ACTELION 2015 – 2020
TRANSFORMATION ON THE WAY

Jean-Paul Clozel
Chief Executive Officer
The following information contains certain “forward-looking statements”, relating to the company’s business, which can be identified by the use of forward-looking terminology such as “estimates”, “believes”, “expects”, “may”, “are expected to”, “will”, “will continue”, “should”, “would be”, “seeks”, “pending” or “anticipates” or similar expressions, or by discussions of strategy, plans or intentions. Such statements include descriptions of the company’s investment and research and development programs and anticipated expenditures in connection therewith, descriptions of new products expected to be introduced by the company and anticipated customer demand for such products and products in the company’s existing portfolio. Such statements reflect the current views of the company with respect to future events and are subject to certain risks, uncertainties and assumptions. Many factors could cause the actual results, performance or achievements of the company to be materially different from any future results, performances or achievements that may be expressed or implied by such forward-looking statements. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those described herein as anticipated, believed, estimated or expected.
1. What we achieved in 2015
2. Transformation of the PAH franchise
3. Transformation of Actelion
4. 2016: What’s ahead
KEY HIGHLIGHTS: A VERY SUCCESSFUL YEAR FOR ACTELION

- **Opsumit**: Outstanding launch momentum
- **Uptravi**: US FDA approval
- **Pipeline**: Significant progress
- **Financial results**: Exceeded expectations
OUTSTANDING LAUNCH MOMENTUM
OUTSTANDING LAUNCH MOMENTUM

- Across all key markets
- 9 months sales: CHF 354 million
- Commercially available in over 30 countries
Selexipag for the Treatment of Pulmonary Arterial Hypertension

Olivier Sitbon, M.D., Richard Channick, M.D., Kelly M. Chin, M.D.,
Aline Frey, Pharm.D., Sean Gaine, M.D., Nazzareno Galiè, M.D.,
Hossein-Ardeshir Ghofrani, M.D., Marius M. Hoeper, M.D., Irene M. Lang, M.D.,
Ralph Preiss, M.D., Lewis J. Rubin, M.D., Lilla Di Scala, Ph.D., Victor Tapson, M.D.,
Igor Adzerikho, M.D., Jinming Liu, M.D., Olga Moiseeva, M.D., Xiaofeng Zeng, M.D.,
Gérald Simonneau, M.D., and Vallerie V. McLaughlin, M.D.,
for the GRIPHON Investigators*
UPTRAVI is indicated for the treatment of pulmonary arterial hypertension (PAH, WHO Group I) to **delay disease progression** and **reduce the risk of hospitalization** for PAH.

Adverse reactions occurring more frequently (>5%) on UPTRAVI compared to placebo are headache, diarrhea, jaw pain, nausea, myalgia, vomiting, pain in extremity, and flushing.

Source: US Prescribing Information, December 2015
LAUNCH PRIORITIES USA

1. Establish as prostacyclin therapy of choice
2. Expand prostacyclin therapy patient base
3. Expand prescriber base

Market Development → LAUNCH
# EXTENDING THE CORE PAH FRANCHISE

<table>
<thead>
<tr>
<th></th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Phase IV</th>
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<tbody>
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<td>Macitentan</td>
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<td>OPUS</td>
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<td>Macitentan &amp; Selexipag</td>
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# DIVERSIFICATION

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<tr>
<th>Drug/Condition</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
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<tr>
<td>Cadazolid</td>
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<tr>
<td><em>Clostridium difficile</em> assoc. diarrhea</td>
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<td>Ponesimod</td>
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<tr>
<td>Multiple Sclerosis</td>
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<tr>
<td>Clazosentan</td>
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<td>✔️</td>
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<tr>
<td>Reversal of vasospasm post-aSAH</td>
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<tr>
<td>Ponesimod</td>
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<td>✔️</td>
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<tr>
<td>Graft vs. host disease</td>
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<tr>
<td>S1P1 modulator</td>
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<tr>
<td>Systemic lupus erythematosus</td>
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<td>Endothelin Receptor Antagonist</td>
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<td>Lucerastat</td>
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<tr>
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<td>Cardiovascular disorders</td>
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**Phase I:** Early phase of clinical development.

**Phase II:** Mid-stage clinical trial.

**Phase III:** Late-stage clinical trial, typically for approval by regulatory agencies.
SELECTED PIPELINE HIGHLIGHTS

- Cadazolid for *Clostridium difficile* associated diarrhea
- Ponesimod for multiple sclerosis
- Clazosentan for reversal of vasospasm post-aSAH

These compounds are investigational drugs in development and not approved or marketed in any country.
International, Multi-center Program Assessing Cadazolid Treatment in patients suffering from Clostridium difficile associated diarrhea (CDAD)

Completion of enrollment is expected by the end of 2016
**CADAZOLID SHOWS MINIMAL EFFECTS ON THE GUT MICROFLORA**

**QRT-PCR QUANTIFICATION OF BACTERIAL NUMBERS IN STOOL SAMPLES FROM PHASE II** (T. LOUIE)

- **C. difficile**
  - Cadazolid is an investigational drug in development and not approved or marketed in any country

- **C. leptum**

- **Prevotella**

- **Bacteroidetes**

- **Bifidobacterium**

- **Lactobacillus**

CFU/g stool

* Cadazolid is an investigational drug in development and not approved or marketed in any country
PHASE II EFFICACY ENDPOINTS

MODIFIED CURE RATE, RECURRENCE RATE, SUSTAINED CURE (MITT)

Cadazolid 250mg bid
Vancomycin 125mg qid

Cadazolid is an investigational drug in development and not approved or marketed in any country
Oral Ponesimod versus Teriflunomide In Multiple sclerosis

Ponesimod is an investigational drug in development and not approved or marketed in any country
PHASE II 1° ENDPOINT: CUMULATIVE NUMBER OF NEW T1 GD+ LESIONS FROM WEEK 12 TO WEEK 24

Per-protocol population

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean ± SE</th>
<th>Reduction</th>
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<tbody>
<tr>
<td>Placebo (N=110)</td>
<td>6.2</td>
<td>43%</td>
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<tr>
<td>Ponesimod 10 mg (N=88)</td>
<td>3.5</td>
<td>*</td>
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<tr>
<td>Ponesimod 20 mg (N=98)</td>
<td>1.1</td>
<td>***</td>
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<tr>
<td>Ponesimod 40 mg (N=93)</td>
<td>1.4</td>
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*P<0.05, ***P<0.0001 vs placebo

Ponesimod is an investigational drug in development and not approved or marketed in any country.
UNIQUE CLINICAL REVERSIBILITY

Return to Baseline

- **Ponesimod**: < 7 days
- **Ozanimod**: >> 14 days
- **Fingolimod**: > 28 days

Comparison based on in-house and published data

Phase II data

Presented at ECTRIMS 2006

Presented at ECTRIMS 2012
CLAZOSENTAN FOR CEREBRAL VASOSPASM POST-ANEURISMAL SUBARACHNOID HEMORRHAGE (aSAH)

- Highly soluble ETA selective ERA ideal for intravenous administration
- >1,500 patients treated with clazosentan providing significant experience in vasospasm post aSAH and a well documented safety profile

- CONSCIOUS-2  aneurysm secured by clipping  Lancet Neurology 2011;10(7):618-625

Clazosentan is an investigational drug in development and not approved or marketed in any country
CONSCIOUS-3 STUDY - EVENT RATE FOR THE COMPONENTS OF THE 1\(^{o}\) COMPOSITE ENDPOINT

- Placebo
- Clazosentan 5 mg/h
- Clazosentan 15 mg/h

DIND = Delayed ischemic neurological deficits; Macdonald R et al. *Stroke* 2012.

Clazosentan is an investigational drug in development and not approved or marketed in any country.
ADAPTED STRATEGY: REVERSAL VS. PREVENTION

- Phase III study under discussion with HA’s
- Primary objective to determine whether clazosentan is an efficacious treatment of cerebral vasospasm
- Open question: How early is the effect of clazosentan on reversing vasospasm?
- REVERSE: Phase II study to evaluate whether clazosentan has an early effect in reversing angiographically-confirmed cerebral vasospasm in approximately 25 subjects

Clazosentan is an investigational drug in development and not approved or marketed in any country
9M 2015

STRONG PERFORMANCE CONTINUES

PRODUCT SALES > CHF 1.5 B
↑ 10%

CORE EPS > CHF 4.90
↑ 20%*

CORE EARNINGS > CHF 650 M
↑ 20%*

CASH RETURN TO SHAREHOLDERS > CHF 800 M

* CER Ex 2014 US rebate reversal
Core earnings growth crossing the 20% mark at CER and excluding 2014 US rebate reversals
ACTELION 2015 – 2020

TRANSFORMATION OF THE PAH FRANCHISE
WE ARE TRANSFORMING OUR PAH PORTFOLIO

MOVING FROM SYMPTOM-BASED TO OUTCOME-BASED THERAPY
WE ARE TRANSFORMING OUR PAH PORTFOLIO

COVERING CONTINUUM OF CARE WITH OUTCOME-BASED MEDICINES

<table>
<thead>
<tr>
<th>FC II</th>
<th>FC III</th>
<th>FC IV</th>
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<tr>
<td>+/- PDE-5 inhibitor</td>
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- **Opsumit** (macitentan)
- **Uptravi** (selexipag)
- **VELETRI** (epoprostenol for injection)
WE ARE TRANSFORMING OUR PAH PORTFOLIO

USE OF DOUBLE AND TRIPLE ORAL COMBINATION THERAPY

Macitentan in the SERAPHIN study
38% RR, p = 0.009

Selexipag in the GRIPHON study
37% RR, p = 0.0058

Patients at risk:
Placebo 154 122 106 90 80 40 10
Macitentan 154 134 119 107 97 53 24

Patients at risk:
Placebo 197 158 119 70 44 27 7
Selexipag 179 140 105 70 43 31 8

On top of single background therapy

On top of double background therapy
ACTELION 2015 – 2020

TRANSFORMATION OF ACTELION
ACTELION 2015 – 2020
TRANSFORMATION ON THE WAY

- We have the products
- We have the ideas and the concepts
- We have a fully integrated infrastructure
- We have the money to finance it without compromising our profitability
A TRANSFORMATIONAL YEAR

- DRIVE our ambition with Opsumit
- LAUNCH Uptravi successfully
- ESTABLISH triple combination therapy in PAH
- ADVANCE the Discovery and Development pipeline
- CONTINUE shareholder value creation
2016 NEWSFLOW

- Cadazolid – IMPACT fully recruited
- Clazosentan – Phase II results
- ERA – Phase II results for specialty cardiovascular disorders
- Lucerastat – Phase Ib results in Fabry disease
- Macitentan – MERIT results

- Ponesimod – Update on Phase III MS program
- S1P₁ modulator – Systemic lupus erythematosus
- Selexipag – CHMP Opinion & EC decision
- Early stage pipeline progression