Disclaimer & Safe Harbor

This presentation includes only summary information and does not purport to be comprehensive. Forward-looking statements, targets and estimates contained herein are for illustrative purposes only and are based on management’s current views and assumptions. Such statements involve known and unknown risks and uncertainties that may cause actual results, performance or events to differ materially from those anticipated in the summary information. Actual results may depart significantly from these targets given the occurrence of certain risks and uncertainties, notably given that a new product can appear to be promising at a preparatory stage of development or after clinical trials but never be launched on the market or be launched on the market but fail to sell notably for regulatory or competitive reasons. The Group must deal with or may have to deal with competition from generic that may result in market share losses, which could affect its current level of growth in sales or profitability. The Company expressly disclaims any obligation or undertaking to update or revise any forward-looking statements, targets or estimates contained in this presentation to reflect any change in events, conditions, assumptions or circumstances on which any such statements are based unless so required by applicable law.

All product names listed in this document are either licensed to the Ipsen Group or are registered trademarks of the Ipsen Group or its partners.

The implementation of the strategy has to be submitted to the relevant staff representation authorities in each country concerned, in compliance with the specific procedures, terms and conditions set forth by each national legislation.

The Group operates in certain geographical regions whose governmental finances, local currencies or inflation rates could be affected by the current crisis, which could in turn erode the local competitiveness of the Group’s products relative to competitors operating in local currency, and/or could be detrimental to the Group’s margins in those regions where the Group’s drugs are billed in local currencies.

In a number of countries, the Group markets its drugs via distributors or agents: some of these partners’ financial strength could be impacted by the crisis, potentially subjecting the Group to difficulties in recovering its receivables. Furthermore, in certain countries whose financial equilibrium is threatened by the crisis and where the Group sells its drugs directly to hospitals, the Group could be forced to lengthen its payment terms or could experience difficulties in recovering its receivables in full.

Finally, in those countries in which public or private health cover is provided, the impact of the financial crisis could cause medical insurance agencies to place added pressure on drug prices, increase financial contributions by patients or adopt a more selective approach to reimbursement criteria.

All of the above risks could affect the Group’s future ability to achieve its financial targets, which were set assuming reasonable macroeconomic conditions based on the information available today.
<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Presenter(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:00pm</td>
<td>01 Vision &amp; Strategy</td>
<td>David Meek</td>
</tr>
<tr>
<td>1:10pm</td>
<td>02 Financials</td>
<td>Aymeric Le Chatelier</td>
</tr>
<tr>
<td>1:20pm</td>
<td>03 R&amp;D strategy/ External innovation strategy</td>
<td>Alexandre LeBeaut/ Ivana Magovčević-Liebisch</td>
</tr>
<tr>
<td>1:35pm</td>
<td>Q&amp;A</td>
<td></td>
</tr>
<tr>
<td>1:55pm</td>
<td>04 Rare Diseases</td>
<td>Harout Semerjian/ Clarissa Desjardins</td>
</tr>
<tr>
<td>2:20pm</td>
<td>05 Neuroscience</td>
<td>Harout Semerjian/ John Chaddock</td>
</tr>
<tr>
<td>2:40pm</td>
<td>Q&amp;A</td>
<td></td>
</tr>
<tr>
<td>2:55pm</td>
<td>Break</td>
<td></td>
</tr>
<tr>
<td>3:10pm</td>
<td>06 Oncology</td>
<td>Richard Paulson, Sandy McEwan, Yan Moore</td>
</tr>
<tr>
<td>4:10pm</td>
<td>Q&amp;A/ Conclusion</td>
<td></td>
</tr>
<tr>
<td>4:30pm</td>
<td>Cocktail reception</td>
<td></td>
</tr>
</tbody>
</table>
Vision and Strategy

David Meek
Chief Executive Officer
VISION

Being a leading global biopharmaceutical company focused on Innovation and Specialty Care
Ipsen at a glance

Industry leading top and bottom-line growth

Specialty Care
- 89% of sales
- #1 or #2 in key markets

Advancing R&D pipeline
- 5 NCEs and multiple LCM programs

Top 14 Oncology company globally
- 2018 sales >€1.5bn

Well-diversified geographically
- Presence in >115 countries

High-performing executive management team
- Focus on culture

NCEs: New Chemical Entities; LCM: Lifecycle Management
## Delivering on our strategy

### Objectives from 2017 Investor Day

<table>
<thead>
<tr>
<th>Objective</th>
<th>Execution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deliver double-digit growth and improving profitability</td>
<td>✓ Industry-leading <strong>20%+ sales growth</strong> in 2017 and 2018 driven by Specialty Care</td>
</tr>
<tr>
<td></td>
<td>✓ <strong>COI margin improvement of 6.7pt</strong> 2016-2018</td>
</tr>
<tr>
<td>Implement R&amp;D transformation with focus on innovative and differentiated assets</td>
<td>✓ <strong>Prioritization</strong> and <strong>acceleration</strong> of key internal programs</td>
</tr>
<tr>
<td></td>
<td>✓ <strong>5 innovative NCEs</strong> advancing in the clinic</td>
</tr>
<tr>
<td>Bolster external sourcing model/ business development to expand innovative Specialty Care pipeline</td>
<td>✓ <strong>Clementia acquisition</strong> in Rare Diseases</td>
</tr>
<tr>
<td></td>
<td>✓ Earlier-stage <strong>in-licensing and partnerships</strong> (MD Anderson for IPN60090)</td>
</tr>
</tbody>
</table>
Strengthening leadership position in three therapeutic areas

**Oncology**
- Differentiated, best-in-class products in niche markets
- LCM programs in additional indications to expand benefits and market potential

**Neuroscience**
- Expertise in research, development, manufacturing, commercialization
- R&D programs for additional indications and to provide innovative solutions along treatment paradigm

**Rare Diseases**
- Proven capabilities and patient-centric model to serve unmet medical needs
- First-in-class anchor asset palovarotene
Roadmap and priorities

Growth
• Maximize growth and market share worldwide for differentiated best-in-class Specialty Care products
• Leverage commercial capabilities and optimize cost base

Pipeline
• Increase value of the pipeline by accelerating key R&D programs
• Identify, execute and integrate successful business development transactions

Culture
• Drive further transformation and ambition through leadership and people
• Purpose to expeditiously bring innovative therapies to patients with unmet medical needs
### Multiple value-driving and differentiated pipeline opportunities

**Five new chemical entities in the clinic; Nine regulatory submissions from 2019 to 2022**

<table>
<thead>
<tr>
<th>Preclinical</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Registration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&quot;177Lu-IPN-01072 (Satoreotide Tetraxetan) GEP-NET, breast cancer imaging&quot;</td>
<td>&quot;177Ga-IPN-01070 (Satoreotide Trizoxetan) GEP-NET, breast cancer imaging&quot;</td>
<td>Cabometyx® RCC 1L combination with nivolumab</td>
<td>Somatuline® New delivery system (U.S.)</td>
</tr>
<tr>
<td></td>
<td>IPN60090 (MD Anderson)</td>
<td>Dysport® PDAC 1L</td>
<td>Cabometyx® HCC 1L combination with atezolizumab</td>
<td>Dysport® Glabellar lines (China)</td>
</tr>
<tr>
<td></td>
<td>Cabometyx® combination with atezolizumab Solid tumors</td>
<td>Dysport® Hallux valgus</td>
<td>Decapeptyl® 3M Endometriosis (China)</td>
<td>Dysport® Acromegaly (China)</td>
</tr>
<tr>
<td></td>
<td>1L HCC combination with nivolumab</td>
<td>Dysport® Vulvodynia</td>
<td>Dysport® solution Glabellar lines</td>
<td>Dysport® PUL spasticity</td>
</tr>
<tr>
<td></td>
<td>Onivyde® Breast cancer</td>
<td>IPN60120 (palovarotene) FOP</td>
<td>IPN60120 (palovarotene) FOP</td>
<td>IPN60120 (palovarotene) FOP chronic</td>
</tr>
<tr>
<td></td>
<td>Fast-acting toxin rBoNT/E</td>
<td>IPN60120 (palovarotene) MO</td>
<td>IPN60120 (palovarotene) MO</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IPN60120 (palovarotene) Dry eye</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Abbreviations:**
- **FOP:** Fibrodysplasia Ossificans Progressiva
- **GEP-NET:** Gastroenteropancreatic Neuroendocrine Tumors
- **HCC:** Hepatocellular Carcinoma
- **MO:** Multiple Osteochondromas
- **PDAC:** Pancreatic ductal adenocarcinoma
- **RCC:** Renal Cell Carcinoma
- **SCLC:** Small Cell Lung Cancer
- **1L:** First line
- **2L:** Second line
- **3M:** 3-month formulation

**Additional notes:**
- MRBoNT/A': Longer-acting toxin
- MRBoNT/A: Longer-acting toxin
- MRBoNT/E: Fast-acting toxin
- rBoNT/E: Fast-acting toxin
- rBoNT/A: Long-acting toxin
- rBoNT/A': Long-acting toxin
- GEP-NET (NET): Gastroenteropancreatic Neuroendocrine Tumors
- NTSR1 solid tumors
- PDAC: Pancreatic ductal adenocarcinoma
- SCLC: Small Cell Lung Cancer
- HCC: Hepatocellular Carcinoma
- 1L: First line
- 2L: Second line
- 3M: 3-month formulation

**IPN60120 (palovarotene)**
- FOP: Fibrodysplasia Ossificans Progressiva
- FOP: Fibrodysplasia Ossificans Progressiva
- GEP-NET: Gastroenteropancreatic Neuroendocrine Tumors
- HCC: Hepatocellular Carcinoma
- MO: Multiple Osteochondromas
- PDAC: Pancreatic ductal adenocarcinoma
- RCC: Renal Cell Carcinoma
- SCLC: Small Cell Lung Cancer
- 1L: First line
- 2L: Second line
- 3M: 3-month formulation

**Other abbreviations:**
- 3M: 3-month formulation
- FOP: Fibrodysplasia Ossificans Progressiva
- GEP-NET: Gastroenteropancreatic Neuroendocrine Tumors
- HCC: Hepatocellular Carcinoma
- MO: Multiple Osteochondromas
- PDAC: Pancreatic ductal adenocarcinoma
- RCC: Renal Cell Carcinoma
- SCLC: Small Cell Lung Cancer
- 1L: First line
- 2L: Second line
- 3M: 3-month formulation
Execution on growth strategy through external innovation

Continued investment in R&D pipeline for long-term growth

- Active business development efforts
  - Strengthened and agile global team focused on three key therapeutics areas

- Driven by strong balance sheet
  - Quickly replenishing firepower through significant cash flow generation

- To build an innovative and sustainable pipeline
  - Execute on top-line, bottom-line and pipeline growth strategy
Transformative company culture with focus on social responsibility

Employees
Caring for and developing employees, encouraging diversity and inclusion, and supporting an open and respectful culture

Patients & Society
Providing innovative solutions for the benefit of patients & society based on trusted relationships and shared commitments

Environment
Protecting the environment, minimizing the impact on it, by making activities safe and sustainable
Objectives of the day

- Provide financial outlook and capital allocation strategy
- Update on R&D and External Innovation strategy
- Provide commercial highlights and deep dive in R&D pipeline by therapeutic area

Create and deliver long-term value by executing on growth strategy
Financial update

Aymeric Le Chatelier
Chief Financial Officer
Top-tier consistent financial performance

Significant top-line growth and margin enhancement
On track to deliver 2020 guidance\(^1\) one year early

<table>
<thead>
<tr>
<th></th>
<th>2016</th>
<th>2019</th>
<th>CAGR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sales</td>
<td>€1.58bn</td>
<td>&gt;€2.5bn</td>
<td>+17%</td>
</tr>
<tr>
<td>Core Operating Income</td>
<td>€364mn</td>
<td>&gt;€750mn</td>
<td>+28%</td>
</tr>
<tr>
<td>Core Operating Margin</td>
<td>23%</td>
<td>~30%(^2)</td>
<td>+7pts(^3)</td>
</tr>
</tbody>
</table>

Business Development transactions for ~€2bn since 2016 (Cabometyx, Onivyde, Clementia)

Total Shareholder Return >23\(^4\)% per year since 2016

Strong cash flow generation while investing in business development

Free cash flow (2016-2018)

<table>
<thead>
<tr>
<th></th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>€m</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2016</td>
<td>229</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2017</td>
<td></td>
<td>309</td>
<td></td>
</tr>
<tr>
<td>2018</td>
<td></td>
<td></td>
<td>458</td>
</tr>
</tbody>
</table>

1. 2020 guidance excluding impact of Clementia acquisition: Sales > €2.5bn and Core Operating Margin > 30%
2. Calculation based on company guidance confirmed 24 April 2019
3. Variance 2016-2019. From Jan 1, 2016 to Dec 31, 2018
4. From Jan 1, 2016 to Dec 31, 2018
Financial outlook 2022

Group Net Sales: ~€3.2bn
(assuming current level of exchange rates)

Core Operating Margin: >32.0%
(as % of net sales)

- Existing portfolio, including palovarotene for FOP indications, assumes no approvals of additional meaningful products or indications
- Assuming earliest possible entry of SSA generics based on current market intelligence
  - Any delays would result in significant upside to sales and Core Operating margin
- Impact of further business development not included

Strong top-line and bottom-line growth while investing to grow pipeline
## Strong growth from key Specialty Care products

<table>
<thead>
<tr>
<th>Brand/ asset</th>
<th>Geographies</th>
<th>Major indications</th>
<th>Growth / Peak sales</th>
</tr>
</thead>
<tbody>
<tr>
<td>Somatuline autogel</td>
<td>Global</td>
<td>Neuroendocrine Tumors (NET)</td>
<td>Double-digit growth until potential impact of generic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Acromegaly</td>
<td></td>
</tr>
<tr>
<td>Decapeptyl® SR triptorelin</td>
<td>Ex-US and Japan</td>
<td>Prostate Cancer</td>
<td>High to mid single-digit growth in all territories</td>
</tr>
<tr>
<td>CABOMETYX® (cabozantinib) tablets</td>
<td>Ex-US and Japan</td>
<td>Renal Cell Carcinoma (RCC)</td>
<td>Expected peak sales of €400mn on current approved indications</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hepatocellular Carcinoma (HCC)</td>
<td></td>
</tr>
<tr>
<td>onivyde™ (riflosin liposome injection)</td>
<td>U.S. only</td>
<td>Pancreatic cancer</td>
<td>Expected peak sales of $300mn for current indication</td>
</tr>
<tr>
<td>Dysport® (abobotulinumtoxinA)</td>
<td>Global</td>
<td>Spasticity (Tx)</td>
<td>Double-digit growth in line with market growth in both markets</td>
</tr>
<tr>
<td>palovarotene clementia</td>
<td>Global</td>
<td>Glabellar lines (Ax)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fibrodysplasia Ossificans Progressiva (FOP)</td>
<td>Expected peak sales of $400mn for FOP indications only (flare-up and chronic)</td>
</tr>
</tbody>
</table>
Somatuline® – Potential SSA competitive environment

Market Intelligence

• Short-acting generic formulations of octreotide and lanreotide available for many years with no impact
• Number of companies identified with an interest in developing long-acting formulations of octreotide or lanreotide
• FDA rejected or delayed several long-acting octreotide generics in past 2 years due to CMC/manufacturing challenges
• Recent filing of long-acting lanreotide generic not expected to result in launch in EU5\(^1\) countries until 2021 at earliest
• No FDA filing for long-acting lanreotide (orphan drug exclusivity in U.S. through December 2021)

Somatuline® outlook

• Long-acting formulations remain standard of care in growing market
• Strong clinical, device and value differentiation of Somatuline vs. octreotide
• Limited patient switch and no interchangeability limiting impact of octreotide generic
• Maximization of Somatuline value in case of lanreotide generic (improved delivery system, loyal patient base, long duration of treatment and patient services)
• Complex and fragmented U.S. injectable oncology market which makes it challenging for generic substitution – strategic partnering and contracting to limit the impact on pricing and patient erosion

---

SSA: Somatostatin Analog; CMC: Chemistry, Manufacturing and Controls; NET: Neuroendocrine Tumors

1. EU5: European Union Five (France, Germany, Italy, Spain, United Kingdom)
## 2022 Core Operating Income growth drivers

<table>
<thead>
<tr>
<th>COGS</th>
<th>Slight increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Higher Cabometyx royalties and lower Somatuline contribution if SSA generics enter</td>
<td></td>
</tr>
<tr>
<td>• Slightly offset by Specialty Care growth and manufacturing efficiencies</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sales &amp; Marketing</th>
<th>Significant reduction as % of sales</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Increasing synergies and leveraging current commercial infrastructure, including mitigation if SSA generics enter</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>R&amp;D</th>
<th>Increase as a % of sales to reach 14%-15% of sales</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Support and accelerate programs for innovative NCEs (including palovarotene) and LCM</td>
<td></td>
</tr>
<tr>
<td>• Incremental investments in business development opportunities to accelerate growth of pipeline not included</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>G&amp;A</th>
<th>Slight decrease as % of sales</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Streamlining of operations and limited growth in support functions</td>
<td></td>
</tr>
</tbody>
</table>

**Other Revenues**

Decrease from impact of Adenuric loss of exclusivity (from 2019) and Galderma milestone amortization (from 2021)
## Capital allocation principles

| Business development | • **Significant financing capacity** to leverage balance sheet up to 2.0x Net Debt to EBITDA  
• **>€1bn business development fire power** by end of 2020  
• **Strict financial discipline** based on IRR, value creation > cost of capital and risk adjusted analysis and structuring  
• **Long-term value and growth creation** outweighs potential short-term, low single-digit Core Operating margin dilution |
| --- | --- |
| Capex | • Investments to support **capacity expansion** for key products and pipeline  
• Investments to support **Group growth and transformation initiatives** |
| Dividends | • **Limited increases** in order to prioritize external growth strategy |
| Share buyback | • **Limited share buybacks** only to prevent dilution from employee incentive plans |

**EBITDA**: Earnings Before Interest, Tax, Depreciation and Amortization; **IRR**: Internal Rate of Return
Priorities to deliver strong shareholder return

**Sales growth**
- Maintain ambition of double-digit top-line growth
- Maximize key product growth
- Build leadership position in attractive Specialty Care markets

**Margin expansion**
- Utilize multiple levers to optimize resource allocation
- Increase synergies through leveraging current commercial infrastructure
- Prioritize R&D investment to grow pipeline

**Capital allocation**
- Increase strong free cash flow generation
- Accelerate Business Development with strong balance sheet
- Invest in sustainable growth through disciplined capital allocation policy

Strong top-line and bottom-line growth while investing to grow pipeline
03
R&D / External Innovation Strategy
R&D Strategy and Portfolio

Alexandre LeBeaut, MD
Chief Scientific Officer
Growing our Pipeline: R&D Strategy

Focus on Oncology, Neuroscience and Rare Diseases

- Addressing unmet medical needs

Aiming for first/best-in-class assets drives differentiation of the pipeline

- Innovative programs: Systemic Radiation Therapy (SRT), recombinant neurotoxins, palovarotene

Be a leading external innovation-sourcing organization

- Open innovation
- Leverage presence and collaborations in strategically located ecosystems

Be a development powerhouse

- Accelerate programs with highest value
- Optimize digital and cutting-edge innovation and technologies
### Accomplishments since Investor Day 2017

<table>
<thead>
<tr>
<th>Oncology</th>
<th>Neuroscience</th>
<th>Rare Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Decapeptyl®</strong> Breast cancer (EU)</td>
<td>Dysport® ALL spasticity (U.S.)</td>
<td>IPN60120 (palovarotene) MO</td>
</tr>
<tr>
<td><strong>Xermelo®</strong> Carcinoid syndrome</td>
<td>Dysport® PLL spasticity (EU)</td>
<td>IPN60120 (palovarotene) POP</td>
</tr>
<tr>
<td><strong>Somatuline®</strong> New delivery system (EU)</td>
<td>Somatuline® GEP NET Japan</td>
<td>IPN60120 (palovarotene) FOP Chronic</td>
</tr>
<tr>
<td><strong>Somatuline® Autogel®</strong> Carcinoid syndrome (U.S.)</td>
<td>Cabometyx® 1L RCC (EU)</td>
<td>IPN60120 (palovarotene) FOP</td>
</tr>
<tr>
<td><strong>Cabometyx® 2L HCC (EU)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cabometyx® 1L RCC combination with nivolumab</strong></td>
<td>Cabometyx® 1L RCC combination with atezolizumab</td>
<td></td>
</tr>
<tr>
<td><strong>Cabometyx® 1L HCC combination with nivolumab</strong></td>
<td>Cabometyx® 1L HCC combination with nivolumab</td>
<td></td>
</tr>
<tr>
<td><strong>Decapeptyl® 6M Prostate cancer (China)</strong></td>
<td>Decapeptyl® 6M Prostate cancer (China)</td>
<td></td>
</tr>
<tr>
<td><strong>177Lu-IPN-01087 NTSR1 solid tumors</strong></td>
<td>Satoreotide GEP-NET imaging</td>
<td></td>
</tr>
<tr>
<td><strong>rBoNT/E Fast-acting toxin</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Decapeptyl®</strong> Breast cancer (EU)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Somatuline®</strong> New delivery system (U.S.)</td>
<td>Somatuline® New delivery system (U.S.)</td>
<td></td>
</tr>
<tr>
<td><strong>Xermelo®</strong> Carcinoid syndrome</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**9** Major indications approved

**16** New projects added into development including

**5** NCEs entering clinical development

---

NET: Neuroendocrine Tumors; RCC: Renal Cell Carcinoma; HCC: Hepatocellular Carcinoma; ALL: Adult Lower Limb; PLL: Pediatric Lower Limb; GEP-NET: Gastroenteropancreatic Neuroendocrine Tumor; FOP: Fibrodysplasia Ossificans Progressiva; MO: Multiple Osteochondromas
Being a Development Powerhouse

- Seasoned experts leading innovation platforms
- Integrated digital solutions (site selection, in silico clinical trials)
- Regulatory science to support innovative study design (e.g. basket trials)
- Integrated pharmaceutical development

- Focus on high unmet needs and well-defined patient populations
- Integration of Patient Reported Outcomes (PROs)
- Patient engagement across drug development

- Lean Governance to streamline decision making process
- To enable rapid reallocation of resources to high priority projects
- To create a risk-balanced and innovative pipeline of differentiated assets in Oncology, Neuroscience and Rare Diseases
Leading a risk-balanced early and late stage innovative proprietary pipeline

Preclinical
- Palovarotene (FOP chronic)
- Palovarotene (FOP episodic)
- Palovarotene (MO)
- Palovarotene (dry eye)
- NTSR1 177Lu-IPN01087 (solid tumors)
- Long-acting toxin mrBoNT/A
- Long-acting toxin mrBoNT/A'

Phase 1
- First-in-class
  - Palovarotene (FOP chronic)
  - Palovarotene (FOP episodic)
  - Palovarotene (MO)
  - Palovarotene (dry eye)
  - NTSR1 177Lu-IPN01087 (solid tumors)
  - Long-acting toxin mrBoNT/A
  - Long-acting toxin mrBoNT/A'
  - Satoreotide (GEP-NET imaging)
  - Fast-acting toxin (rBoNT/E)
  - Satoreotide (GEP-NET and non NET)
  - IPN60090 (MD Anderson)

Phase 2

Phase 3

First-in-class

Best-in-class

Oncology
Neuroscience
Rare Diseases/ Other

FOP: Fibrodysplasia Ossificans Progressiva; GEP-NET: Gastroenteropancreatic Neuroendocrine Tumors; MO: Multiple Osteochondromas; rBoNT/A: recombinant Botulinum Toxin Type A; rBoNT/E: recombinant Botulinum Toxin Type E
# Targeted regulatory submissions

Delivering >1 NCE / significant new indication per year

<table>
<thead>
<tr>
<th>Year</th>
<th>2019</th>
<th>2020</th>
<th>2021</th>
<th>2022</th>
<th>2023</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Somatuline</strong>&lt;sup&gt;*&lt;/sup&gt;</td>
<td>Dysport&lt;sup&gt;*&lt;/sup&gt; PUL spasticity (U.S., EU)</td>
<td>Dysport&lt;sup&gt;*&lt;/sup&gt; Glabellar lines (China)</td>
<td>Dysport&lt;sup&gt;*&lt;/sup&gt; solution Glabellar lines (EU)</td>
<td>IPN 60120 (palovarotene) FOP episodic (U.S.*)</td>
<td>Onivyde&lt;sup&gt;*&lt;/sup&gt; SCLC (U.S.)</td>
</tr>
<tr>
<td>GEP-NET (China)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Decapeptyl 3M Endometriosis (China)</td>
<td>Decapeptyl 6M Breast cancer (China)</td>
<td>IPN 60120 (palovarotene) FOP chronic (U.S.*)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cabometytx</strong>&lt;sup&gt;*&lt;/sup&gt; 1L RCC combo with nivolumab</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cabometytx</strong>&lt;sup&gt;*&lt;/sup&gt; 1L HCC combo with atezolizumab</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>IPN01070</strong>&lt;sup&gt;*&lt;/sup&gt; GEP-NET imaging (U.S., EU)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>IPN01072</strong>&lt;sup&gt;*&lt;/sup&gt; GEP-NET (U.S., EU)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Decapeptyl 3M</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Decapeptyl 6M</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Onivyde</strong>&lt;sup&gt;*&lt;/sup&gt; 1L PDAC (U.S.)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dysport</strong>&lt;sup&gt;*&lt;/sup&gt; Hallux valgus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dysport</strong>&lt;sup&gt;*&lt;/sup&gt; Glabellar lines (U.S., EU)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>IPN01070</strong>&lt;sup&gt;*&lt;/sup&gt; GEP-NET imaging (U.S., EU)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Onivyde</strong>&lt;sup&gt;*&lt;/sup&gt; 1L PDAC (U.S.)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>IPN01072</strong>&lt;sup&gt;*&lt;/sup&gt; GEP-NET (U.S., EU)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Onivyde</strong>&lt;sup&gt;*&lt;/sup&gt; SCLC (U.S.)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dysport</strong>&lt;sup&gt;*&lt;/sup&gt; Glabellar lines (U.S., EU)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Somatuline</strong>&lt;sup&gt;*&lt;/sup&gt; GEP-NET (China)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>GEP-NET</strong>: Gastroenteropancreatic Neuroendocrine Tumor; <strong>PUL</strong>: Pediatric Upper Limb; <strong>FOP</strong>: Fibrodysplasia Ossificans Progressiva; <strong>RCC</strong>: Renal Cell Carcinoma; <strong>HCC</strong>: Hepatocellular Carcinoma; <strong>MO</strong>: Multiple Osteochondromas; <strong>SCLC</strong>: Small Cell Lung Cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* To be followed by EU and RoW filing
R&D strategy: Creating value with advancing pipeline

• Strongest pipeline in Ipsen's history risk-balanced across three therapeutics areas and phases development
• 5 New Chemical Entities progressing in clinical development
• Innovative programs with potential to expand into additional indications – Systemic Radiation Therapy, recombinant neurotoxins, palovarotene
• Development powerhouse with disciplined resource allocation
• Focused execution of external innovation strategy to build innovative and sustainable pipeline
External Innovation Strategy

Ivana Magovčević-Liebisch, Ph.D., J.D.
Chief Business Officer
External innovation-focused organization actively searching for new assets

- **Dedicated team** – ~30 scientific and business professionals based across global hubs
- **Integrative & collaborative organization** – Ability to move quickly and effectively from opportunity identification through decision making
- **Differentiating philosophy** – Treat all partners as equals, sharing their passion to develop and commercialize innovation globally
- **Compelling value proposition** – Global development and commercial powerhouse with a strong track record of delivering results
- **Creativity & flexibility** – Commitment, financial strength and size allow for transactional flexibility and creativity

External innovation fuels R&D pipeline to deliver at least one new product or meaningful indication annually
### Areas of Focus

| **Oncology** | • Focus on rare or niche solid tumors  
• All stages of development candidates and marketed products  
• All modalities excluding vaccines, oncolytic viruses, cell therapies, gene therapies |
| **Rare Diseases** | • Rare bone and musculoskeletal diseases and their adjacencies  
• All stages of development candidates and marketed products  
• All modalities |
| **Neuroscience** | • Novel neurotoxins  
• Technologies/ solutions to enhance Ipsen’s neurotoxin therapies and R&D capabilities  
• Movement disorders, spasticity and adjacencies |
| **Early Innovation** | • Strategic alliances with biotech-focused venture capital firms, start-up incubators and major academic centers |
Track Record of Success Through Diverse Partnerships & Transactions

Early Innovation Partnerships

- ARIX BIOSCIENCE plc
- IPSEN INNOVATION CENTER
- biolabs
- bpi France
- InnoBio

New venture capital fund
Cambridge, MA (U.S.)

Academic Alliances

- Harvard Catalyst
- Harvard University
- Gustave Roussy
- Institute of Molecular and Cell Biology

Partnerships/ Licensing

- MD Anderson Cancer Center
- Galderma
- Exelixis
- Debiopharm Group
- 3B Pharmaceuticals
- Lexicon Pharmaceuticals

Asset & Company Acquisitions

- Clementia
- Onivyde (irinotecan liposome injection)
- OctreoPharm Sciences
- Syntaxin
Clementia: Successful Execution of External Innovation Strategy

- Proactively identified Clementia as transformative opportunity in Rare Diseases
- Agility in moving quickly to initiate and drive the process forward
- Collaborative and integrated teamwork internally and with Clementia along the process
- Focused on seamless integration to bring palovarotene to patients worldwide as quickly as possible
Rare Diseases
Rare Diseases

Harout Semerjian
Chief Commercial Officer
Rare Diseases background

Affecting fewer than 1 in 2,000 people

~7000 Rare Diseases
Most are genetic or have a genetic component

~5% have therapeutic treatment available

>560 medicines in development for Rare Diseases
Relatively quicker regulatory pathway and limited competition

Significant unmet medical needs remain

Source: Pharmaceutical Research and Manufacturers of America
Ipsen’s Rare Diseases capabilities

Mission: To develop and bring innovative solutions to people living with debilitating or life-threatening conditions as quickly as possible

• Established legacy of Rare Disease assets in Endocrinology (Nutropin®, Increlex®, Somatuline® in acromegaly); Oncology (Somatuline® in Neuroendocrine Tumors, carcinoid syndrome) and Neuroscience (Dysport® in pediatric spasticity)

• Specialized, non-traditional skill-set in clinical and regulatory

• Global infrastructure including medical advocacy and commercial across key geographies

• Highly patient-centric business model (patient finding and retention, advocacy groups, reimbursement assistance)
Acquisition of Clementia Pharmaceuticals: A Rare Disease company

**Acquisition**
Announced 25 February and closed 17 April

**Key asset**
Palovarotene, an investigational retinoic acid receptor gamma (RARγ) selective agonist, for the treatment of fibrodysplasia ossificans progressiva (FOP), multiple osteochondromas (MO), dry eye and other diseases; IP protection into the early 2030s

**Integration**
Ipsen and Clementia working closely together to ensure smooth transition of operations while maintaining patient-centric culture

Accelerate strong global Rare Disease organization to expeditiously deliver palovarotene to patients worldwide
FOP is a severely disabling bone disorder

Skeleton of Harry Eastlack

- Harry passed away 6 days before his 40th birthday
- Fused skeleton exemplifies harsh reality of FOP
- Reminder of how much work remains to help FOP patients
- On display at the Mutter Museum of The College of Physicians in Philadelphia

Source: IFOPA website; FOP: Fibrodysplasia Ossificans Progressiva
High unmet medical need for FOP

Currently no approved therapies to prevent or treat the formation of heterotopic ossifications (HO, new bone) in FOP

High-dose corticosteroids started within the first 24 hours of a flare-up may help reduce the inflammation\textsuperscript{1,2}

Surgical intervention not recommended – risks new, trauma-induced HO\textsuperscript{1}

Activities that trigger flare-ups should be avoided\textsuperscript{2}

\textbf{FOP}: Fibrodysplasia Ossificans Progressiva; \textbf{HO}: Heterotopic Ossification

FOP patients treated by specialists in centers of excellence

Centers of excellence identified in major markets

Patients managed by variety of specialists

- Pediatricians
- Endocrinologists specializing in bone/mineral disorders
- Orthopedic surgeons
- Medical geneticists

Very active and engaged global and national patient groups

U.S. 10
Germany 3
Spain 2
UK 4
Italy 4
France 2

FOP: Fibrodysplasia Ossificans Progressiva
Significant commercial opportunity for FOP

Well-defined patient population

- Prevalence: 1.3/1 million lives¹: ~9,000 patients
- >800 identified addressable patients in U.S. and EU5
- Characteristic big toe malformation at birth
- Symptoms start ~2-4 years of age
- Progressive disease leading to immobility by mid-twenties
- Median age at death: 40 years
- No available therapies: steroids and NSAIDs are used for symptomatic relief

Limited commercial investments

- Focused commercial investments required for U.S. and ex-US launch based on existing capabilities
- Early access program underway to support patients worldwide
- Worldwide patient-finding efforts underway
- Plan to launch in the U.S., EU and other territories

Favorable FOP launch dynamics expected

<table>
<thead>
<tr>
<th>Well-characterized disease</th>
<th>Favorable product profile</th>
<th>Ultra-rare disease pricing expected based on</th>
<th>Relatively quick ramp expected</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Genetic mutation</td>
<td>• Strong clinical efficacy</td>
<td>• Serious unmet need</td>
<td>• First-in-class treatment option</td>
</tr>
<tr>
<td>• Characteristic big toe malformation at birth</td>
<td>• Daily oral therapy</td>
<td>• Compelling clinical profile</td>
<td>• Patients expected to initiate therapy upon first flare</td>
</tr>
<tr>
<td></td>
<td>• Good safety profile</td>
<td>• Potentially disease modifying</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Functional endpoints forthcoming</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Patient identification

- >800 pts identified many months before expected launch
- Ongoing and active patient identification efforts worldwide
- Historically, many more patients emerge when first therapy for a rare disease becomes available

Peak sales of approximately $400mn for FOP (assuming flare-up and chronic approvals)
Additional significant upside with more FOP patients, MO and other potential indications
Multiple Osteochondromas (MO) – Significant upside opportunity

Another disabling bone disorder with no therapeutic treatment options

- Ultra-rare, debilitating, bone disorder in which multiple benign bone tumors, also known as osteochondromas (OCs), develop on bones
- Diagnosed prevalence\(^1,2,3\): \textbf{1 in 40,000: nearly 200,000 patients}
  \(\rightarrow 20\%\) pre-puberty and \textbf{65\%} moderate to severe disease
  \(\rightarrow \approx 24,000\) patients initially eligible for treatment
- Most common inherited musculoskeletal condition
- Symptoms include functional limitations and skeletal abnormalities
- Supportive care, \textbf{~70\%} of affected individuals undergo multiple surgeries over their lifetime
Palovarotene R&D

Clarissa Desjardins, PhD
Chief Executive Officer, Clementia
Palovarotene for Fibrodysplasia Ossificans Progressiva (FOP)

- Disease of uncontrolled new bone formation
- Symptoms start ~2-4 years of age
- Progressive, irreversible, cumulative
- Immobility by mid-twenties
- Median age at death 40 years
- No available therapies: steroids and NSAIDs are used for symptomatic relief

Connor JM et al., 1982; Cohen RB et al., 1993
FOP is caused by mutations in the ACVR1 gene. Mutant ACVR1 is believed to be overactive on its own, and in the presence of BMP ligands, which induces the BMP signalling pathway.

This leads to muscles, ligaments and tendons progressively turning to bone ('heterotopic ossification') throughout an individual's lifetime.

Palovarotene is an agonist (activator) of a specific subtype of the retinoic acid receptor (RAR-γ). RAR-γ is highly expressed in cartilage-forming cells.

Palovarotene reduces levels of phosphorylated Smads, as well as overall Smad abundance, repressing excess BMP signalling and abnormal bone formation.
Palovarotene Phase 2 and extension study

-201 Study
-202 Study Part A & Part B

10 mg, 5 mg, or Placebo
5 mg, 2.5 mg, or Placebo
No Treatment

14 days
28 days

Enroll within 1 week of flare-up
Treatment period (6 wks)
Observational period (6 wks)
Open-label extension trial for new flare-ups

**Imaging endpoints**
- X-ray
- CT scan
- MRI or ultrasound (US)

**Functional endpoints**
- FOP Patient Reported Outcome (PRO)
- Range of motion
- Global Health scales

**Symptom and other measures**
- NRS pain and swelling
- Cartilage, bone and inflammatory biomarkers
- Device questionnaire

- Randomized, double-blind, multicenter, placebo-controlled (3:1 randomization)
- Adaptive (for dose, duration and timing of assessments)
- All subjects who successfully completed 12 week DB trial participated in OLE
Natural history study of 114 patients

3-year non-interventional study to gain insight into FOP disease progression¹

- Annual in-clinic visits, telephone interviews between visits, in-clinic visits to study new flare ups
- Primary endpoint is change from baseline in total body HO at 3 years
- Other endpoints include physical functioning, patient-reported physical and mental health, and biomarkers

Baseline data from first 101 patients

- All but one subject (99%) had great toe malformations²; thumb malformations (51%) and tibial osteochondromas (37%) also common
- Initial flare-ups (median onset 4.5 years) in the cervical spine (20%), upper back/thoracic spine (20%), and head (19%)²
- Older subjects had more flare-ups in the hip
- Baseline results with respect to mobility, as measured by CAJIS³, are similar to a previous retrospective, international survey in 500 patients⁴

Phase 2 study: 12-week flare-up data

72–75% reduction in new bone growth (HO volumes) at 12 weeks for patients receiving palovarotene at the time of flare-up relative to placebo/untreated flare-ups\(^1,2\)

- The reduction with the episodic 20/10 mg regimen was statistically significant (p=0.02)\(^1,2\)

\(\text{HO: heterotopic ossification; PBO: placebo; PVO: palovarotene}\)

Palovarotene has established safety profile with manageable tolerability

Phase 2 studies

- Dose-related increases in adverse events (AEs); most mild or moderate in severity
- 10/35 subjects had at least one dose-reduction, mainly due to retinoid-associated AEs; most (68%) during 20 mg dosing
- Retinoid-associated AEs include dry skin, dry lips, rash and dry mouth, and can be treated prophylactically
- No apparent effects on growth in skeletally immature subjects

Established safety profile in earlier studies

- Palovarotene was previously investigated in 800 individuals as a possible therapy for COPD
- More than 450 patients received 5 mg palovarotene daily for up to 2 years\textsuperscript{1,2}
- Palovarotene was generally well tolerated, with the exception of mild mucocutaneous events\textsuperscript{1,2}
- Safety profile consistent with other retinoids\textsuperscript{1}

FOP Phase 2 data supports NDA submission

Extensive Phase 2 clinical development program

- FDA has agreed that Phase 2 flare-up data supports NDA submission for the episodic dosing regimen of palovarotene in FOP in children and adults
- NDA submission targeted for H2 2019
- Fast-track, breakthrough therapy, orphan drug and rare pediatric disease designations from the FDA
- Phase 3 trial evaluating chronic treatment to support potential supplemental NDA submission

Potential FDA approval in H1 2020 and EMA approval in H2 2020
Evaluating a new dosing regimen for FOP: Phase 3 MOVE Trial

Efficacy and safety study of chronic oral palovarotene for the treatment of FOP

**HO Primary Endpoint**
annualized volume of new HO measured by whole body CT scan

**Global Study**
15 sites, 11 countries, using natural history study as external control

**>80 Patients Enrolled**
>4 years of age with no current flare-up symptoms

Oral palovarotene at 5 mg once-daily (or weight based equivalent for children)

Flare-up based dosing of 20 mg for 4 weeks followed by 10 mg for 8 weeks

24-month treatment with two interim analyses in 2019 and one in 2020

* Dosing will be weight-adjusted for skeletally immature subjects
** These analyses will assess safety and check tracking of the primary endpoint

FOP: Fibrodysplasia Ossificans Progressiva; HO: Heterotopic Ossification
1. Available at clinicaltrials.gov.uk [NCT03312634]
Palovarotene for Multiple Osteochondromas (MO)

• MO, also known as HME, is the most common inherited musculoskeletal condition

• MO is characterized by the development of multiple, benign, cartilage-capped bone tumors (osteochoondromas)

• Development of osteochondromas (OCs) results in functional limitations and skeletal abnormalities, including;
  • Decreased range of motion, short stature, joint deformities, limb length discrepancies, entrapment of vessels, spinal cord compression, plus a small risk of cancerous growths
Multiple osteochondromas (MO): Excess BMP signaling plays a role

- The majority of patients with MO carry loss-of-function mutations in the **EXT1** or **EXT2** gene, which encode proteins essential for biosynthesis of heparan sulfate (HS) chains on specific proteoglycans (HSPGs)
- Decreases in or absence of HSPGs cause local increases in BMP and Smads 1/5/8 leading to abnormal budding of OCs
- Palovarotene shown to inhibit BMP signaling and OC development and could potentially inhibit OC growth

OC: Osteochondromas; BMP: bone morphogenetic signalling

Phase 2 trial of palovarotene in MO

Excess BMP signaling plays a role

- Double-blind, randomized, placebo-controlled trial
  - Palovarotene 2.5 mg daily vs 5 mg daily vs placebo for 2 years
- 240 patients age 2–14 years with symptomatic MO
- Primary endpoint: Annualized rate of new osteochondromas (OCs)
- Secondary endpoints include the total volume of OCs, the rate of new/worsening deformities, and the rate of MO-related surgeries
- Completion of enrolment: Q3 2019
  Interim analysis: Q3 2020
  Final readout: 2021
- Potential registrational trial

**Patients**
- 2–14 years old with symptomatic MO and confirmed EXT1 or EXT2 mutations

**Palovarotene 2.5 mg daily**
- Palovarotene 5 mg daily
- Placebo

MO: Multiple Osteochondromas; Clinicaltrials.gov.uk [NCT03442985]
Advancing palovarotene clinical trial pipeline

<table>
<thead>
<tr>
<th>Indication</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Next Milestone</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FOP</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flare-up episodic treatment (registrational trial)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>NDA submission H2 2019</td>
</tr>
<tr>
<td><strong>FOP</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(registrational trial)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Interim analyses 2019</td>
</tr>
<tr>
<td><strong>Multiple Osteochondromas (MO)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(potential registrational trial)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Complete enrolment Q3 2019</td>
</tr>
<tr>
<td><strong>Dry eye disease</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- NDA submission H2 2019
- Interim analyses 2019
- Complete enrolment Q3 2019
- Phase 1 completed Q1 2019
Neuroscience
Dynamic and attractive neurotoxin market

- Market split between Therapeutics (~55%) and Aesthetics (~45%)
- Market split between U.S. (~58%) and ex-U.S. (~42%)
- Market growth rate expected to continue for the foreseeable future
- High barriers to entry with specialized and highly regulated biologic and highly-regulated manufacturing process
- Dysport® has leading market position: #2 globally, #1 in some significant emerging markets

Source: Daeadal Research, Global Botulinum Toxin Market: Size, Trends and Forecasts 2018
Dysport®: A unique neurotoxin to manufacture

Cornerstone product to Ipsen’s Neurotoxin franchise, ~30 years of manufacturing expertise

- Highly complex production processes difficult to replicate and executed by staff with substantial and unique expertise in toxin manufacturing
- State-of-the-art drug product manufacturing facility which utilizes a technology that isolates the product, not only from the environment, but the people working in the area
- Biohazard subject to strict governmental oversight and compliance with stringent Good Manufacturing Practice regulations
Strong commercial execution

### Ipsen Dysport® sales 2014-2018

- Ipsen’s Dysport® 2018 sales up 12.6% at CER
- Solid volume growth in therapeutics
- Strong performance of Galderma in aesthetics

Global in-market sales under Dysport brand: >€500 million

Source: Daedal Research, Global Botulinum Toxin Market: Size, Trends and Forecasts 2018
Aesthetics: Well-positioned in attractive growing market

Drivers of continued growth

• Growth driven by the U.S. and emerging markets (China)
• Favorable market dynamics:\n  • Growing awareness among consumers
  • Shift in preference from surgical to non-surgical procedures
  • Increasing consumer spending in emerging markets
  • Strong brand loyalty for leading products

Successful Galderma partnership

• Commercial partner in all geographies except Russia and Middle East
• Global leader in aesthetics
• Territories >75% world aesthetics market, ongoing geographic expansion
• Strong growth in Ipsen-led aesthetics sales

1. Market Research Engine, Global Medical Aesthetics Market, 2019
Significant opportunity remains in Therapeutics

Dysport addressing >40% of therapeutics market

2018 Global therapeutic neurotoxin sales per indication¹

- Spasticity: 27%
- Overactive Bladder: 19%
- Cervical dystonia: 15%
- Blepharospasm: 5%
- Other: 5%
- Chronic Migraine: 29%

Performance by geography

- #2 in EU markets (UK, Germany, Italy)
- Market leader in Brazil and Russia
- Limited but growing market share in U.S.

Strategic objectives

- Grow share in adult and pediatric spasticity
- Increase treatment in eligible patients:
  - Only ~4.5% eligible adult spasticity patients receive neurotoxin treatment²
- Differentiate as toxin delivering longer-lasting symptom relief between injections
- Expand into select indications beyond spasticity

---

¹ Daedal Research, Global Botulinum Toxin Market: Size, Trends and Forecasts (2016-2020); ² Adelphi: Understanding and Sizing the Spasticity Patient Journey 22312b; Dysport AS Tracking Global Report PR30624
Lifecycle management: Hallux valgus (bunions)

Disease characterization

• High prevalence worldwide: 23%\(^1\) → 15% consult specialist → 10%\(^2\) moderate to severe patients

• Chronic foot deformity characterized by lateral deviation of the big toe (hallux) leading to debilitating foot pain, functional impairments

• No effective treatment with exception of surgery - long and painful recovery time

• Treatment with neurotoxin expected to relieve an underlying cause through muscle relaxing action resulting in clinically meaningful changes in hallux valgus angle, foot pain and functional mobility\(^3,4\)

Phase 2 clinical development

• Multiple-dose, double-blind, randomized, placebo-controlled study of ~165 patients

• Primary endpoint: Change from baseline in daily Numeric Pain Rating Scale (NPRS) score

• Top-line results: Q1 2020

• Patent protection for treatment protocol until 2038

Lifecycle management: Vulvodynia

Disease characterization

• Underestimated prevalence worldwide: 6.5%\(^1\) of female population \(\rightarrow\) 69%\(^2\) consult specialist \(\rightarrow\) 40% vulvodynia diagnosis \(\rightarrow\) 60%\(^3\) provoked vulvodynia
• Vulvar pain for at least 3 months, without a clear identifiable cause often associated with sexual dysfunction and affective distress
• No therapeutic treatments available – remains underdiagnosed and inadequately treated
• Strong evidence of Dysport causing muscle relaxation of the affected pelvic floor muscles and inhibiting the release of neuropeptides and neurotransmitters involved in chronic pain and inflammation\(^4,5,6\)

Phase 2 clinical development

• Double-blind, randomized, placebo controlled, dose escalation and dose finding study in ~93 patients
• Primary endpoint: safety and mean change from baseline to week 6 in vaginal pain as reported on a 11-point pain Numeric Rating Scale (NRS)
• Top-line results: Q4 2020

Next-generation neurotoxins

John Chaddock, PhD
VP, Head of Neuroscience Area Operations
Pioneering research in next-generation toxins

From experts in natural neurotoxins

~30 years of expertise in:

• Pharmacology
• Preclinical/ clinical development
• Manufacturing/ scale up

To leaders in recombinant toxins

• Enhanced, well-characterized, high quality molecules
• High level of understanding of mechanism of action leading to effectively-targeted therapies
### Creating recombinant toxins

- Ability to modify aspects of neurotoxin function to enhance therapeutic applications
  - Synthesize the gene encoding the desired neurotoxin
  - Incorporate the gene into the bacteria *E. coli*, which expresses the protein, which is harvested and purified

### Expected benefits of recombinant toxins

- Enhanced characteristics – potency, stability, duration, spread, onset of action, immunogenicity
- Extended indications – application, delivery method, alternative payloads, formulation
- Improved manufacturing – solubility, activation, expression, post-translational modification

---

Modified recombinant neurotoxins: Modify catalytic site for new intracellular targets

Identification and Characterization of Botulium Neurotoxin A Substrate Binding Pockets and Their Re-Engineering for Human SNAP-23

Stefan Sikorra1, Christa Litschko1, Carina Müller1, Nadine Thiel1, Thierry Galli2, Timo Elchner3 and Thomas Binz1

Detailed knowledge of the structure of BoNT + collaboration with experts in the field + recombinant BoNT platform =

- Engineered BoNT LC/A that cleaves human SNAP-23 (non-neuronal homologue of SNAP-25)
- Establishes the potential for BoNT LCs to be used to inhibit secretory processes beyond the neuron
- Expands the potential utility of engineered BoNT-based biologics to a suite of non-neuronal indications
Modified recombinant neurotoxins: Optimize receptor binding to increase potency

Detailed knowledge of the structure of BoNT + collaboration with experts in the field + recombinant BoNT platform =

- Engineered BoNT/B binding domain with improved affinity for the human motor neuron
- Establishes the potential for improved BoNT/B binding domains in the design of innovative NMEs
- Increases the range of options for design of new patient solutions

Detailed knowledge of the structure of BoNT + collaboration with experts in the field + recombinant BoNT platform =

- Engineered BoNT/B binding domain with improved affinity for the human motor neuron
- Establishes the potential for improved BoNT/B binding domains in the design of innovative NMEs
- Increases the range of options for design of new patient solutions
Clinical translation: Paving the way for a new treatment paradigm

Developing a unique portfolio of existing and new neurotoxins with different pharmacodynamics profiles, allowing physicians to choose the neurotoxin that will fit patients’ unique medical needs.

**Fast-acting recombinant**
**Type E toxin**

- Fast onset (1 to 2 days) and 2 to 6 week duration of action
- This novel toxin could give clinicians the opportunity to treat conditions that require a significant and early effect.

**Natural Abobotulinum**
**Type A toxin**

- Long effect (3-4 months, up to 5 months)
- This toxin is the standard solution benefiting most patients today.

**Long-acting recombinant**
**Type A toxin**

- Longer effect than current natural Type A toxin (at least 6 months)
- This toxin could improve patients’ quality of life and open new therapeutic windows.

---

Discovering a New Class of Biopharmaceuticals: Targeted Secretion Inhibitors (TSIs)

Developing a new class of proteins by incorporating toxin/non-toxin domains: Targeted secretion inhibitors (TSI)\(^1\) with the ability to not only target neurons but also other types of cells in the body leading to a wide array of clinical applications\(^2\).

**TSI platform technology**

- **Re-targeting**
  Replace neurotoxin binding domain with cell receptor ligands

- **Substrate Specificity**
  Multiple serotypes provide a range of potential SNARE protein targets

- **Molecular Toolbox**
  Targeted to disease-related cell type and relevant SNARE population

**Wide array of clinical applications**

- Neuromuscular
- Pain
- Endocrine
- Proliferative disease
- Inflammatory disorders

---


SNARE: Soluble NSF attachment protein receptor
Extending neurotoxin leadership with next-generation toxins

• Pioneers in cutting-edge innovation leveraging long legacy and expertise in neurotoxin field
• Uniquely broad portfolio to serve patient needs across the treatment spectrum
• Fast and long-acting neurotoxin programs advancing in the clinic
• Expanding into new modalities - Targeted Secretion Inhibitors
06 Oncology
Oncology Commercial Highlights

Richard Paulson
Executive Vice-President and Chief Executive Officer of North America
Global Oncology Strategy

To be a leader in solid tumors with high unmet needs in well-defined patient populations

Maximize leadership position in Specialty Oncology markets

- Leading #1 or #2 market share against formidable oncology players
- Differentiated first/best-in-class assets
- Market share gains worldwide
- Strengthening portfolio through partnerships (IO) and business development
- Leveraging current Oncology infrastructure
Ipsen Oncology sales double 2015-2018

- Oncology sales reach €1.5bn in 2018, +30% at CER
- Franchise accounts for 68% of Ipsen sales vs. 52% in 2015
- Ipsen #14 in global Oncology rankings
- Decapeptyl® mid to high-single digit growth
- Encouraging launches of Cabometyx® and Onivyde®
- Strong momentum and double-digit growth of Somatuline® continues
- 11 programs in clinical development

CER: Constant Exchange Rates
Decapeptyl

Mid to high single-digit growth expected to continue

Attractive market dynamics
- Androgen deprivation therapy (ADT) is the standard of care in metastatic prostate cancer
- China ~18% CAGR over last 4 years driven by prostate and breast cancer

Strengthened commercial organization
- 30+ years of experience
- Launched in >70 markets
- Continued commitment to uro-oncology field

6-month formulation
- Cost and time efficient with no loss of prostate-specific antigen (PSA) control
- Higher compliance
- Patient-preferred choice

---

Cabometyx®
TKI of choice in 2L RCC

Unique mechanism of action, strong clinical profile

- Oral, small molecule that targets MET and AXL beyond VEGF receptors, with the potential to overcome the resistance induced by prior antiangiogenic therapies
- Consistent results across patient subgroups regardless of risk group, duration of prior treatment, presence of bone or visceral metastases
- Median time to response: 1.9 months
- Known and manageable class effect adverse event profile

TKI market share in 2L aRCC – Q1 2019

1. CABOMETYX® SmPC, 2016. 2. Rx Tracker – Kantar HealthBase March 2019: aRCC 2L patients currently TKI treated, excluding clinical trials EU4 data (France, Germany, Italy and UK); TKI: Tyrosine Kinase Inhibitor
Cabometyx® securing solid position along RCC treatment paradigm

Evolving RCC market dynamics

- Evolving RCC market dynamics
- First IO combination approved in Europe January 2019
- Currently IO monotherapy has ~50% 2L RCC market share
- IO combinations expected to rapidly move into 1L and gain majority share
- Significant 2L market share gains expected for Cabometyx as IO combinations move into 1L
  - Precedent in U.S. where Cabometyx has ~90% 2L market share post-IO therapy in 1L

Support for Cabometyx® use post-IO therapy

- Retrospective multicenter analysis
- Cabometyx: clinical efficacy post-IO independent of mono/combo or concomitant therapies:
  - Objective Response Rate: 36%
  - Median time to treatment failure: 6.5 months
  - 79% of patients derived clinical benefit
- Retrospective analysis of Cabometyx post IO: Encouraging anti-tumor activity observed, safety profile consistent with that described previously

IO: Immuno-Oncology; RCC: Renal Cell Carcinoma; TKI: Tyrosine-Kinase Inhibitor; 1. Bradley McGregor Dana Farber Cancer Institute, ESMO 2018
Expected sequencing of evolving RCC market

1L

IO combinations

Other targeted therapies

Cabometyx

2L

Other targeted therapies

Cabometyx

IO monotherapy

New treatments that have demonstrated superiority over standard of care

Significant 2L market share gains expected for Cabometyx® as IO combinations move into 1L
Supported by European Association of Urology and NCCN treatment guidelines
Cabometyx® in Hepatocellular Carcinoma (HCC) market

Strong clinical profile

- Approval in EU in November 2018 based on Phase 3 CELESTIAL trial:
  - Efficacy benefit vs. placebo (OS: 10.2 mo vs 8.0) demonstrated in a broad patient population
  - Benefit even greater in pure 2L subgroup (OS: 11.3 mo vs 7.2 mo)
  - Broad and clinically relevant 2L+ patient population

Cabometyx® included in ESMO HCC treatment guidelines

HCC market opportunity

- High unmet medical need with numerous negative Phase 3 trials in recent years
- ~26K 1L patients and ~15K 2L patients in Ipsen territories ex-China
- Currently, sorafenib dominates in 1L, while regorafenib dominates in 2L
- Competitive landscape expected to change substantially due to recent and impending launches
- Increasing numbers of available treatments may increase patient pool

OS: Overall Survival; ESMO: European Society for Medical Oncology
Expansion of Cabometyx opportunity

1L RCC
- Approved May 2018 in EU
- Launched in 8 countries

2L RCC
- TKI of choice
- Launched in 27 countries including EU, Can, AU, BZ

2L HCC
- Approved November 2018 in EU
- Launched in 5 countries

IO combination

Peak year sales:
- €300mn RCC
- €100mn 2L HCC
- Upside opportunity from ongoing IO combo trials

>40 ongoing Investigator Sponsored Trials

IP (EU):
Compound patent, including Supplementary Protection Certificate (SPC), expires March 2029

RCC: Renal Cell Carcinoma; HCC: Hepatocellular Carcinoma; IO: Immuno-Oncology; IP: Intellectual property
Significant U.S. opportunity in metastatic pancreatic cancer

Half of patients diagnosed in metastatic setting

- Accounting for <5% of all new cancer cases but is the #3 cancer in number of deaths
- 5-year survival rates for metastatic pancreatic cancer: 2.6%
- High failure rate of pancreatic cancer trials
- High unmet need remains

Onivyde® is enabling the evolution of the pancreatic cancer treatment paradigm to maximize outcomes in multiple lines of therapy

Metastatic Pancreatic Cancer Patients¹: ~37,000


Onivyde® strong clinical profile and differentiation

Differentiated product for metastatic pancreatic cancer

- First and only FDA-approved therapy for post-gemcitabine pancreatic cancer
- Novel encapsulation of irinotecan
  - Superior PK profile
  - Selective accumulation at tumor site
- Patents covering the liposome composition expire 2025-2028; additional granted patents covering the approved use expire 2033

Category 1 evidence in NCCN guidelines

- Onivyde + 5-FU/LV significantly improved OS among patients previously treated with gemcitabine-based therapy
- Superior PFS, ORR and TTF in patients receiving ONIVYDE + 5-FU/LV
- NAPOLI-1 study published in Lancet, final survival data published in European Journal of Cancer

FU/LV: Fluorouracil/Leucovorin; NCCN: National Comprehensive Cancer Network; ORR: Objective Response Rate; OS: Overall Survival; PFS: Progression-Free Survival; PK: Pharmacokinetics; TTF: Time to Treatment Failure
Global pancreatic cancer market could triple by 2024 as treatment paradigm evolves to sequencing of therapies

Since Onivyde® launched, the number of patients receiving 2L and 3L has increased 18% and 10%, respectively, but ~38% of 2L patients remain untreated

Source: Evaluate Pharma
Onivyde®: Significant synergies from U.S. Oncology commercial team

- Dedicated and experienced team of ~180 professionals including sales, marketing, reimbursement, medical affairs, patient/payer services
- Extensive Oncology experience in pancreatic cancer
- ~65% overlap with Somatuline® call points - Somatuline® performance also benefitting
- Demand growth 19% year-over-year in Q1 2019
- Acceptances on key pathways
- 2019 publications¹ to further support use in current approved and possible other indications

¹. NAPOLI-1 phase 3 study of liposomal irinotecan in metastatic pancreatic cancer: Final overall survival analysis and characteristics of long term survivors, A. Wang-Gillam et al., Eur J of Ca, 108 (2019) 78-87 Phase 1 expansion study of irinotecan liposome injection (nal-IRI) in patients with metastatic breast cancer (mBC), J. Sachdev, AACR, Abstract CT048, April 1, 2019
Expansion potential of Onivyde® franchise

2L PDAC
launch ongoing
• PYS: $300mn

1L PDAC
Ph 2 trial interim readout mid-2019
• 28K patients eligible for treatment

2L SCLC
Ph 2 trial readout H2 2019
• 35K new cases/yr in U.S.
• 14K patients treated in 2L
• Topotecan only FDA-approved 2L treatment:
  • OS: 7.8 months
  • PFS: 12-14 weeks

Other indications

Expansion potential of Onivyde® franchise

Expansion potential of Onivyde® franchise

Expansion potential of Onivyde® franchise
Somatuline®
Somatuline®: Best-in-class product in attractive Neuroendocrine Tumor (NET) market

Attractive NET market dynamics

- Somatostatin analog (SSA) market
  - Two main competitors - Somatuline (Ipsen) and Sandostatin LAR (Novartis)
  - High barriers to entry
- Long-acting SSAs - to remain:
  - Standard of care for 1L therapy
  - Backbone of SSA treatment
  - Radiotherapy used in 2L and complementary to SSA treatment

SSA market growing double digits

Differentiated product profile

- Best-in-class SSA with real-world evidence and more extensive label in the U.S.
  - Tumor control
  - Symptom control
  - Significantly extended PFS
- Favorable administration
  - Prefilled, ready-to-use syringe administered as deep subcutaneous injection
  - Predictable and sustained PK/PD dynamics
  - Preferred by HCPs, patients
  - Delivering enhanced value to the system

PFS: Progression-Free Survival; PK: Pharmacokinetics; PD: Pharmacodynamics; HCPs: Health Care Professionals
SSA competitive environment

**IP position**
- Somatuline® Depot (U.S.) – March 2020 acromegaly, December 2021 orphan drug designation in NET
- Sandostatin® LAR (U.S.) – January 2017
- EU patents expired years ago for both products

**Constraints to entry**
- Specialized peptide manufacturing process
- Chronic therapy - patients on therapy for 3-7+ years
- Very limited switch patients (two SSAs are not interchangeable)
- Risk of share loss first primarily in new patients

**Manufacturing unique depot formulation**
- Unique formulation manufactured using advanced liquid crystal technology
- Engineered to provide sustained release for once-monthly dosing
- Significant know-how required to scale up, increase yields and maintain high quality standards

PFS: Progression-Free Survival; PK: Pharmacokinetics; PD: Pharmacodynamics; HCPs: Health Care Professionals
Exceptional Somatuline® performance driving Specialty Care business

3-year sales growth

Attractive financial profile

- Wholly-owned global asset
- Largest, fast-growing and most profitable product
- Achieved blockbuster status in 2018
- Market share increasing steadily worldwide
  - U.S.: ~30% TRx and ~40% NRx
  - EU: ~50% TRx
- Volume growth in expanding markets is key driver

EU5: France, Germany, Italy, United Kingdom, Spain; ROW: Rest of World; TRx: Total Prescriptions; NRx: New Prescriptions
Expanding leadership in NET market

Growth strategy in resilient NET market

- Strong growth market (11%) to continue
  - Expansion of SSA market to over $2bn since Somatuline NET launch in U.S. in early 2015
  - Over 5x increase in NET incidence over last 40 years¹
- Market share increasing steadily WW
- Chronic treatment market with loyal patients
  - Patients continue on therapy for years
  - 10-15% new patients per year
- PRRT approved for 2L or in combination with SSA expands and extends patient treatment duration
- Dedicated, motivated Oncology commercial team with proven track record

Momentum driven by continuing patients and growing new patient share²

Somatuline® momentum driven by real-world evidence, new delivery system and continued investment

Delivery systems matter

• Delivery system important to HCPs
• Patient experience matters
• Real-world evidence demonstrates value of delivery system
  • 99% full dose delivery
  • Shorter injection prep time
  • Safety and efficacy
  • Low risk of clogging, easy to teach and inject
• New delivery system building on established benefits of existing Somatuline delivery system with even sturdier device
• EU initial launch in progress, U.S. approval pending
Systemic Radiation Therapy

Sandy McEwan, MB, FRCPC, FSNMMI
Vice President, Radiopharmaceuticals
Building Systemic Radiation Therapy (SRT) platform

Ipsen’s commitment to SRT:

Developing innovative radiolabeled diagnostics and therapeutics for enhanced care through precision medicine

• Entered the field via OctreoPharm acquisition in 2015
  • Strategic alignment with Ipsen’s NET/oncology franchise
• Strengthening a dedicated and growing team with new talent and expertise
• Understanding the science
• Optimizing manufacturing supply chain
• Two SRT programs currently under development:
  • Satoreotide (SSTR2 antagonist) – potential best in class
  • IPN-01087 – first in class
Rationale of Systemic Radiation Therapy (SRT)

**SRT**: Precision targeted treatment strategy using radiolabelled peptides or other molecules to deliver therapeutic doses of radiation to cancer cells which overexpress specific receptors

Precision targeting of overexpressed receptor

Imaging diagnostic used as a predictive biomarker for treatment selection and treatment outcome

Therapeutic **MoA** – targeted radiation causes cell death through direct DNA damage and biological bystander effects

Platform technology that can be applied to multiple tumor types and also as combination therapy
Systemic Radiation Therapy Characteristics

- Companion imaging diagnostic/imaging biomarker
  - Patient selection defined by image
  - Identification of tumor heterogeneity
- Fractionated schedules are most effective
- High clinical response rate
- Stable disease is common
- Low toxicity, high patient acceptance
- Can be used in combination
Theranostics: Companion diagnostic imaging agent defines treatment potential for SRT

Therapeutic strategy uses same targeting strategy as Dx but delivers therapeutic amounts of radiation to treat the cancer.

Theranostics
Merging drug therapy and diagnostics to advance personalized medicine.

Companion Diagnostic may be IHC or an image - targeting strategy delivers small amount of radiation to make an image.

https://breast-cancer.ca/histogy/
Complex manufacturing/ supply chain management capabilities

<table>
<thead>
<tr>
<th>Lutetium-177 Production</th>
<th>CMO Central Manufacturing</th>
<th>Clinical Site</th>
<th>Diagnostic Availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Precursor Irradiation in Reactor</td>
<td>Receive Lutetium-177 Manufacturing in Hot Cell Dispensing Shipment (Regulations)</td>
<td>Required licenses Radiopharmacy Treatment facility Trained Staff</td>
<td>Gallium-68 Diagnostic Synthesis Unit Radiopharmacy PET Scanners</td>
</tr>
</tbody>
</table>

Ipsen has developed significant internal and external capabilities in radiopharmaceutical manufacturing
Comparison of Satoreotide binding with DOTA-TATE

SSTR2 (Somatostatin Receptor type 2) antagonist
Satoreotide has 3-4 more binding sites than the agonist
Diagnostic: $^{68}$Ga-IPN-01070
Therapeutic: $^{177}$Lu-IPN-01072

Quantitatively 3-4x binding seen with Satoreotide = increased therapeutic index

Significantly increased therapeutic index
Satoreotide background and strategy

- Ipsen’s commitment to NET patient population
  - Provide solutions along the treatment journey and extend leadership position in the market
  - Commitment to improving lives of patients
- Antagonist, potential first- and best-in-class systemic radiation therapeutic
- Primary focus - NET indications
  - >80% of GEP-NET patients have overexpression of SSTR2
  - Consider new indications with high unmet needs which permit registration, differentiation and data generation (e.g. 1L Grade 3 NET; 3L GEP-NET; lung NET)
Satoreotide development program

Therapeutic: $^{177}$Lu-IPN-01072

- Mass dose, administered dose selected
- Treatment regimen selected
- Trial design underway
- Phase 2/3 trial to start Q1 2020
Satoreotide development program

Diagnostic: $^{68}$Ga-IPN-01070

- Potential best-in-class asset: non-inferiority study vs. approved competitor
  - Showed superior detection capability
  - Positive indicator of treatment success
- Next steps: Phase 2/3 trial to start Q4 2019/ Q1 2020
  - Europe and North America
  - Testing diagnostic accuracy and role
  - Confirming theranostic role
IPN01087 - First-in-class asset targeting tumours expressing NTSR1

- Diagnostic: $^{111}$In-IPN01087
- Therapeutic: $^{177}$Lu-IPN01087
- Platform applicable to multiple possible indications:
  - Lead indication: PDAC in which 40-75% of patients overexpress NTSR-1
    → Possibility of combining with Ipsen and other assets
  - Other possible indications: colorectal cancer, Ewing sarcoma, glioblastoma multiforme
NTSR-1 overexpressed in multiple cancers

NTSR-1 Background

• NTSR-1 Background
• NTSR-1 mediates multiple functions of neurotensin
• Overexpressed in many cancers
• Overexpression associated with
  • Tumor growth
  • Poorer prognosis
  • Increased aggressiveness
  • Poorer outcomes

Literature Evidence for NTSR-1 Expression

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Expression</th>
</tr>
</thead>
<tbody>
<tr>
<td>PDAC</td>
<td>61 – 80% (IHC)</td>
</tr>
<tr>
<td>CRC</td>
<td>93 – 100% (IHC, mRNA)</td>
</tr>
<tr>
<td>Gastric</td>
<td>71% (IHC)</td>
</tr>
<tr>
<td>SCCHN</td>
<td>50% (mRNA)</td>
</tr>
<tr>
<td>Ewings</td>
<td>65% (autoradiography)</td>
</tr>
<tr>
<td>GBM</td>
<td>80%</td>
</tr>
</tbody>
</table>

PDAC: Pancreatic Ductal Adenocarcinoma; IHC: Immunohistochemistry; CRC: Colorectal Cancer; SCCHN: Squamous Cell Carcinoma of the Head and Neck; GBM: Glioblastoma Multiforme 1. e.g. Korner, 2015; Bossard, 2007; Zhou, 2015; Shimizu, 2015; Reubi, 1999
Screening images in mCRC support high therapeutic index

Screening Images - Patient with CRC metastatic to liver
High tumour : Background ratio = High therapeutic index
IPN01087 clinical development strategy

Phase 1 study:

- Open-label Phase 1/2 study to evaluate the safety, tolerability, biodistribution and antitumor activity of 177Lu-IPN-01087 for the treatment of subjects with solid tumors expressing NTSR-1
- Companion imaging biomarker in clinic Q4 2019

Partnership with the Pancreatic Cancer Action Network (PanCAN) to leverage its scientific/medical expertise and strong network with the pancreatic cancer community

- Opportunity to participate in the Phase 2/3 Precision Promise registration trial in combination with Gem/Abx or Folfirinox that has been pre-approved by the FDA
- Next steps: Generate safety data of IPN-01087 plus Gem/Abx or Folfirinox and validate diagnostic - to be integrated in ongoing study

NTSR1: Neurotensin Receptor 1; PDAC: Pancreatic Ductal Adenocarcinoma
Conclusion

Building world-class Systemic Radiation Therapy platform with potential first/best-in-class assets

Providing solutions across the treatment paradigm and expanding Ipsen’s presence in markets with unmet needs (NET, PDAC)

Rationale to expand into other tumor types and to combine with other therapies, including Ipsen assets
Oncology R&D

Yan Moore, MD
SVP, Global Head of Oncology R&D
Strategic Vision for Oncology R&D

**Strategy**

- Build streamlined and innovative oncology “development powerhouse”
- Maximize data-driven lifecycle management
- Synergize with internal/external assets
- Bring in first/best-in-class targeted assets to balance, diversify and expand portfolio

**Vision**

- Become global leader in well-characterized rare/selected cancers with defined patient populations
- Become partner of choice for other organizations
- Be an early adopter of digital solutions and AI platforms in order to enhance development and improve chances of success
## Ipsen in Oncology: Current landscape

<table>
<thead>
<tr>
<th>Neuroendocrine Tumors (NET)</th>
<th>Prostate Cancer</th>
<th>Renal Cell Carcinoma (RCC)</th>
<th>Pancreatic Cancer</th>
<th>Hepatocellular Carcinoma (HCC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Somatostatin analog with market leadership position</td>
<td>Established and growing product in EU and RoW (China)</td>
<td>Ongoing EU launch in 1L &amp; 2L RCC supported by best-in-class clinical profile</td>
<td>Differentiated product with OS benefit for high unmet medical need</td>
<td>Ongoing EU launch in 2L HCC supported by best-in-class clinical profile</td>
</tr>
<tr>
<td>Somatuline autogel (Global)</td>
<td>Decapeptyl®SR triptorelin (Ex-U.S. and Japan)</td>
<td>CABOMETYX™ (caldacetumab) tablets 40 mg, 160 mg, 250 mg (Ex-U.S. and Japan)</td>
<td>onivyde™ (trinitrancap liposome injection) (U.S. only)</td>
<td>CABOMETYX™ (caldacetumab) tablets 40 mg, 160 mg, 250 mg (Ex-U.S. and Japan)</td>
</tr>
</tbody>
</table>
Cabometyx®
(cabozantinib)
Expanding Clinical Benefit of Cabometyx®

• Establish Cabometyx® as standard of care in advanced renal cell carcinoma (RCC) and advanced hepatocellular carcinoma (HCC)
• Expand monotherapy into additional indications beyond RCC and HCC
• Become TKI of choice for IO combinations
• Focus on China as a primary expansion opportunity
Rationale For Cabozantinib/ IO Combinations

Cabozantinib

Promotes an immune-permissive environment

Increases
- Tumor MHC class 1 expression
- T-cell mediated killing
- Levels of circulating and tumor infiltrating cytotoxic T cells

Decreases
- Number and/or function of immune-suppressive cells ($T_{regs}$, MDSCs)

Inhibits targets that promote tumor immune-suppression
e.g. VEGFRs, MET, AXL, MER, TYRO3

Increases
- $CD8 + T$-cells

Decreases
- $T_{regs} + CD14 + Monocytes$

Based on preclinical and clinical data
Become TKI of choice across indications, monotherapy or combination

>100 ISTs in >25 tumors

March 2016

2L RCC

1L RCC

2L HCC

2016

2017

2018

2022

Various Combinations in Development with Immunotherapies

- RCC 1L: Phase 3 CheckMate 9ER (cabozantinib + nivolumab)
- HCC 1L: Phase 3 Cosmic-312 (cabozantinib + atezolizumab)
- HCC 1L/2L: Phase 1/2 Checkmate 040 (cabozantinib + nivolumab)
- Other indications: Phase 1b COSMIC-021 (cabozantinib + atezolizumab)

RCC: Renal Cell Carcinoma, HCC: HepatoCellular Carcinoma, NSCLC: Non Small Cell Lung Cancer, IST: Investigator Sponsored Trial
COSMIC-312: Phase 3 Trial in 1L HCC in combination with IO

COSMIC-312
Randomized, Open-Label in advanced 1L HCC (N = 640)
- No prior systemic anticancer therapy
- Child-Pugh Class A
- ECOG PS 0 or 1

Stratification factors:
- Etiology (HBV, HCV, other)
- Region (Asia, other)
- Extra Hepatic Spread or Macro Vascular Invasion

Experimental arm A:
Cabozantinib at 40 mg qd +
Atezolizumab 1200 mg q3w

Control arm:
Sorafenib 400 mg bid

Exploratory arm B:
Cabozantinib 60 mg qd

Randomization
6:3:1

Primary endpoint: PFS, OS
Secondary endpoint: ORR, safety

Sponsored by Exelixis/Roche

COSMIC-312 serves as regulatory pathway to China with >50% of new liver cancer cases and deaths

IO: Immuno-Oncology; HCC: Hepatocellular Carcinoma; PFS: Progression-Free Survival; OS: Overall Survival; ORR: Objective Response Rate

CheckMate 9ER: Phase 3 Cabometyx®/IO combination in 1L RCC

CheckMate 9ER
• Randomized, Open-Label, Ph3
• Cabozantinib + Nivolumab vs. sunitinib
• All risk groups with previously-untreated advanced RCC

N= ~650 patients

Randomization 1:1

Primary endpoint: PFS
Secondary endpoint: OS, ORR, Safety

Top-line results expected: early 2020

Sponsored by BMS/Exelixis

Cabozantinib 40mg QD + Nivolumab 240mg Q2W

Sunitinib 50mg daily (4w/2w)

1. Expanded from 580 to approximately 650 patients globally, Exelixis 25 April 2019
Additional potential indications for Cabometyx®

COSMIC-021: Cabometyx® / atezolizumab in multiple tumors (sponsored by Exelixis/Roche)
- 20 cohorts ongoing
- Top-line results (from multiple cohorts) expected when cohort are fully enrolled and data has matured

Cabometyx® monotherapy
- Ewing sarcoma
- Osteosarcomas

Cabometyx® + Immune-therapy
Onivyde®
(irinotecan liposomal injection)
Part 1: Single-arm study of previously untreated, metastatic pancreatic cancer patients

Phase 1 (dose finding): Completed; Phase 2 dose selection

NAPOX = Onivyde 50mg/m2, Oxaliplatin 60mg/m2, 5-FU 2400mg/m2, and LV 400mg/m2

Phase 2 (Dose expansion)

• Enrollment completed, interim analysis completed (with mFU=7mo)
  → Disease Control Rate (DCR): encouraging results, supports further development
  → mOS, mPFS: are still maturing

Accepted for oral presentation at the 2019 ESMO World Congress on GI Cancers, July 3-6 2019

Part 2: Planned Pivotal Study

• Superiority design vs. Gem/Abx
• Futility and Interim analyses included
2L SCLC Development: Phase 2/3 Seamless Design

Part 1: Phase 2a single arm study in 2L SCLC patients who progressed from 1L platinum treatment

- Enrollment completed (n=30)
- Part 1 results expected: H2 2019
  - Primary endpoint: safety and tolerability
  - Secondary endpoint: ORR, PFS, OS
  - Results from Dose finding phase will be presented at 2019 ASCO Annual Meeting

Part 2: Phase 3 randomized controlled trial

- Superiority design vs. Topotecan (SOC)
  - Primary endpoint: OS
  - Secondary endpoint: ORR, PFS, QOL
  - Futility and interim analyses included
  - Recent data: supports use of IO + Chemotherapy in 1L, lack of efficacy in 2L

Phase 3 Study in 2L SCLC

- Arm 1: Onivyde
- Arm 2: Topotecan

---

Phase 1 trial in Metastatic Breast Cancer (mBC)

**Phase 1 study**
- Phase 1 study completed (n=30)
- Results suggest Onivyde monotherapy has clinically meaningful anti-tumor activity, presented at 2019 AACR Meeting\(^1\)
  - HER2-, HR+ mBC patients: ORR 40%
  - TNBC patients: ORR 33%
  - Patients with active metastases [systemic and CNS] ORR 30%
- Historical ORR for physician’s choice of chemo (a.k.a, Beacon Study) estimated to be approximately < 20% \(^2\)

**Next steps/Potential development pathways**
- Development and regulatory consideration ongoing
  - SAB recommended further development
  - Potential indication: HER2-, HR+ / TNBC with active brain metastases
  - Opportunity for accelerated development d/t high unmet need and efficacy signals

---
\(^1\) https://www.abstractsonline.com/pp8/#!/6812/presentation/9863
\(^2\) Perez et al Lancet Oncol. 2015 Nov;16(15):1556-1568
Additional potential indications for Onivyde®

**Recurrent glioblastoma multiforme (rGBM)**
- Significant unmet medical need
- Ongoing IST (UCSF): Promising signal of Onivyde intrathecal injection in recurrent GBM\(^1\)
  - 7 of 10 patients on study

**Pediatric Solid Tumors**
- Ongoing IST (South Plains Oncology Consortium): Promising signal of Onivyde in Ewing’s sarcoma\(^2\)

**Onivyde in combination**
- Synergistic effects of combining Onivyde with DDRs in preclinical models\(^3\)
- Potential indications include TNBC, pancreatic cancer, SCLC, ovarian cancer, and prostate cancer

**Other potential indications: 2L HGSOC (platinum resistant)**
Evidence-based strategy working towards Onivyde® as backbone therapy for multiple tumor types

<table>
<thead>
<tr>
<th>Combinations with novel agents (DDR, IO)</th>
<th>Pediatric (Ewing sarcoma, pediatric brain tumors)</th>
<th>Others indications (glioblastoma, ovarian)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1L PDAC</td>
<td>2L SCLC</td>
<td>mBC</td>
</tr>
<tr>
<td>Phase 2 ongoing</td>
<td>Phase 2 interim readout: mid-2019</td>
<td>Encouraging clinical signals</td>
</tr>
<tr>
<td>Phase 2 readout: H2 2019</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Maximizing the potential of Onivyde®

1L PDAC: Pancreatic Ductal Adenocarcinoma; SCLC: Small-Cell Lung Cancer; mBC: metastatic breast cancer

Potential new indication

Currently under development

DDR: DNA Damage Repair; IO: Immuno-Oncology
IPN60090
IPN60090: Novel potent oral selective GLS1 inhibitor

Innovative approach

• Targeted therapy for unmet medical need in multiple solid tumors
• Targeting tumor metabolism in biomarker-selected population
• Potential for best-in-class agent
• Multiple development opportunities in combinations
• In-licensed from MD Anderson Cancer Center (May 2018)

Development strategy

<table>
<thead>
<tr>
<th>Monotherapy (biomarker strategy)</th>
<th>Tumor Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blocks Glutamine Metabolism</td>
<td>Nutrient Deprivation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Combo with chemotherapy (Onivyde, paclitaxel)</th>
<th>Oxidative Stress</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blocks DNA &amp; Glutathione Synthesis</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Combo with IO (anti-PD-1)</th>
<th>T-cell Activation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supplies Glutamine to T-cells</td>
<td></td>
</tr>
</tbody>
</table>
Phase 1 Trial Ongoing

Open-label, dose escalation/expansion study to investigate safety, PK, PD and anti-tumor activity

Part 1
IPN60090 Monotherapy

Part 2
IPN60090 + Chemotherapy

Part 3
IPN60090 + I/O

Advanced solid tumor susceptible to:
• Undisclosed mutations
• Undisclosed Expression Level

Biomarker Selected Population

NSCLC
With Undisclosed Biomarker
Potential to combine with Onivyde®

HGSOC
With Undisclosed Biomarker
Potential to combine with Onivyde®

• Potential to expand to other Glutaminase-dependent solid tumors in biomarker selected population
→ HNSCC, endometrial, HCC, SCLC, melanoma, RCC, bladder

• Combinations: leveraging Ipsen portfolio (Onivyde®, Cabometyx®) and other molecules (DDRs, PI3K α or mTOR inhibitors; CDK4/6 inhibitor; EGFR inhibitor; chemotherapies)

NSCLC: Non-Small Cell Lung Cancer; HGSOC: High-Grade Serous Ovarian Cancer; PK: Pharmacokinetics; PD: Pharmacodynamics; ASNS: Asparagine Synthetase; HNSCC: Head and Neck Squamous Cell Carcinoma; HCC: Hepatocellular Carcinoma; SCLC: Small Cell Lung Cancer; RCC: Renal Cell Carcinoma
Multiple development opportunities

- **Onivyde®**
  - PDAC, SCLC, BC, HGSOC

- Paclitaxel
  - Endometrial cancer

- PARP inhibitors
  - HGSOC, endometrial cancer

- PI3K α or mTOR inhibitors
  - Breast cancer

- CDK4/6 inhibitors
  - Breast cancer

- EGFR inhibitors
  - NSCLC and HNSCC

**Indications in italics are not yet approved/no Phase III results**

Leveraging Ipsen portfolio

Expanding through combinations

PDAC: Pancreatic Ductal Adenocarcinoma; SCLC: Small Cell Lung Cancer; BC: Breast Cancer; HGSOC: High-Grade Serous Ovarian Cancer; NSCLC: Non-Small Cell Lung Cancer; HNSCC: Head and Neck Squamous Cell Carcinoma
Oncology R&D

Creating value with Oncology pipeline

- Focus on rare/ niche cancers with unmet needs
- Maximize benefits of existing portfolio
- Develop innovative assets with potential to synergize with existing pipeline
- Continue to search for externally sourced assets
Q&A
Conclusion

→ Excellent business momentum across all major Specialty Care products and geographies

→ Maintain strong top-line growth and continued margin expansion

→ Strongest ever company R&D pipeline advancing first/best-in-class innovative assets

→ Mission to bring innovative, life-altering treatments to patients

Please join us for a cocktail reception in Le Salon de Famille.