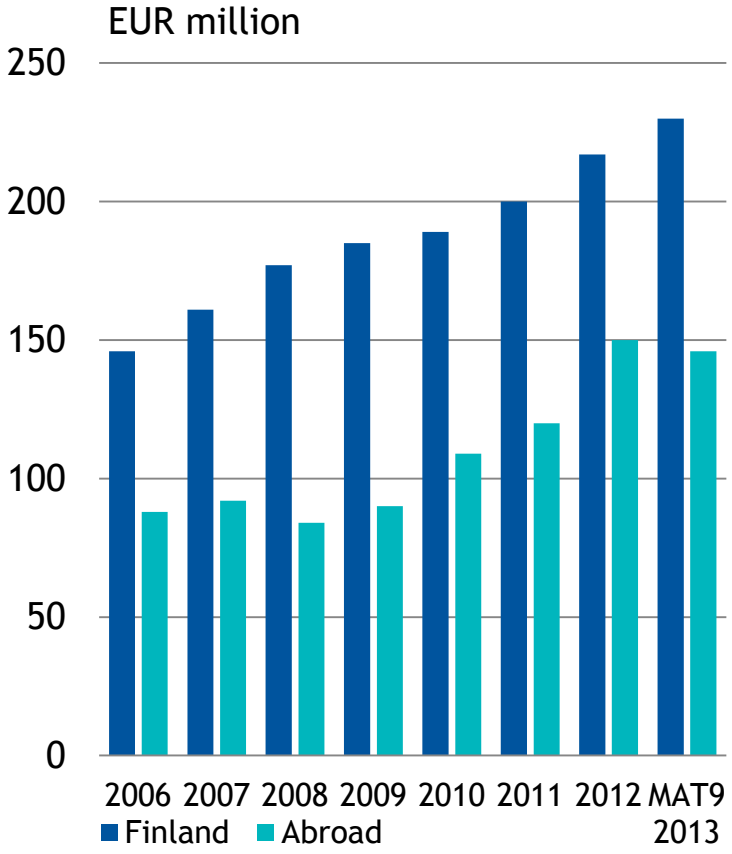
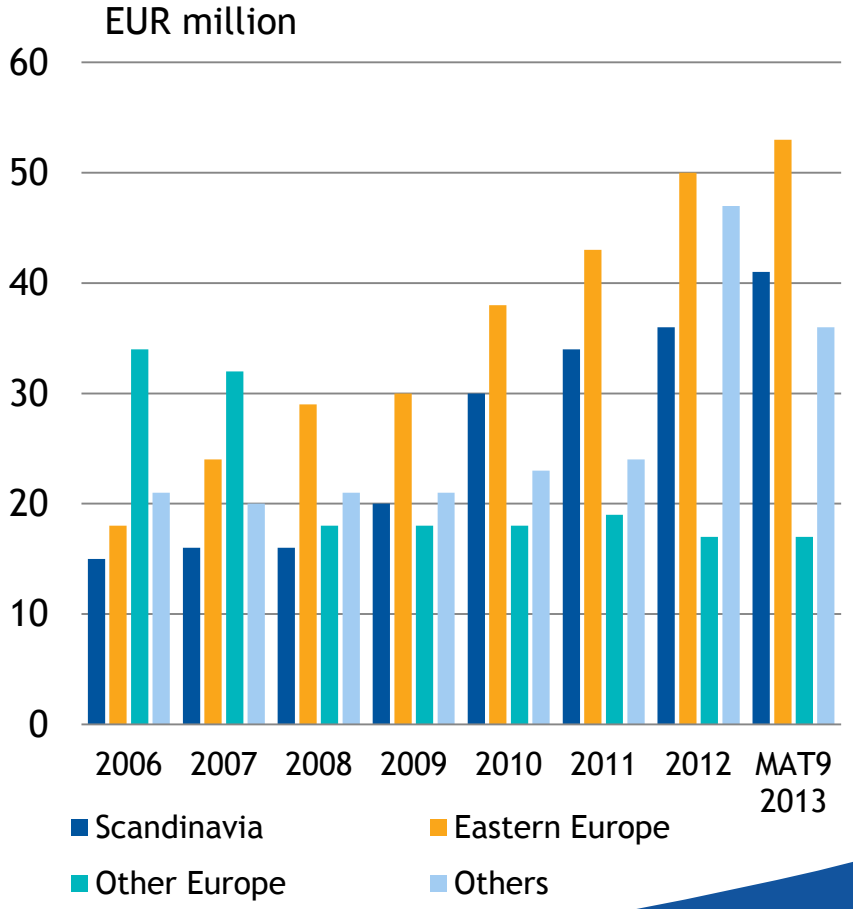
# Where is our growth coming?
## Geographical areas



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# Orion Diagnostica

Jaakko Rissanen
President

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# Orion Diagnostica – Building Well-being

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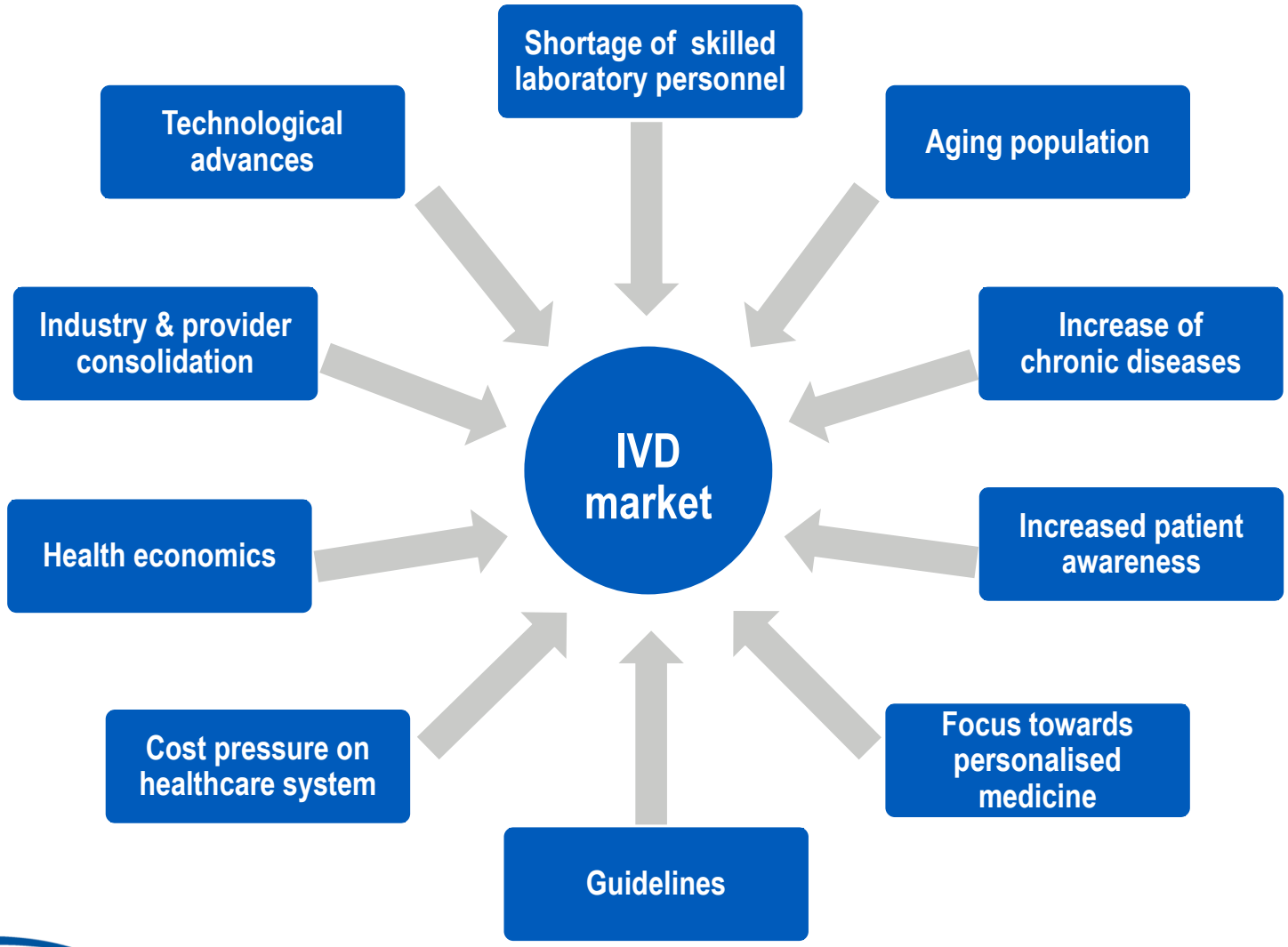
# The In Vitro Diagnostics (IVD) market is changing - Openings for growth potential




***Sources:***

- *Kalorama Information: The Worldwide Market for In Vitro Diagnostic Tests, 8th Edition, July 2012 & several articles*

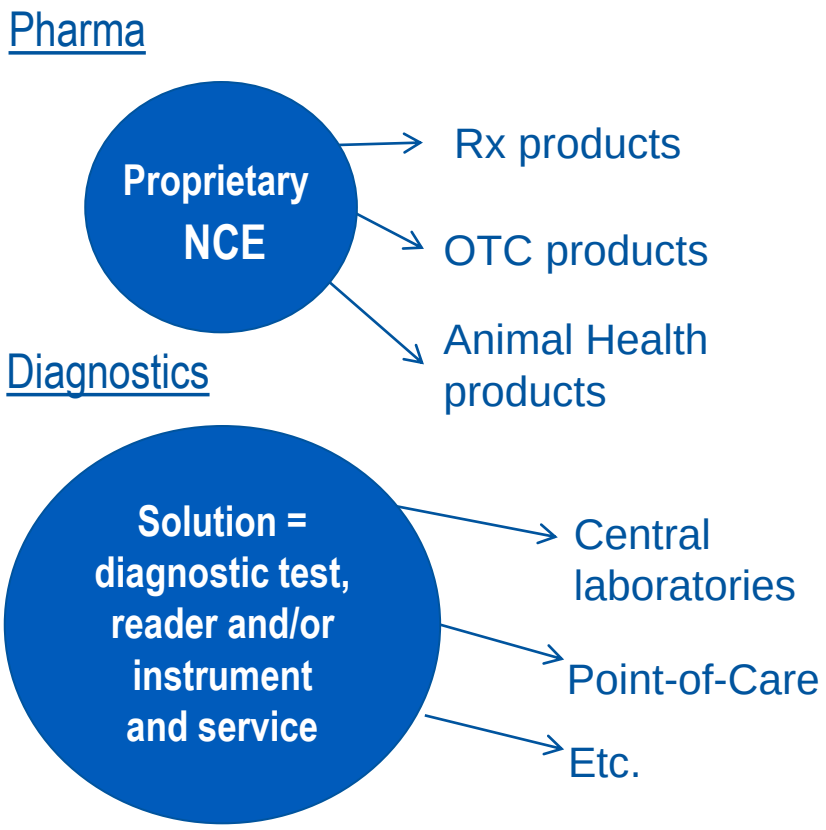
# Characteristics of diagnostics business

## Time, cost and risk level

### Diagnostics compared with Pharmaceutical business

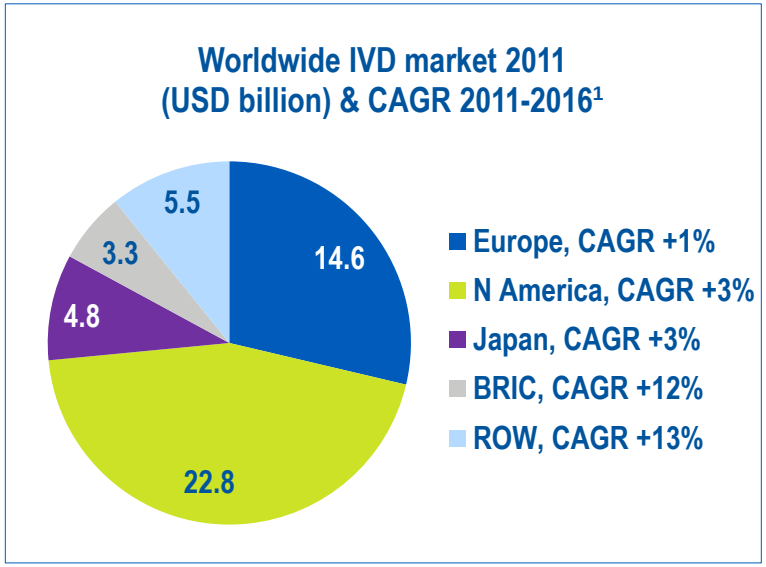
- **Shorter time**
  - typical time to market 2-5 yrs
- **Lower cost**
  - 0.1- 10 mEur
- **Lower technical risk**
  - not 0/1, can be managed
- **Different type of market risk**
  - influenced mainly by changes in business environment – can be managed by strong intellectual property (IP) and/or by complex technical solutions

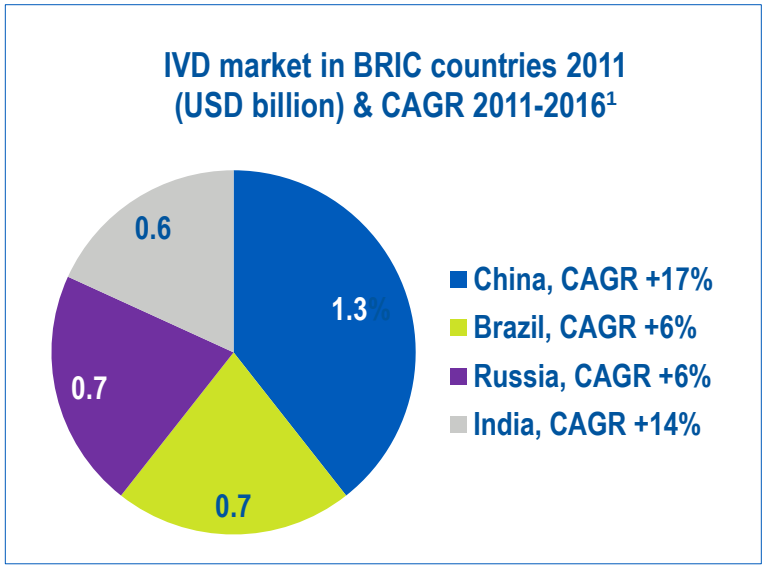
### Leveraging the assets



# Global IVD market is expected to grow 5% annually

- An estimated USD 50 billion market. Expected to exceed USD 64 billion in 2016. Annual growth in developed countries ~5%.[1]
- Europe, North America and Japan about 75% of the total IVD market.[1]
- BRIC countries (Brazil, Russia, India, China) are expected to grow at a 12% rate.[1]
- Molecular testing forecasted to grow 7-11% annually.[1,2]
- POC testing expected to see continued growth at an annual rate of 4 -7%.[1,2]





***Sources:***

1. *Kalorama Information: The Worldwide Market for In Vitro Diagnostic Tests, 8th Edition, July 2012*
2. *Genetic Engineering & biotechnology News. IVD Market Moving Rapidly on an Upward Trajectory. 1 Dec 2012.*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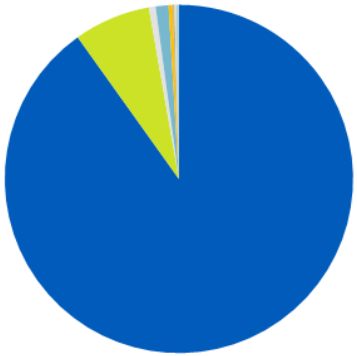
# Point-of-Care market is broad & fragmented - and growing

**Total POC testing market**
- **2011: USD 15.300 million**
- **2016: USD 18.400 million**
- **CAGR: 4%**

**OTC/Self testing market**
- 2011: USD 9.624 million
- 2016: USD 11.616 million
- CAGR: +4%

**Professional POC market**
- 2011: USD 5.660 million
- 2016: USD 6.765 million
- CAGR: +4%

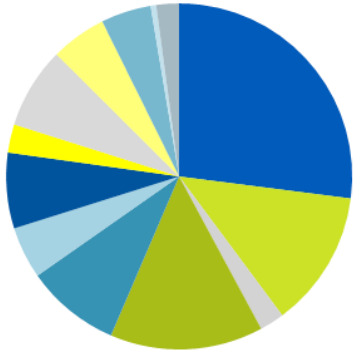
## OTC/Self testing market



**Sales by test category & percentage of market, CAGR**

- Glucose ($ 8.673, 90%, CAGR 4%)
- Pregnancy, ovulation ($ 685, 7%, CAGR 1%)
- Coagulation / PT ($ 60, 1%, CAGR 5%)
- Faecal occult blood ($ 115, 1%, CAGR 1%)
- Drugs of abuse ($ 35, 0.4%, CAGR 3%)
- H pylori ($ 5, 0.1%, CAGR 4%)
- HIV ($ 11, 0.1%, CAGR 22%)
- Cholesterol ($ 15, 0.2%, CAGR 0%)
- Other ($ 25, 0.3%, CAGR 4%)

## Professional POC market



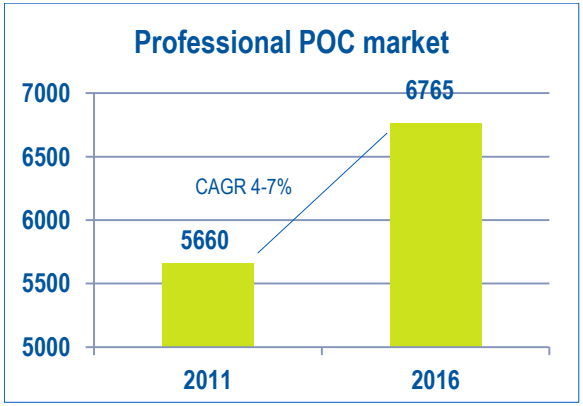
**Sales by test category & percentage of market, CAGR**

- Glucose ($ 1.530, 27%, CAGR 1%)
- Critical care ($ 725, 13%, CAGR 4%)
- Pregnancy ($ 130, 2%, CAGR 1%)
- Infectious disease ($ 810, 14%, CAGR 3%
- Cardiac markers ($ 500, 9%, CAGR 5%)
- Cholesterol / Lipids ($ 275, 5%, CAGR 5%)
- Coagulation / PT, ACT ($ 400, 7%, CAGR 2%)
- HbA1c ($ 150, 3%, CAGR 15%)
- Haematology ($430, 8%, CAGR 3%)
- Faecal occult blood ($ 295, 5%, CAGR 9%)
- Drugs of abuse ($ 265, 5%, CAGR 0%)
- Bilirubin ($ 30, 1%, CAGR 6%)
- Other ($ 120, 2%, CAGR 5%)

*Source:*
- *Kalorama Information: The Worldwide Market for In Vitro Diagnostic Tests, 8th Edition, July 2012*

# Point-of-Care testing holds a lot of promise

- **POC testing**
  - shortens time between sample taking and analysis
  - speeds up diagnosis and treatment
  - improves clinical outcome
  - allows patients to be managed efficiently and more cost effectively




- **POC tests are used in**
  - primary care locations, remote settings with no laboratory infrastructure and by patients themselves for home-testing

- **Success of POC systems will rely on**
  - easy and error-free operation, portability, robustness, low cost, miniaturisation, small sample volume, simple sample preparation and improved sensitivity
  - POC instrument connectivity to electronic medical records for device control, management of patient and user data as well as test results
  - smartphones?

***Sources:***

- *Kalorama Information: The Worldwide Market for In Vitro Diagnostic Tests, 8th Edition, July 2012 & several articles*

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# Orion Diagnostica:
## Smart Solutions for Healthcare & Hygiene Monitoring



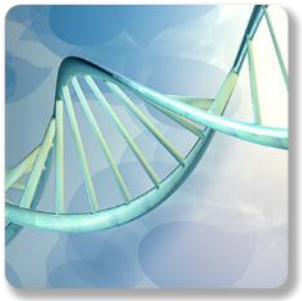

- Accurate and affordable clinical diagnostic and hygiene monitoring tests, which are easy to use and provide fast results.
- Focus on point-of-care diagnostic (POC) tools, which enable healthcare professionals to detect disease quicker, make evidence based diagnoses and treatment decisions and follow up treatment outcome.
- Close to 40 years' experience in clinical diagnostics and hygiene monitoring businesses.
- Quality and regulatory requirements form the foundation of our activities. Full compliance with ISO 9001, ISO 13585 and FDA requirements.

# Business areas

- Point-of-Care
  - **QuikRead®**
    Rapid tests to general practitioners, family doctors, paediatricians, healthcare centres, occupational healthcare, nursing homes, emergency departments

**Point-of-Care testing**

- Small and mid-sized laboratories
  - **High quality test kits and reagents**
    For clinical chemistry laboratories
    - **Orion GenRead®**
      Front line Nucleic Acid Tests (NAT = Molecular Diagnostics) for microbiology labs



**Laboratory testing**

- Healthcare, industrial processes
  - **Orion CleanCard® PRO**
  - **Dipslides**
    Novel and conventional tests for monitoring cleanliness and contamination

**Hygiene testing**

# Point-of-Care Tests

Easy to use solutions to our customers

## The QuikRead® System



- For measuring C-reactive protein (CRP) from a small finger-stick blood sample
- Result in two minutes
- A CRP test performed during patient consultation helps clinicians to differentiate between bacterial and viral infections and target antibiotic treatment
- Includes also tests for **Strep A**, **CRP+Hb**, **hsCRP+Hb**, FOB (faecal occult blood) and U-ALB (urinary albumin)
- Over 30.000 QuikRead units in use globally

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# Orion GenRead®

## Our newest platform for Molecular Diagnostics

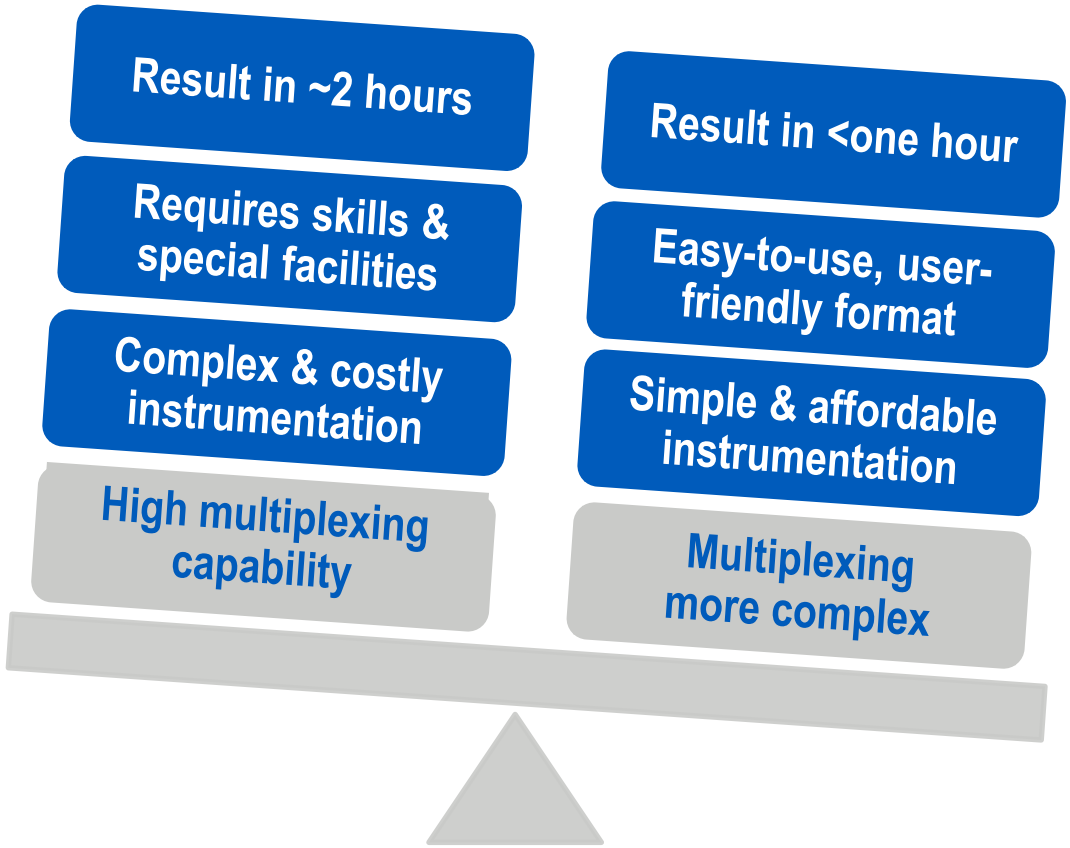
- Built on SIBA®, a rapid and reliable isothermal nucleic acid amplification technology.
- Orion Diagnostica has all rights to this patented, proprietary technology.
- A flexible benchtop solution including a small instrument and ready to use kits.

orion genread®

- First-phase tests will target pathogens causing gastrointestinal disease. Future product portfolio will cover a wider range of pathogen tests.

# Conventional PCR vs. Isothermal NAT

## Some features



# Hygiene Monitoring

Easy to use solutions to our customers

**Simple and practical tools for settings where surface cleanliness is crucial**

- Healthcare settings:
  For effective infection control
- Food processing and food service:
  For ensuring a safe food chain
- Industrial enterprises:
  For checking microbial burden in various industrial fluids

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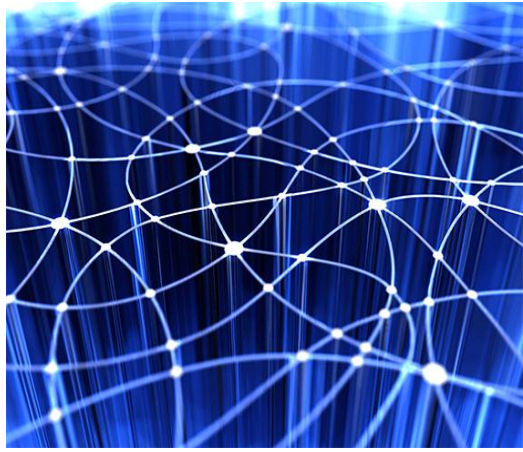
# Orion Diagnostica Network



## Distributor

- In addition to own products, Orion Diagnostica sells products by well-established diagnostics manufacturers.
- Own sales units in Finland, Sweden, Norway, Denmark, Czech Republic, and Germany with an established customer base, local market insight and a motivated and professional sales team.

## OEM partner

- With a close to 40 years' experience in clinical diagnostics and hygiene monitoring businesses and a certified quality management system, Orion Diagnostica offers its expertise and top-quality solutions to companies interested in OEM cooperation.

## Collaborator / Partner

- Orion Diagnostica collaborates with research groups and development partners to discover new ways to address customers' needs for novel and rapid diagnostics.

# THANK YOU!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