



**Diana**  
Living with post-stroke spasticity  
Sintra, Portugal



# Investor Presentation

Spring 2021



## **Our Vision**

**To be a leading global mid-size biopharmaceutical company  
with a focus on transformative medicines  
in oncology, rare disease & neuroscience**



# Focus. Together. For patients & society

Maximize  
*our brands*



Strengthen  
*pipeline*



Drive  
*efficiencies*



Focus on  
*culture*

# Strong & expanding global footprint

**North America**  
**33% of Total Sales<sup>1</sup>**

From 11% to 33% of  
Total Sales over the last  
five years<sup>2</sup>

**Western Europe<sup>3</sup>**  
**51% of Total Sales<sup>1</sup>**

Continued market share  
gains in all TAs

**Rest of World**  
**16% of Total Sales<sup>1</sup>**

Accelerated  
development in China  
Expansion in new  
geographies

**34**

countries with an  
Ipsen presence

**115+**

countries where  
Ipsen products  
are marketed

# Growth drivers

## Oncology



**Continued growth driven by 1L RCC & other potential indications**



**Limited growth until potential indication expansion**



**Attractive growth until generic erosion**



**Continued growth despite challenging Chinese environment**

## Rare disease

**Palovarotene**

**Sales contribution depending on potential FOP label**

## Neuroscience



**Solid growth in line with attractive market**

**Group net sales<sup>1</sup>  
CAGR 20-24 between  
+2% & 5%**

- At constant exchange rates and scope
- Assuming potential additional indications

# Investing in R&D for growth



## Build a strong and best-in-class R&D organization

- Streamline organization and increase efficiencies
- Build clinical operations excellence



## Prioritize key internal development programs

- Accelerate high-value programs
- Discontinue or partner low-priority programs



## Increase R&D investment through external innovation

- Early to late-stage transactions
- Leverage existing development organization

**Increase R&D as  
a % of net sales**

---

driven by external  
innovation strategy

# Accelerate external innovation & strengthen pipeline



## Oncology

- Solid & hematological tumors
- Niche tumors or biomarker segments in broad tumors
- LCM potential



## Rare disease

- Disease areas with **unmet needs** beyond endocrinology & bone disease
- Established & innovative **technologies** including gene-based modalities



## Neuroscience

- Focus on in-house recombinant long-acting toxins & TSIs
- Rare neurological disorders

**€3bn  
cumulative  
firepower for  
pipeline  
expansion  
by 2024<sup>1</sup>**

**Focus on assets across all stages of development  
with strengthened organization to execute on external innovation**

# Transforming Ipsen R&D



## Organizational transformation

- Defined therapeutic area units
- Centralized clinical operations
- Strengthened R&D operations team



## Portfolio governance

- New governance model for major decisions
- Alignment of decisions with R&D strategy, priorities & resources
- Assessment & prioritization of portfolio



## Scientific rigor

- New leadership with biotech & industry experience
- Strengthen links to key opinion leaders




## External innovation

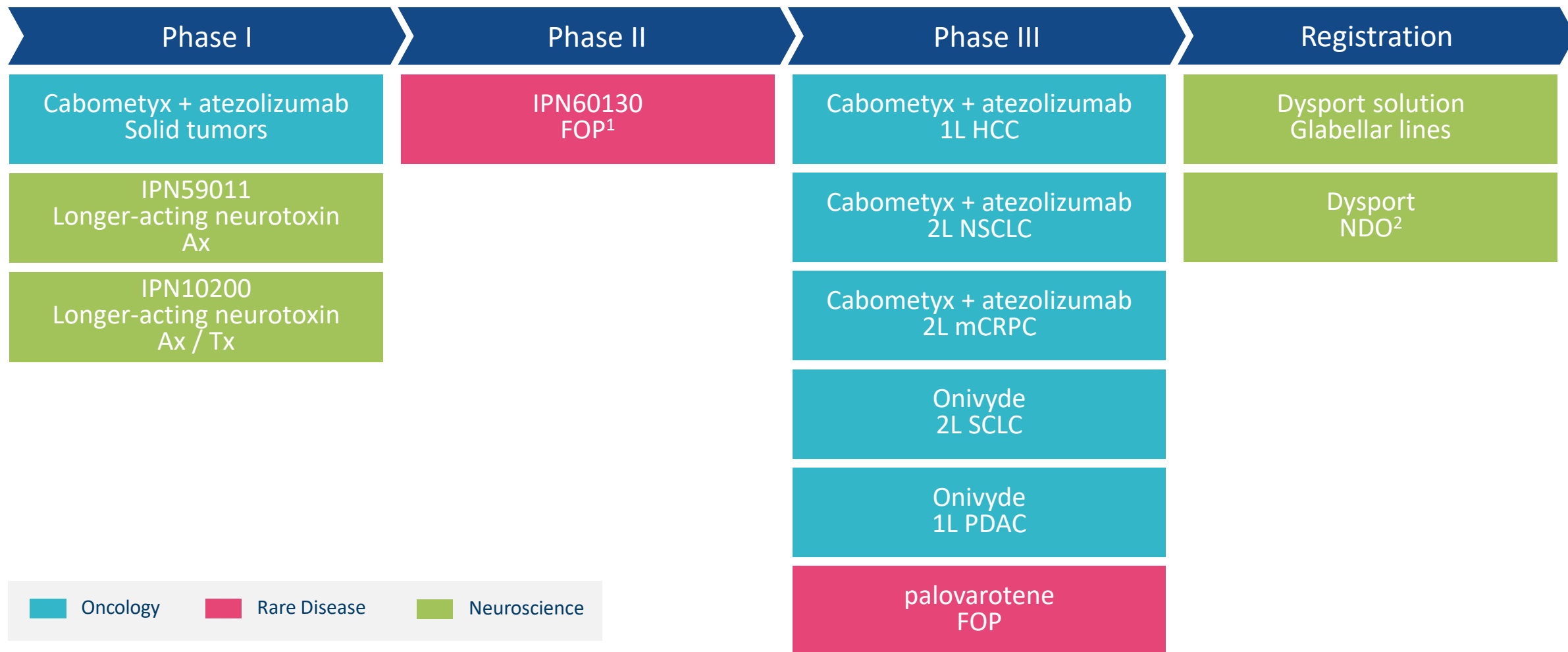
- External innovation further integrated into R&D
- Expand team & broaden the scope & geographical footprint



# Significant potential in late-stage pipeline

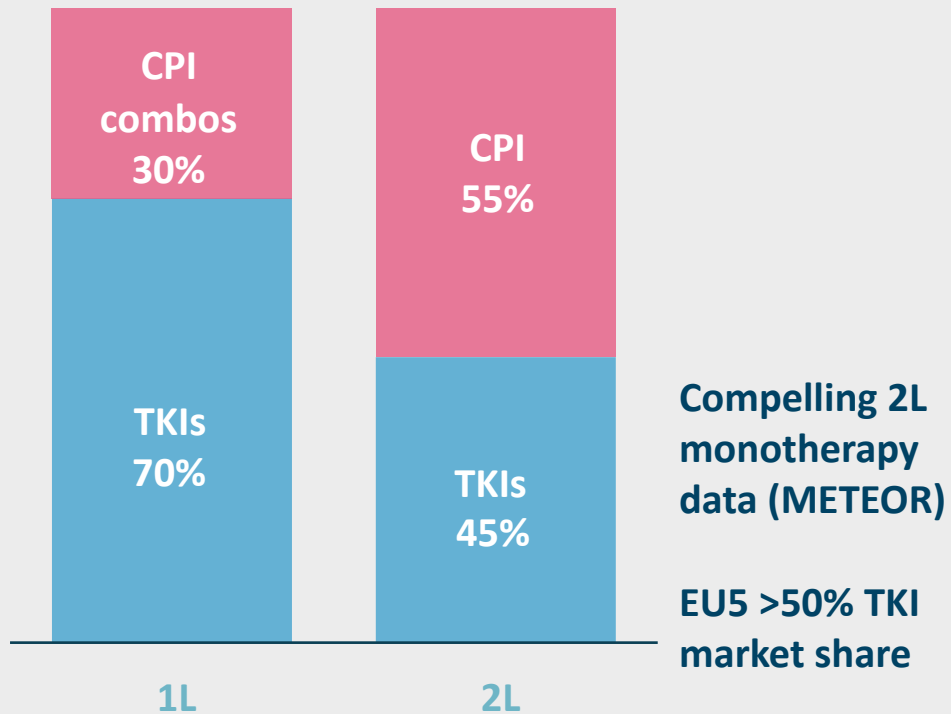
|  |   | Expected regulatory submission |         |  | Potential peak sales <sup>1</sup> |
|--|---|--------------------------------|---------|--|-----------------------------------|
|  |   | 2021                           | 2022    | 2023   |                                   |
| <br><b>CABOMETYX®</b><br>(cabozantinib) tablets | Pipeline in a product                               | 1L HCC<br>with<br>atezolizumab |         | 2L NSCLC<br>with<br>atezolizumab<br><br>2L mCRPC<br>with<br>atezolizumab | >€700M                            |
|  | Potential to establish SoC in hard-to-treat cancers |                                | 2L SCLC | 1L PDAC  | >€300M                            |
| <b>Palovarotene</b><br><br>Establish leadership in FOP   |   | Chronic /<br>Episodic FOP      |         |  | Depending on potential FOP label  |

# Pipeline

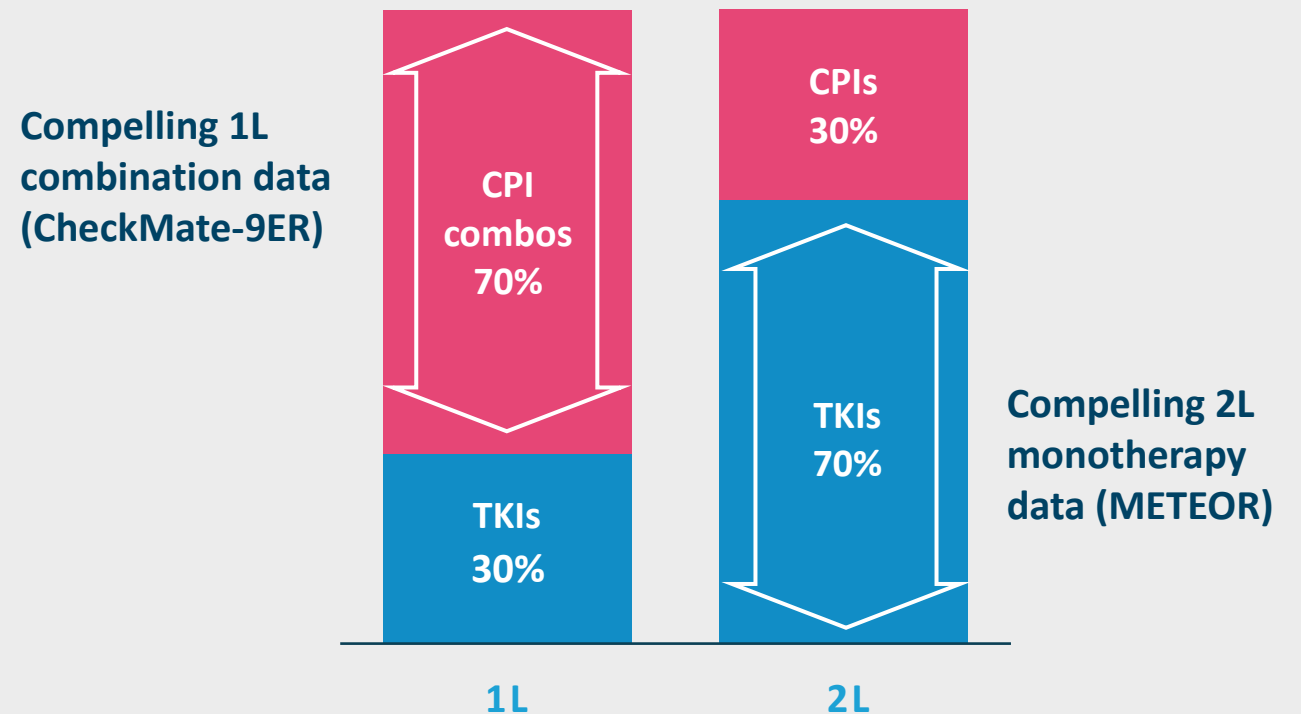


# Cabometyx<sup>®</sup>: shifting landscape in 1&2L aRCC

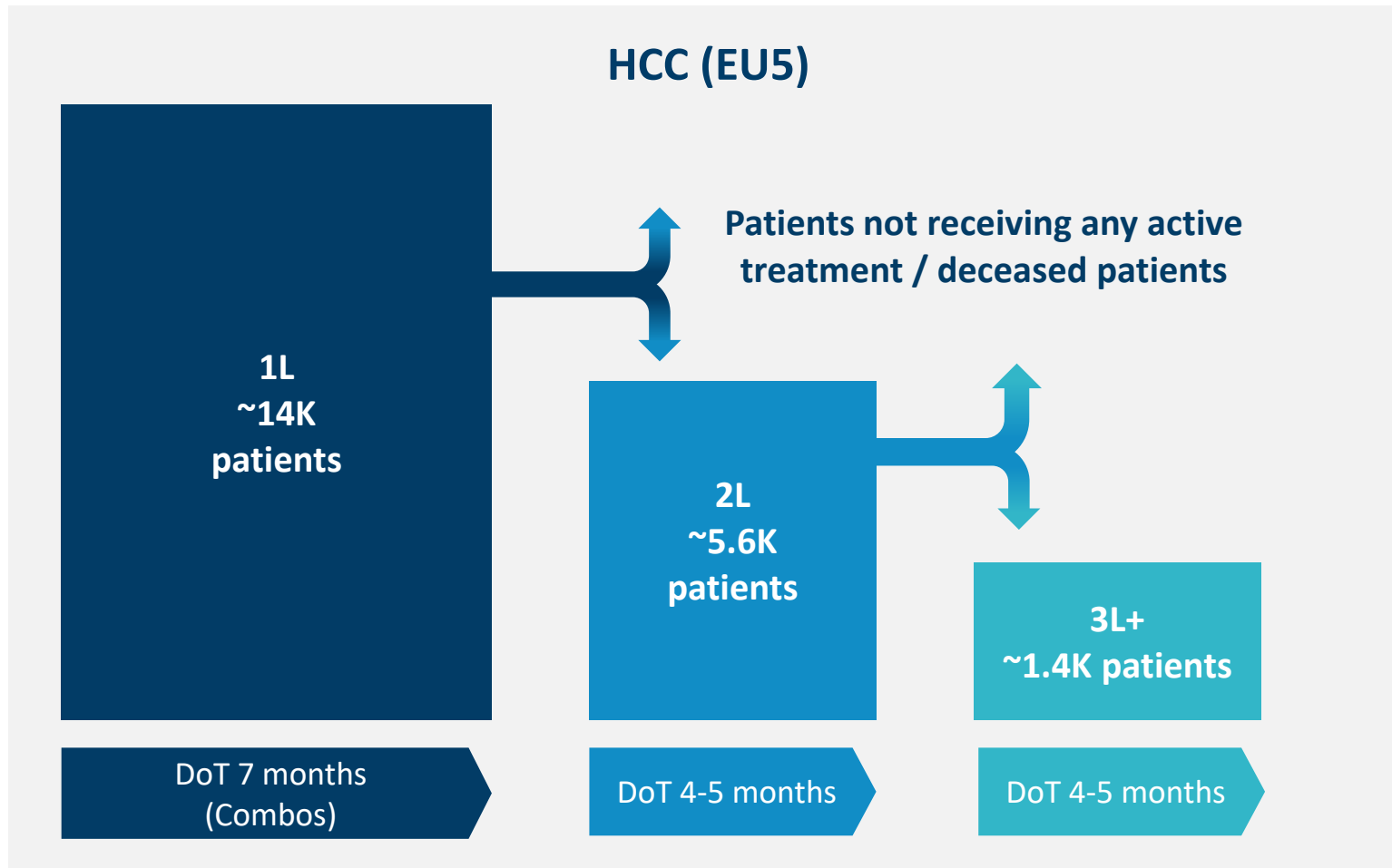
## Today's landscape



## Tomorrow's landscape



# Cabometyx<sup>®</sup> | COSMIC-312: significant expansion opportunity in HCC



## 1L HCC

- CPI combinations to become new SoC
- Approval expected in 2022

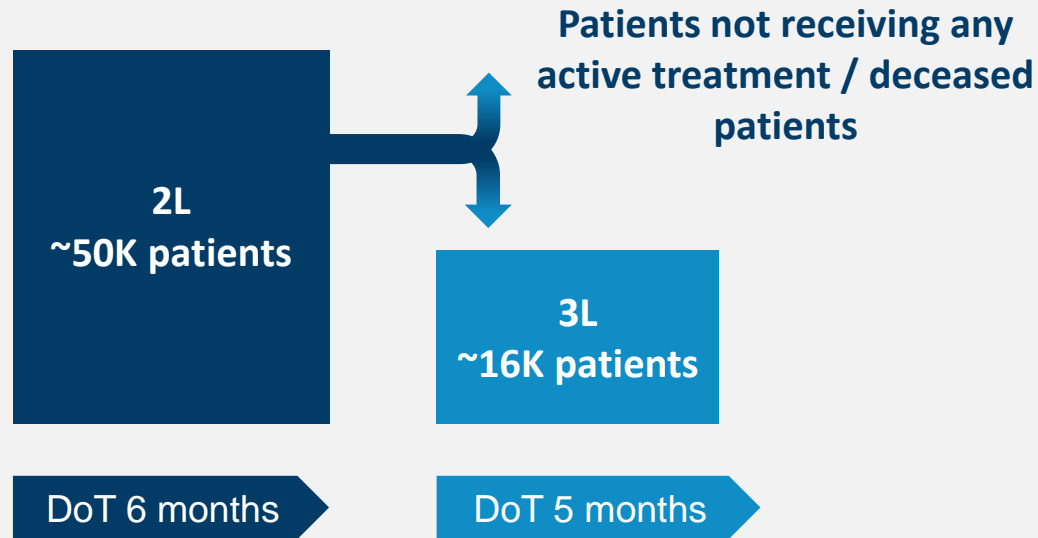
## 2L HCC

- Strong performance in key markets
- Geographic expansion to new markets 2021+

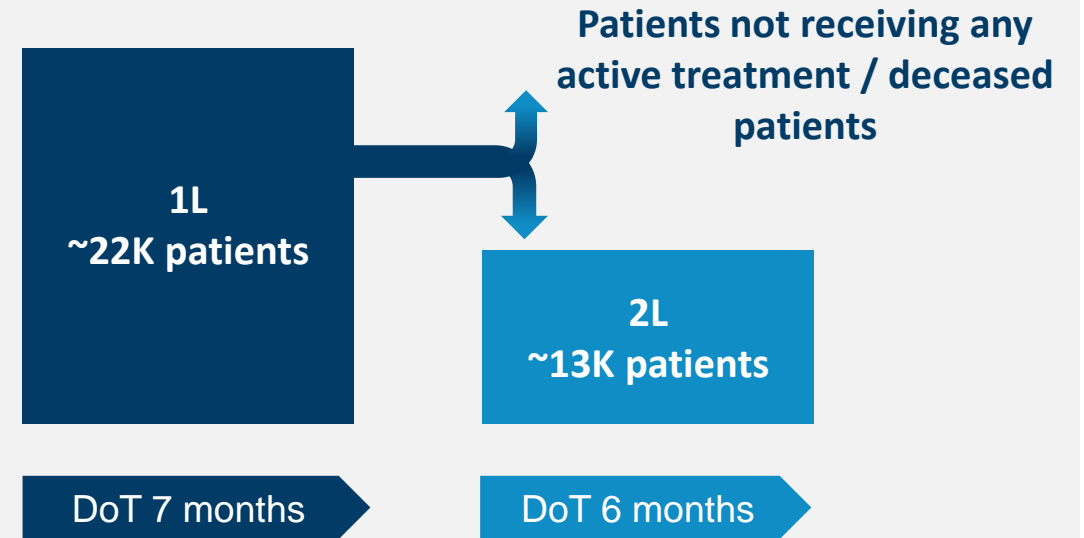


# Expanding Cabometyx<sup>®</sup> potential: NSCLC & mCRPC

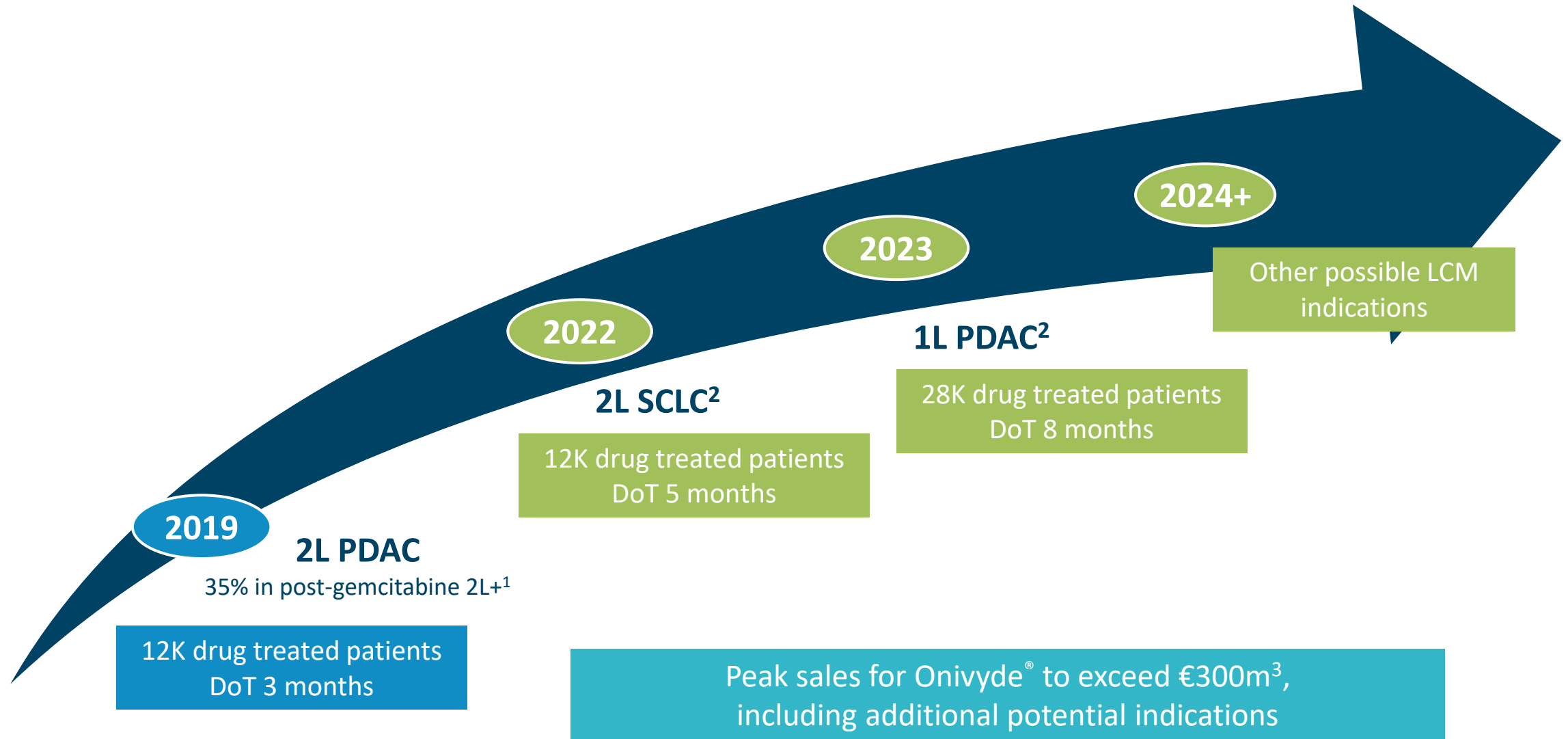
## Non-mutated NSCLC 2L+ (EU5)



## High risk mCRPC (EU5)



# Onivyde® LCM: expansion into new tumor types



# Decapeptyl®: ongoing growth story

## Key Facts



**+3% CAGR**

Net sales growth 2015-2020



**Market Leader** in the EU



Commercialized in

**70+** countries worldwide

**ADTs remain backbone  
therapy in PC<sup>1</sup>**

## Growth drivers

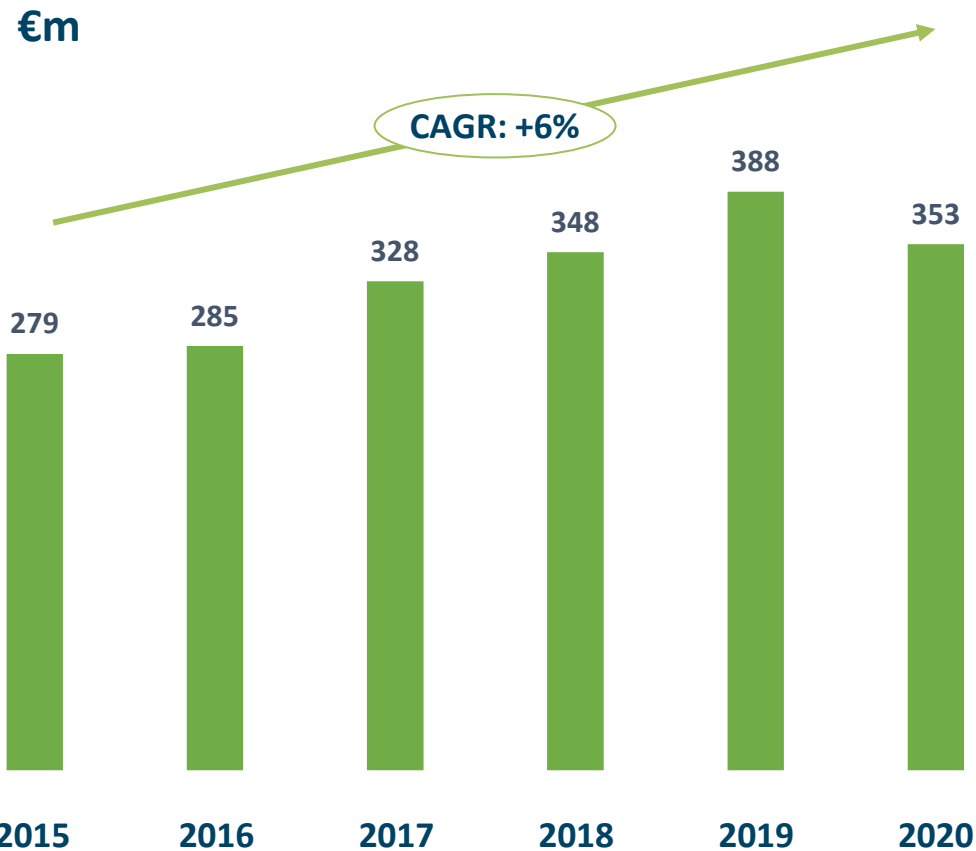
- Attractive market dynamics
- Market share gains in EU and RoW
- China performance impacted by competitive environment
- Focus on long-acting formulations, especially 6 months



Continued growth despite challenging environment in China

# Dysport®: excellence in neurotoxins

Ipsen Dysport® Total Sales 2015-2020



## Key Facts



**+6% CAGR** Total Sales growth  
2015-2020



### Leading market position

Dysport® #2 globally  
#1 in several markets



### Complexity hurdles

Specialized & highly regulated  
manufacturing process



# Efficiency, focus and agility to fuel growth

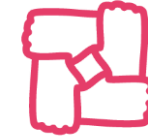


## Generate efficiencies

Smart spending

Manufacturing efficiencies

Digital enablement



## Focused and agile operating model

Simpler operations

Excellence in execution

Transformed R&D organization

# Focus & optimize resources



## Smart spending

- Focus on high priority projects
- Procurement savings
- Centralization, outsourcing and right-sizing



## Simpler operations

- Process optimization & simplification
- Organization & footprint adjustment
- Adoption of new ways of working



## Manufacturing efficiencies

- Relocation of Onivyde<sup>®</sup> manufacturing
- Productivity initiatives
- Process improvement program



## Digital transformation

- Manufacturing 4.0
- Leverage implementation of S4/Hana
- Digitalization of go-to-market

**Lower SG&A as a % of net sales by 2024**

---

**Improve COGS to limit negative impact of product mix**

# 5,700+ employees committed to society with clear KPIs by 2024



## Employees

- **Best place to work** certification in >75% of countries
- **Gender balance**<sup>1</sup> in global leadership team
- Fill 65% of leadership roles via **internal promotion**



## Communities

- **1/3+** of employees supporting healthcare and environment **communities**<sup>1</sup>
- Continue support for **IFPMA Access Accelerated** initiative<sup>3</sup>



## Environment

- **21% reduction of greenhouse gas emissions**<sup>1,2</sup>
- **24% reduction of water consumption**
- **20% reduction of process waste**

Compensation of management & credit facility include social responsibility metrics<sup>1</sup>

# Financial outlook<sup>1</sup> 2020 to 2024



## Group net sales CAGR 2020-24 between +2% & +5%

- At constant exchange rates and scope
- Assuming potential additional indications



## Commitment to invest in R&D supported by SG&A efficiencies

- Lower SG&A as a % of net sales driven by focus & optimization
- Higher R&D as a % of net sales driven by external innovation strategy

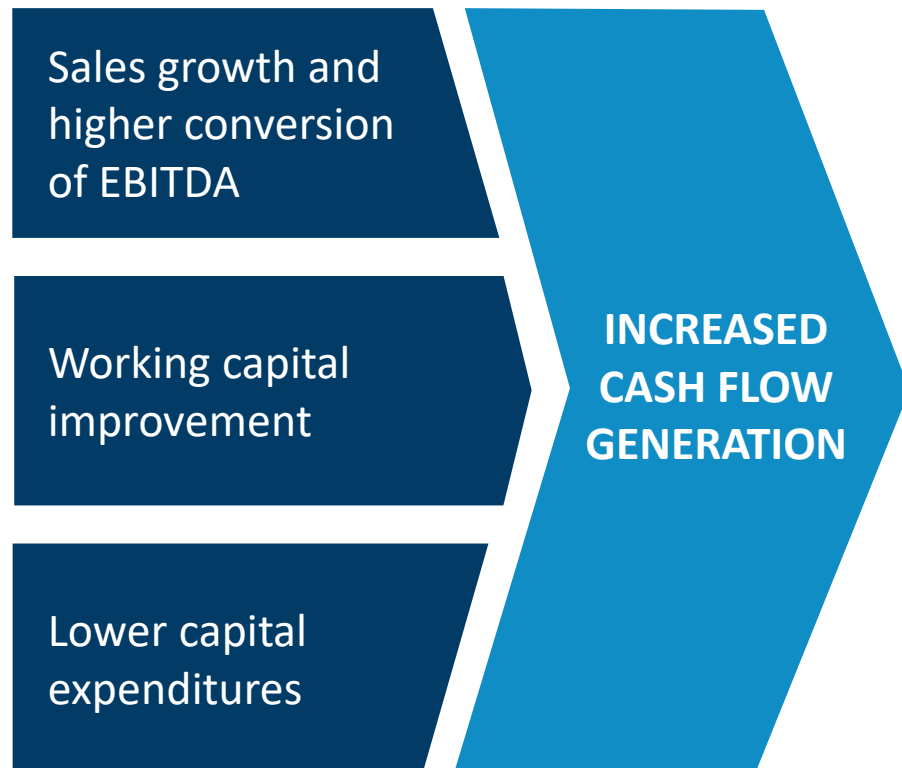


## €3bn cumulative firepower for pipeline expansion

- Excluding the sale of any assets
- Based on net debt below 2.0x EBITDA



# Capital allocation prioritized to external innovation



## PRIORITIES FOR CAPITAL ALLOCATION

- **Priority to external innovation and business development**
- Limited evolution of dividend
- Share buyback only to cover management incentive plan
- Limited milestone payments except contingent Onivyde<sup>®</sup> payment for new indications

**€3bn cumulative firepower for pipeline expansion by 2024**

based on net debt below 2.0x EBITDA



**Diana**  
Living with post-stroke spasticity  
Sintra, Portugal



# Investor Presentation

Spring 2021



# APPENDIX

# Q1 2021

## Encouraging top-line and pipeline progress

### Key highlights



**Total Sales** +5.5% to €659m

- **Specialty Care** +6.4% to €612m



**Regulatory EU approval**

- Cabometyx + nivolumab in 1L aRCC



**COVID-19**

- Limiting diagnoses, treatments and patient care



**Near term**

- **Cabometyx** 1L HCC data readout
- **Palovarotene** regulatory progress



**Full-year guidance confirmed**

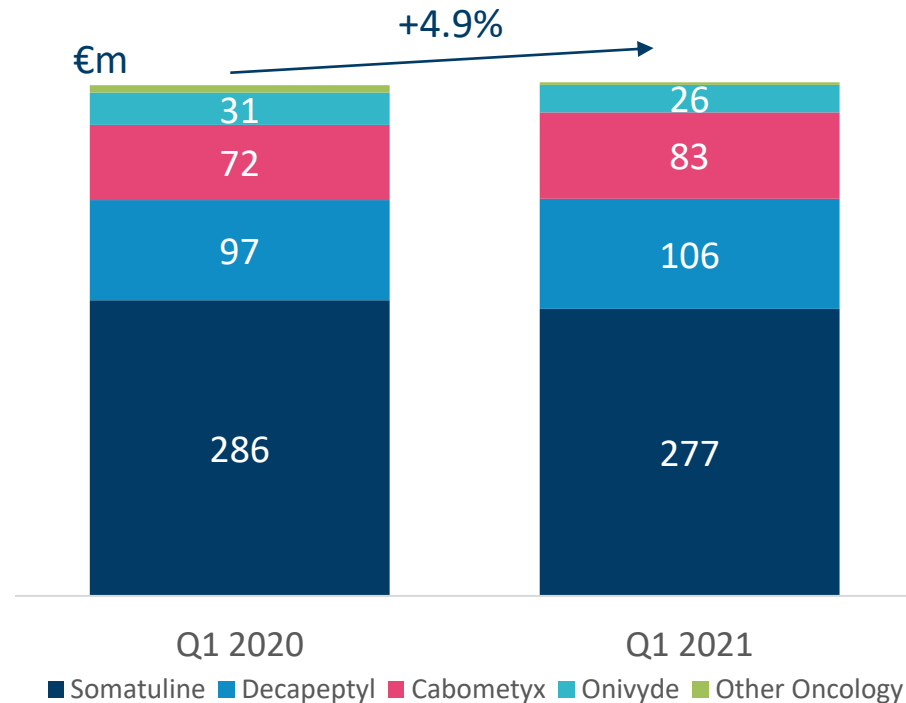


# Q1 2021 sales highlights

## Oncology

**+4.9%**

€495m: 75% of Total Sales



## COVID-19

limiting diagnoses and treatments



**+2.5%**, driven by North America (+5.1%)  
Some stocking in Europe in Q1 2020  
Continued share growth



**+12.0%**, driven by recovery in China  
Gaining market share  
Focusing on the 6m formulation



**+16.4%**  
Strong volumes across most geographies  
Approval in combination in 1L aRCC



**-6.9%**  
Particular adverse COVID-19 impact in the U.S.

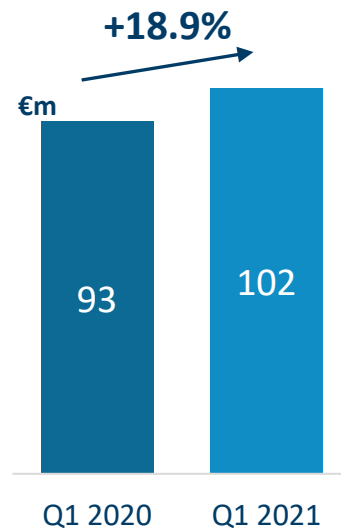
# Q1 2021 sales highlights



**+18.9%**

€102m: 15% of Total Sales

- Aesthetics driving the performance
- Therapeutics and Europe overall still impacted by the pandemic

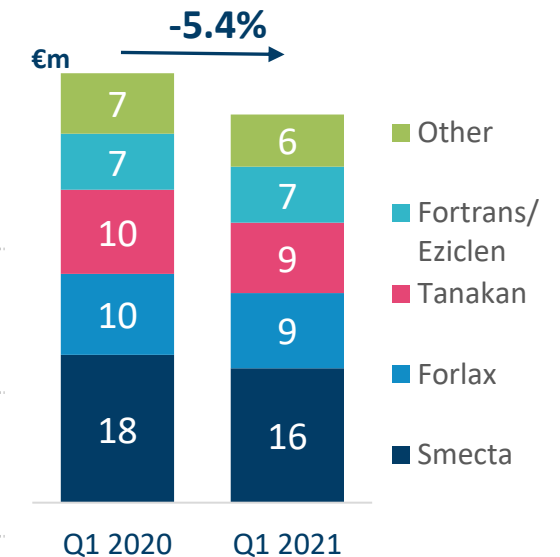


## Consumer Healthcare

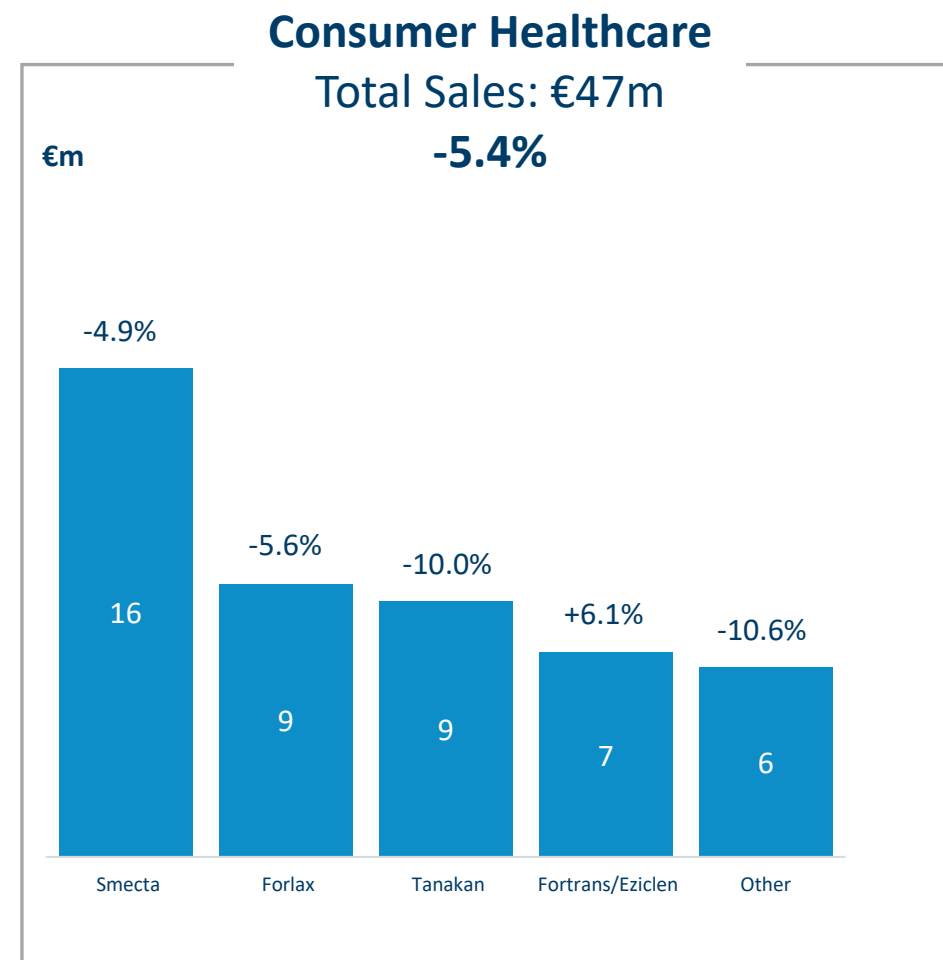
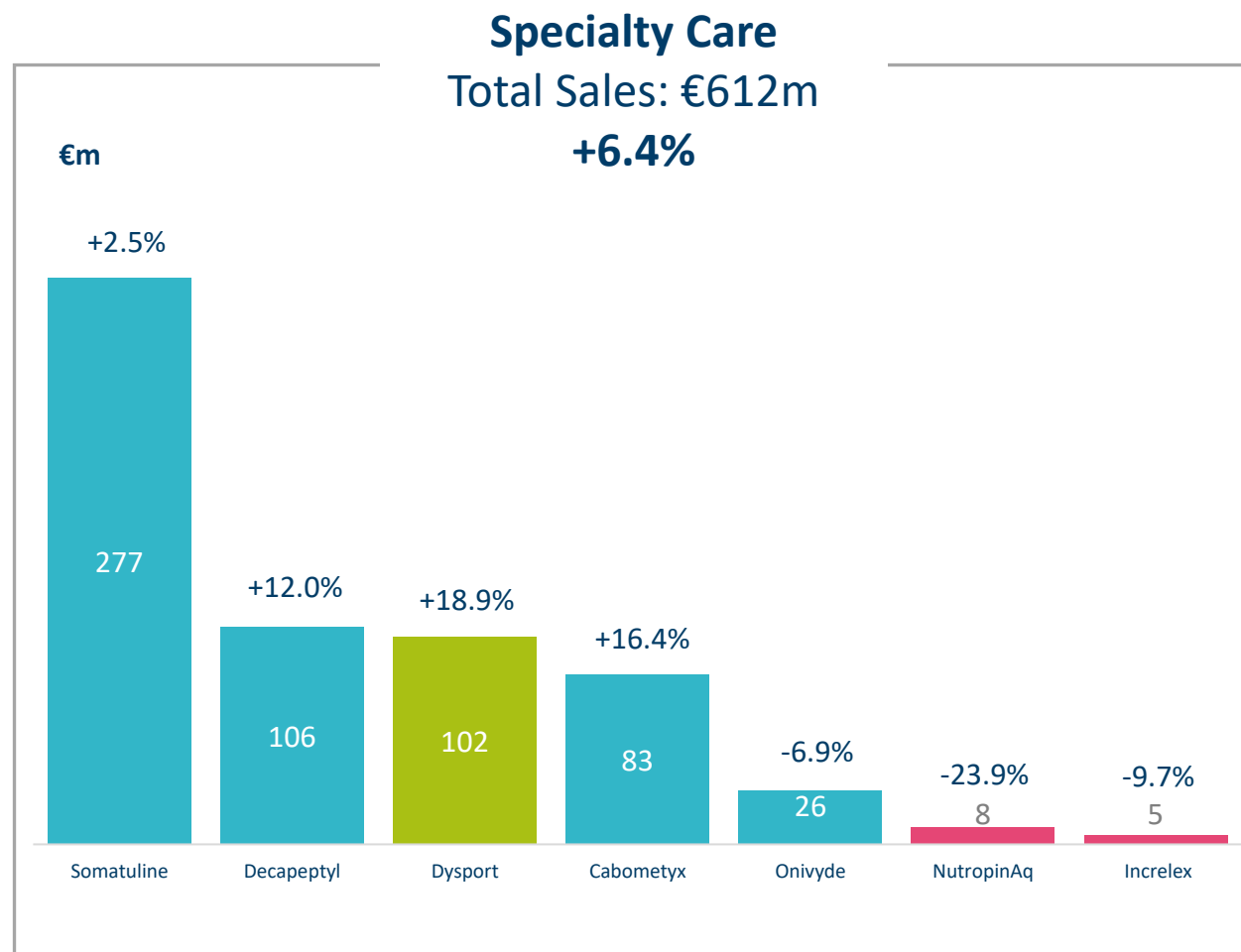
**-5.4%**

€47m: 7% of Total Sales

- Smecta -4.9%, driven by the slowdown of the diarrhea market
- Improving conditions in China
- Strategic review ongoing



# Q1 2021 sales growth driven by Specialty Care



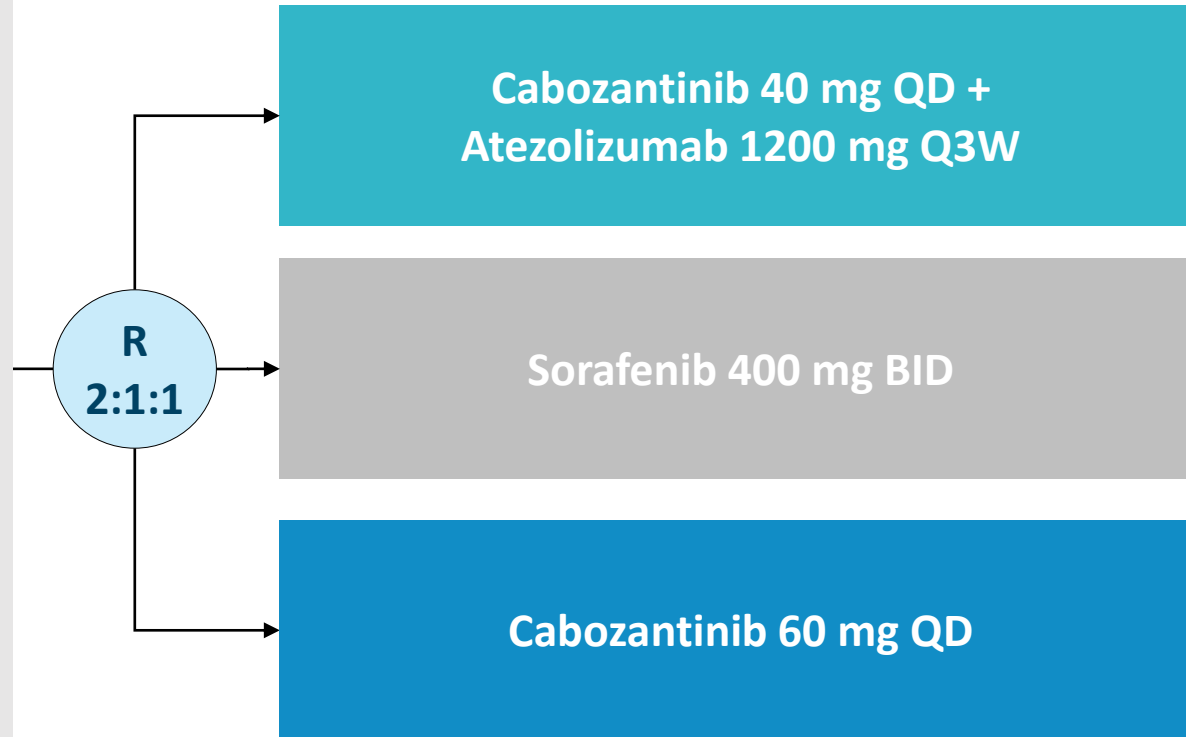
# Cabometyx® | COSMIC-312: 1L HCC study design

**Key inclusion criteria** (N=740, global enrollment completed; continued extended enrollment for China)

- No prior systemic anticancer therapy
- Child-Pugh Class A
- BCLC Stage B or C
- ECOG PS  $\leq 1$
- Measurable disease per RECIST v1.1

**Stratification factors**

- Disease etiology (HBV, HCV, other)
- Region (Asia, other)
- Extrahepatic spread (yes, no)



**Primary endpoint**

- PFS-BIRC/OS (cabozantinib + atezolizumab vs. sorafenib)

**Secondary endpoint**

- PFS (cabozantinib vs. sorafenib)

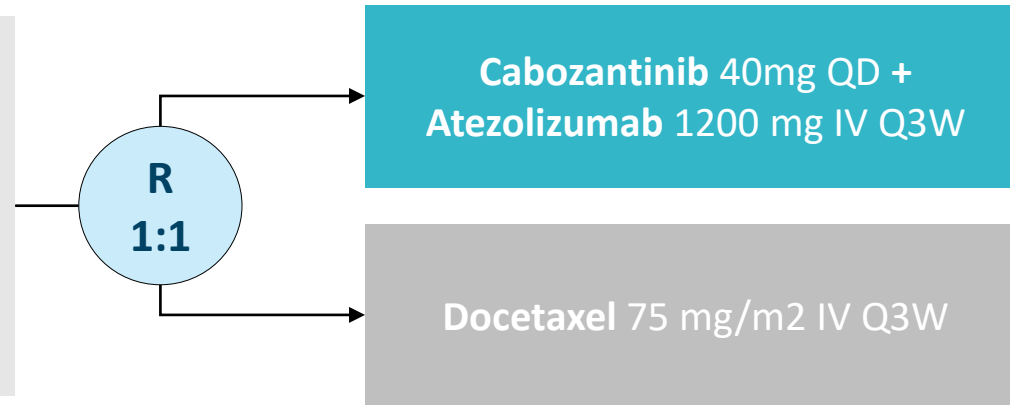
Global topline results expected H1 2021; EU filing in 2021, assuming positive results

# Cabometyx® | CONTACT-01<sup>1</sup> & CONTACT-02<sup>1</sup>: trial designs

## Phase III – NSCLC - CONTACT 01

Enrollment: N = 350; Key milestones: expected topline readout in 2022

- Radiographic progression during or following platinum-containing and anti-PD-L1 therapy for metastatic NSCLC
- Measurable disease per RECIST 1.1
- Known PD-L1 status or availability of tumor tissue for central PD-L1 testing
- ECOG 0-1



### Primary endpoint

- OS

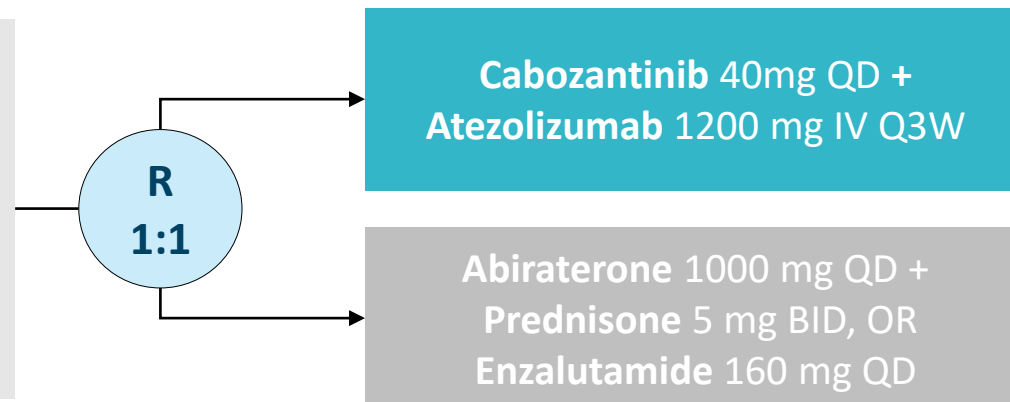
### Secondary endpoints

- PFS per investigator
- ORR
- DOR
- QoL

## Phase III – mCRPC - CONTACT 02

Enrollment: N = 580; Key milestones: expected topline readout in 2023

- Measurable visceral metastases, OR measurable extrapelvic lymph node metastases
- Received 1 NHT for mCSPC, M0 CRPC, or 1L mCRPC
- No prior chemotherapy for mCRPC
- ECOG 0-1



### Primary endpoints

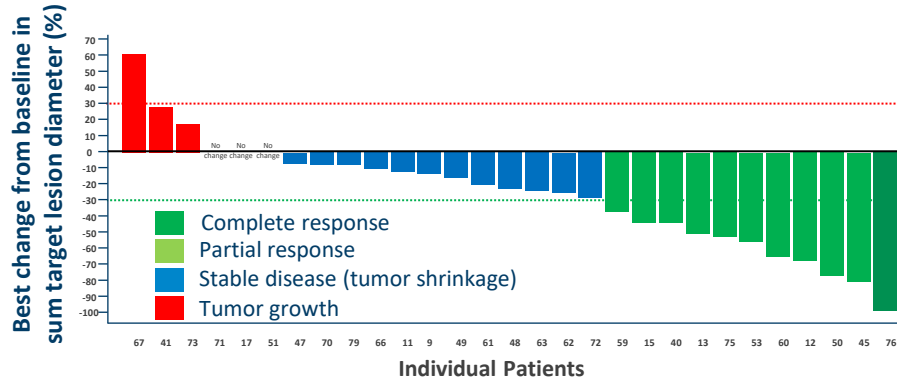
- OS, PFS by RECIST 1.1 per BICR

### Secondary endpoint

- ORR per BICR

# Onivyde®: 1L pancreatic ductal adenocarcinoma (PDAC)

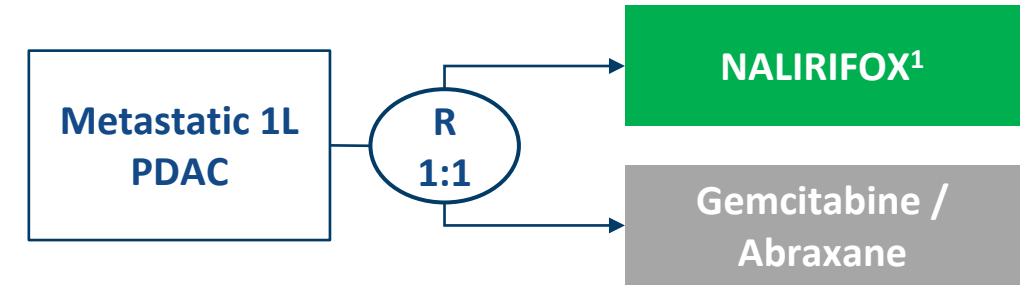
## Phase 2 results



| NALIRIFOX <sup>1</sup> Phase 1/2 - 50/60 Cohort |   |
|---|---|
| N   | 32 (29 metastatic & 3 locally advanced) |
| Complete Response                               | 1 (3.1%)                                |
| Partial Response                                | 10 (31.3%)                              |
| Stable Disease                                  | 15 (46.9%)                              |
| ORR; % (95%)                                    | 11 (34.4%)                              |
| DCR; % (95%)                                    | 26 (81.3%)                              |
| DOR (median); % (95% CI)                        | 9.4 months (3.52-NE)                    |
| PFS (median); % (95% CI)                        | 9.2 months (7.69-11.96)                 |
| OS (median); % (95% CI)                         | 12.6 months (8.74-18.69)                |

## Phase 3 NAPOLI-3 study status & design

- Phase 3 study ongoing
- Received FDA Fast Track designation in June 2020
- Expected topline readout: 2023



### 1L mPDAC (N=750)

- Histologically/cytologically confirmed PDAC
- Not previously treated in the metastatic setting
- >1 metastatic tumor measurable per RECIST v1.1
- ECOG performance status of 0 or 1

### Primary endpoint

- OS

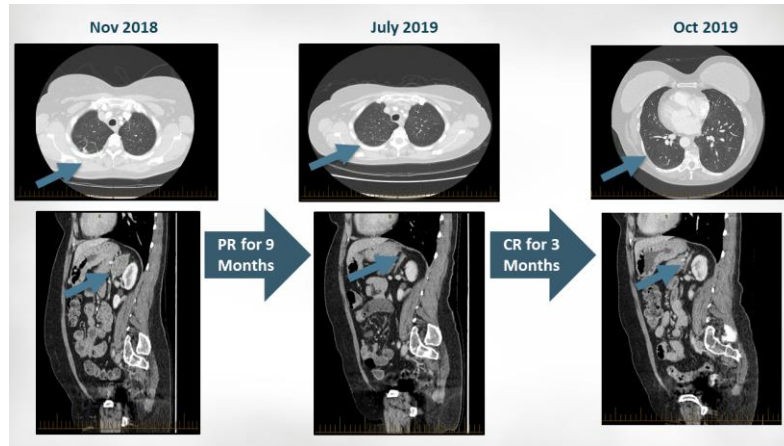
### Secondary endpoints

- PFS
- ORR
- Safety



# Onivyde®: 2L small cell lung cancer (SCLC)

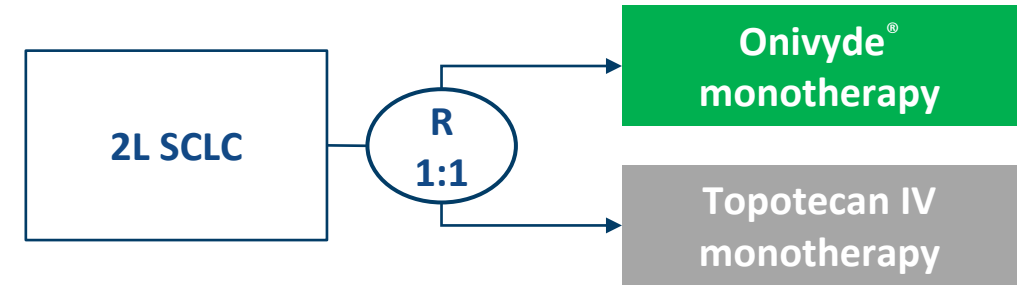
## Phase 2 results



| Resilient Study Part 1 – 70 mg/m <sup>2</sup> Cohort |          |
|--|----------|
| <b>N</b>   | 25       |
| <b>Complete Response</b>                             | 1 (4%)   |
| <b>Partial Response</b>                              | 10 (40%) |
| <b>Stable Disease</b>                                | 7 (28%)  |
| <b>ORR; % (95%)</b>                                  | 11 (44%) |
| <b>DCR; % (95%)</b>                                  | 18 (72%) |

## Phase 3 RESILIENT study status & design

- Phase 3 study ongoing
- Expected topline readout 2022
- **Potential for accelerated regulatory review**



### 2L SCLC (N=450)

- Histologically/cytologically confirmed SCLC with evaluable disease per RECIST v1.1
- Progression after 1L platinum-based therapy
- Prior immunotherapy is allowed
- ECOG performance status of 0 or 1

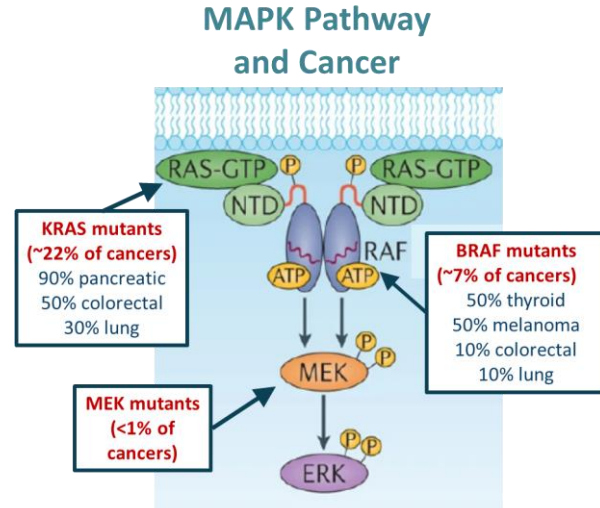
### Primary endpoint

- OS

### Secondary endpoints

- PFS
- ORR
- Safety

# Targeting best-in-class approach to MAPK driven tumors



**MAPK pathway is one of the most commonly mutated** oncogenic driver pathways in cancers with high unmet medical need

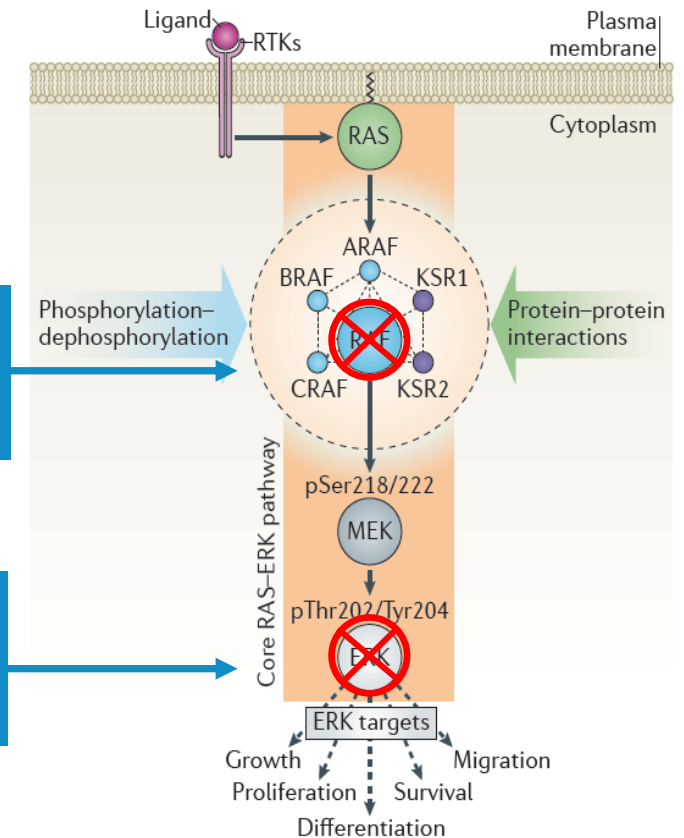
**Room for improvement** as existing approaches provide insufficient pathway inhibition against a subset of the mutations

**Pan-RAFi: broader & more complete activity than current agents**

*IRICoR*

**ERKi: prevent pathway reactivation, more durable pathway inhibition**

*AGV Discovery*



**A portfolio with both pan-RAFi & ERKi programs enables us to develop best-in-class wholly owned monotherapy & combination treatments for MAPK-driven cancers**

# FOP is an ultra-rare, severely disabling genetic disorder

- FOP characterized by bilateral malformations of the great toes, & the formation of bone in soft connective tissues known as **heterotopic ossification (HO)**<sup>1</sup>
- HO leading to progressive, cumulative **disability**
- Sporadic episodes of painful soft tissue swelling called ‘**flare-ups**’ can precede new HO<sup>1</sup>
- Prevalence of FOP being up to **1.36 per million** individuals<sup>2</sup>
- 97% of patients with FOP have classic FOP, associated with an R206H mutation in the gene **ACVR1** (also known as **ALK2**)<sup>3</sup>

Characteristic malformed great toes & hallux valgus<sup>4</sup>



Illustration of HO progression over time<sup>5</sup>



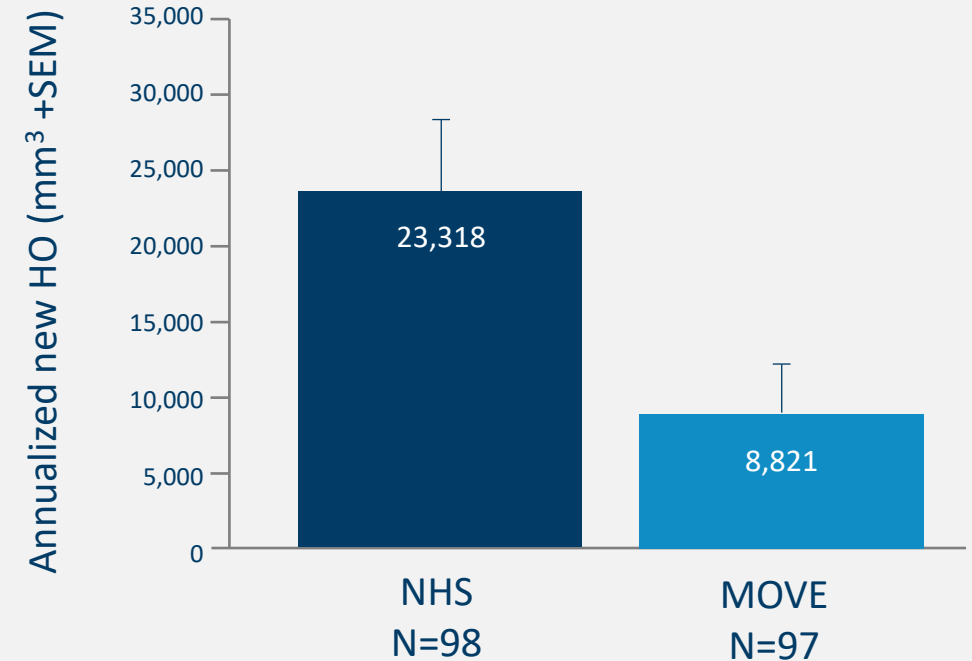
4-year old

10-year old

31-year old

# Palovarotene: 62% reduction in mean annualized new HO volume<sup>1</sup> in Phase 3 MOVE trial

- Demographics & baseline characteristics **sufficiently similar between MOVE & NHS** to support comparison
- New HO volume used as a study endpoint to **measure FOP disease progression**
- **Post hoc analyses showed substantial efficacy** at 3<sup>rd</sup> interim analysis, despite pre-specified futility
- Most common AEs **retinoid-associated** & managed with prophylactic and/or symptomatic therapy
  - Identified **risk of premature physeal closure** in children



- Weighted linear mixed effects (wLME) model estimate: **-11,611 mm<sup>3</sup>**
- wLME nominal p-value: **p=0.0292**

# LANTs: differentiated therapeutic properties



**Therapeutic efficacy benefits:** longer duration of action



**Safety benefits: higher therapeutic index** enabling wider range of possible doses



**Less local and contralateral spread vs native toxins** in non-clinical model



**Increased convenience:** fewer injections/year



**Strong IP protection**

**First-patient dosing in the program**

# Oncology

## Key ongoing clinical-trial highlights

| Trial   | Population   | Patients | Design   | Endpoints  | Status  |
|---|--------------|----------|--|--|---|
| Cabometyx<br>COSMIC 312<br>Phase III<br>NCT03755791 | 1L HCC       | 740      | Sorafenib<br>or<br>Cabometyx + atezolizumab<br>or<br>Cabometyx   | Primary: PFS, OS<br>Secondary: PFS single-agent<br>Cabometyx arm   | Recruiting<br><br>Data anticipated<br>Q2 2021 |
| Cabometyx<br>CONTACT-01<br>Phase III<br>NCT04471428 | 2L NSCLC     | 350      | Docetaxel<br>or<br>Cabometyx + atezolizumab  | Primary: OS<br>Secondary: PFS, ORR, duration<br>of response  | Recruiting<br><br>Data anticipated<br>2023    |
| Cabometyx<br>CONTACT-02<br>Phase III<br>NCT04446117 | 2L CRPC      | 580      | Second novel hormonal<br>therapy (abiraterone and<br>prednisone or enzalutamide)<br>or<br>Cabometyx + atezolizumab | Primary: OS, PFS<br>Additional endpoints: ORR,<br>prostate-specific antigen<br>response rate and duration of<br>response | Recruiting<br><br>Data anticipated<br>2024    |
| Cabometyx<br>Phase Ib<br>NCT03170960                | Solid tumors | 1,732    | Cabometyx + atezolizumab   | Primary: maximum tolerated<br>dose / recommended dose,<br>ORR<br>Secondary: safety                                       | Recruiting                                    |

**CRPC:** castration-resistant prostate cancer; **ORR:** objective response rate; **OS:** overall survival; **PFS:** progression-free survival.



# Oncology

## Key ongoing clinical-trial highlights

| Trial  | Population | Patients | Design   | Endpoints                                  | Status   |
|--|------------|----------|--|--|--|
| Onivyde<br>NAPOLI 3<br>Phase III<br>NCT04083235  | 1L PDAC    | 750      | Nab-paclitaxel + gemcitabine<br>or<br>Onivyde + 5-FU/LV +<br>oxaliplatin | Primary: OS<br>Secondary: PFS, ORR, safety | Recruiting<br><br>Data anticipated<br>2023             |
| Onivyde<br>RESILIENT<br>Phase III<br>NCT03088813 | 2L SCLC    | 461      | Topotecan<br>or<br>Onivyde   | Primary: OS<br>Secondary: PFS, ORR, safety | Active, not recruiting<br><br>Data anticipated<br>2022 |

# Neuroscience

## Key ongoing clinical-trial highlights

| Trial   | Population                                      | Patients | Design  | Endpoints                              | Status     |
|---|---|----------|---|--|------------|
| IPN59011 Ax<br>LONG-SET<br>Phase I<br>NCT04736745 | Moderate to<br>severe upper<br>facial lines     | 424      | Dose escalation and dose finding<br>versus Dysport or placebo | Primary: Safety<br>Secondary: Efficacy | Recruiting |
| IPN10200 Ax<br>LANTIC<br>Phase I<br>NCT04821089   | Moderate to<br>severe upper<br>facial lines     | 424      | Dose escalation and dose finding<br>versus Dysport or placebo | Primary: Safety<br>Secondary: Efficacy | Recruiting |
| IPN10200 Tx<br>LANTIMA<br>Phase I<br>NCT04752774  | Adult patients<br>with upper limb<br>spasticity | 209      | Dose escalation and dose finding<br>versus Dysport or placebo | Primary: Safety<br>Secondary: Efficacy | Recruiting |

# Rare Disease

## Key ongoing clinical-trial highlights

| Trial  | Population       | Patients | Design  | Endpoints   | Status                 |
|--|------------------|----------|---|---|------------------------|
| Palovarotene<br>MOVE<br>Phase III<br>NCT03312634 | FOP<br>(chronic) | 107      | Palovarotene - 5mg QD and<br>upon flare-up, 20mg QD for<br>28 days, followed by 10mg<br>for 56 days | Primary: annualized change in<br>new HO volume<br>Secondary: subjects with new<br>HO, number of body regions<br>with HO, subjects with flare-<br>ups, rate of flare-ups, safety | Active, not recruiting |



**Diana**  
Living with post-stroke spasticity  
Sintra, Portugal



# Investor Presentation

Spring 2021