Tarceva
Proven to prolong survival

*Don Maclean, LCL Tarceva*

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**Tarceva – Key Objectives**

- Establish benefits of Tarceva in 2nd line
  - over chemotherapy
  - as treatment option in untreated patients
    - increase number of patients being treated
- Lower/ remove barriers to utilisation
- Launch successfully in pancreatic cancer
- Establish in 1st line and adjuvant NSCLC
Tarceva Today

Overall survival in two tumor types

- **NSCLC**
  - locally advanced or metastatic NSCLC after failure of at least one prior chemotherapy regimen (monotherapy)
  - approved US, EU and many other countries
- **Pancreatic cancer**
  - in combination with gemcitabine for first-line treatment of locally advanced, unresectable or metastatic pancreatic cancer
  - approved US, under review EU

*HR and p (log-rank test) adjusted for stratification factors at randomisation and HER1/EGFR status

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Tarceva in NSCLC (BR.21)

Improvement in overall survival

⇒ 42.5% improvement in median survival

<table>
<thead>
<tr>
<th>Survival distribution function</th>
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</thead>
<tbody>
<tr>
<td>Survival time (months)</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>5</td>
</tr>
<tr>
<td>10</td>
</tr>
<tr>
<td>15</td>
</tr>
<tr>
<td>20</td>
</tr>
<tr>
<td>25</td>
</tr>
<tr>
<td>30</td>
</tr>
<tr>
<td>1.00</td>
</tr>
<tr>
<td>0.75</td>
</tr>
<tr>
<td>0.50</td>
</tr>
<tr>
<td>0.25</td>
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<tr>
<td>0.00</td>
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- **Tarceva** (n=488)
- **Placebo** (n=243)

<table>
<thead>
<tr>
<th></th>
<th>Tarceva</th>
<th>Placebo</th>
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</thead>
<tbody>
<tr>
<td>Median survival (months)</td>
<td>6.7</td>
<td>4.7</td>
</tr>
<tr>
<td>1-year survival (%)</td>
<td>31</td>
<td>21</td>
</tr>
</tbody>
</table>

HR= 0.73, p< 0.001*

*HR and p (log-rank test) adjusted for stratification factors at randomisation and HER1/EGFR status
Tarceva in pancreatic cancer (PA 3)

*Improvement in overall survival 100mg cohort*

- 19% reduction in risk of death
- 23% increase in survival

**Survival probability**

- **Tarceva + gemcitabine**
  - Median survival (months) 6.4
  - 1-year survival (%) 23.8

- **Placebo + gemcitabine**
  - Median survival (months) 6.0
  - 1-year survival (%) 19.4

*HR 0.81 (0.68–0.97), p=0.028

**Impressive launch in US and Europe**

- 62 countries approved worldwide

**Group sales (CHF m)**

- Reimbursed and launched – Germany, France, Spain, Canada amongst others
- Strong uptake
- Early penetration rates
  - France: 15% in 2nd line Q4 ’05
  - Germany: 17% in 2nd line Q4 ’05
- Launch in Italy imminent
- China planned for Q4 ’06
- Current competition
  - Alimta
  - Taxotere
  - (Iressa - Asia)
**Market**

*High medical need in NSCLC & pancreatic cancer*

**NSCLC: diagnosed incidence cases in 2004**

<table>
<thead>
<tr>
<th>Region</th>
<th>Cases</th>
<th>Growth</th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
<td>200,000</td>
<td>+2.4%</td>
</tr>
<tr>
<td>Europe</td>
<td>150,000</td>
<td>+1.3%</td>
</tr>
<tr>
<td>Japan</td>
<td>50,000</td>
<td>+2.1-2.6%</td>
</tr>
</tbody>
</table>

**Pancreas: diagnosed incidence cases in 2003**

<table>
<thead>
<tr>
<th>Region</th>
<th>Cases</th>
<th>Growth</th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
<td>30,000</td>
<td>+1.9-2.1%</td>
</tr>
<tr>
<td>Europe</td>
<td>25,000</td>
<td>+1.4%</td>
</tr>
<tr>
<td>Japan</td>
<td>10,000</td>
<td>+2.3-2.7%</td>
</tr>
</tbody>
</table>

Source: Decision Resources

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**The Non-Small Cell Lung Cancer market - 1st line**

*Different treatment algorithms in US & EU*

**EU**

- Platinum Mono 1%
- EGFR (SM) 3%
- Platinum + Gemcitabine 33%
- Platinum + Vinorelbine mono 9%
- Vinorelbine mono 9%
- Platin Mono 1%
- Other 16%
- Taxane mono 3%
- Platinum + Taxane 16%

**US**

- Platinum Mono 4%
- EGFR (SM) 9%
- Platinum + Gemcitabine 16%
- Platinum + Vinorelbine mono 3%
- Vinorelbine mono 7%
- Platin Mono 1%
- Other 16%
- Taxane mono 4%
- Platinum + Taxane 43%

Source: Synovate Healthcare 2005
The Non-Small Cell Lung Cancer market – 2nd line

Rapid penetration of Tarceva following launch

EU

US

Source: Synovate Healthcare 2005

Tarceva - current and future filings

Pancreatic Cancer

NSCLC Tarceva 2nd line vs SOC (TITAN)

NSCLC Avastin + Tarceva 2nd Line (Beta Lung)

NSCLC Tarceva 1st Line (SATURN)

NSCLC Tarceva Adjuvant

NSCLC Tarceva/Avastin Maintenance (ATLAS)


Data available  Filing  Expected launch
Tarceva: targeting all lines of treatment in NSCLC
Also in combination with Avastin

- **Phase III**
  - **Adjuvant** (Stage I-IIIA), chemo (+/-) then Tarceva 2 years (OSI)
  - **1st line** Chemotherapy followed by Tarceva (Roche - SATURN)
  - **1st line** (non-squamous) Chemotherapy + Avastin followed by Avastin + Tarceva (Genentech - ATLAS)
  - **2nd line** Tarceva vs. pemetrexed or docetaxel (Roche - TITAN)
  - **2nd line** Avastin + Tarceva vs. Tarceva (Genentech – BETA Lung)

- **Phase II**
  - **2nd line** AT vs. A + docetaxel/ pemetrexed vs. docetaxel/ pemetrexed (Genentech)
  - **2nd line** Marker discover/Clinical outcome (Roche – MERIT)

Combining targeted therapies without chemo
Promising efficacy and favorable safety profile

- Exploratory phase II trial
- Primary endpoint: PFS vs. chemotherapy alone
- Adverse events: No unexpected side effects

Phase III Tarceva + Avastin in 2nd line NSCLC ongoing, data available 2008
**Tarceva product strategy**

*In summary*

- **Where to go**
  - NSCLC is the primary focus
  - Pancreas under HA review

- **How to get there**
  - 5 global phase III trials running in NSCLC
  - 1st line, combination with Avastin and Adjuvant

- **What are the challenges**
  - Large global trials
  - Patient selection
  - Competitive market now in 2nd line

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**Appendix**
# Product profile

**Tarceva**

| **Indication**               | NSCLC – metastatic/locally advanced, relapsed  
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<th>Pancreatic Ca – metastatic, locally advanced</th>
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</table>
| **Dosing**                  | 150mg in NSCLC; 100mg in pancreatic Ca (with  
|                             | gemcitabine)                                  |
| **Adverse reactions**       | Rash, diarrhea                                |
| **Incidence NSCLC**         | ~177,000 (US); ~174,000 (Europe)              |
| **Incidence pancreatic Ca** | ~27,000 (US); ~28,000 (Europe)                |
| **Current sales**           | 2005 - CHF 387m global                        |
|                             | 2006 Q1 - CHF 228m global                     |
| **Further development**     | 1st line NSCLC, combination with Avastin, adjuvant  
|                             | NSCLC                                         |

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## Tarceva development history

- **Pre-1996** Discovery and preclinical development of Tarceva
- **Q3 1997** First in-vitro data published in *Cancer Research*
- **Q2 1999** Positive phase I data presented  
  Large-scale, multi-center, phase II trials started
- **Q2 2000** Full development rights returned to OSIP
- **Q1 2001** OSIP, Genentech and Roche sign joint agreement for development of Tarceva
- **Q2 2001** Positive phase II data presented ASCO
- **Q3/4 2001** Phase III trials started (NSCLC and pancreatic Ca)
- **Q1 2003** BR.21 completed accrual
- **Sept 2003** 1st line trials in combination with chemo negative (Talent & Tribute)
- **April 2004** BR.21 – Positive (2nd/3rd line NSCLC)
- **Sept 2004** PA.3 – Positive (1st line pancreatic Cancer)