Building a Global Solution
Abbott’s Commitment to Pediatric HIV Treatment
Since 2001, Abbott and the Abbott Fund’s efforts to address HIV in Africa have focused in four areas:

- Prevention of mother to child transmission
- Pediatric HIV and support for orphans and vulnerable children
- Strengthening of health systems
- Access to Abbott’s HIV tests and medicines
Access to anti-retroviral therapy has begun to accelerate, especially in Sub-Saharan Africa.

More People Are Receiving ART in Low and Middle-Income Countries, 2002 – 2007

Children Receiving ART in Low and Middle-Income Countries, 2005 – 2007

Pediatric HIV is an epidemic centered primarily on Africa

90% of HIV infected children live in Africa

90% of pediatric infections result from vertical transmission

- Issues of prenatal care
  - Maternal diagnosis
  - Low, but increasing rates of PMTCT
  - PMTCT using single-dose NVP or AZT + Sd NVP
- Difficult infant diagnosis
- Infant Feeding
- Limited treatment options

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- Donation of Determine rapid HIV test
- Healthcare worker education

- Developing formulations suitable for pediatric patients
- Broad registration
- Building ongoing, quality supply
- Offering tiered, affordable prices
- Continued innovation
A Unique Approach to Meeting the Needs of the Developing World

Developing formulations suitable for pediatric patients

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Kaletra/Aluvia: Recommended as Second-line ARV for Children in Developing World

<table>
<thead>
<tr>
<th>First-line regimen at failure</th>
<th>Preferred second-line regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 NRTI + 1 NNRTI AZT- or d4T-containing</td>
<td>RTI components (NRTI/NNRTI)(^5)</td>
</tr>
<tr>
<td>ABC-containing</td>
<td>ddl(^6) + ABC(^7)</td>
</tr>
<tr>
<td>Triple NRTI</td>
<td>ddl(^6) + AZT</td>
</tr>
<tr>
<td></td>
<td>ddl(^6) + EFV(^8) or NVP</td>
</tr>
</tbody>
</table>

- **PI component\(^1\)**
  - LPV/r\(^2\)
  - SQV/r\(^3\)
  - or NFV\(^4\)

1. PI components are listed in order of potency/acceptability.
2. LPV/r is available coformulated as solid and liquid.
3. SQV/r should not be used in children or adolescents weighing less than 25kg.
4. Unboosted NFV may need to be used where no cold chain is in place for liquid LPV/r or SQV/r; it should be taken with food to improve bioavailability and high doses are needed in young children (e.g. >150 mg/kg per day).
5. Continuation of 3TC in second-line regimens may be considered
6. Ddi may not need to be taken on an empty stomach in children.
7. It is not recommend to introduce AZT after use of d4T or vice versa.
8. EFV is not currently recommended for children <3 years of age, and should be avoided in postpubertal adolescent girls who are either in first trimester of pregnancy or are sexually active and not using adequate contraception.

Recent WHO recommendation for treatment for all infants with confirmed HIV infection <12 months of age

Guidelines recommend LPV/r as 1st-line for HIV+ infants with a history of exposure to nevirapine

Most women receiving PMTCT either receive single-dose NVP (50%) or a two-drug regimen (27%) (typically AZT+Sd NVP)

Source:

Lower Strength Tablet: Progress for Children in Developing World

Kaletra Oral Solution
• Indicated for children >14 days (US FDA)
• Requires refrigeration
• Must be taken with food
• Taste challenges
• Requires dosing by syringe or cup

Reduced strength tablet
• 100mg/25mg lopinavir/ritonavir
• Provides flexible dosing for children
• No refrigeration required
• No food requirement
Abbott now has the broadest 2\textsuperscript{nd} line offering for children and a unique new product in the half strength tablet

**US and EU approvals**
- FDA – November 2007
- EMEA – March 2008

**Developing world**
- Regulatory filings in process
- Filings prioritized by disease burden
- First launch anywhere in the world – Uganda, December 1, 2007.

**Waivers**
- Abbott ships on waivers where possible based on local approvals.
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Continued innovation
Kaletra or Aluvia 200/50mg tablets are filed in over 150 countries – more than any other protease inhibitor
Commitment to Broad Registration: Strong Success Registering Kaletra and Aluvia Tablets

<table>
<thead>
<tr>
<th></th>
<th>Number of Countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Filed (not yet approved)</td>
<td>42</td>
</tr>
<tr>
<td>Approvals</td>
<td>115</td>
</tr>
<tr>
<td>Total</td>
<td>157</td>
</tr>
</tbody>
</table>
Commitment to Broad Registration:
Half strength tablet will quickly be filed as broadly

<table>
<thead>
<tr>
<th>Number of Countries</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Filed</td>
<td>30</td>
</tr>
<tr>
<td>(not yet approved)</td>
<td></td>
</tr>
<tr>
<td>Approvals</td>
<td>60</td>
</tr>
<tr>
<td>Total</td>
<td>90</td>
</tr>
</tbody>
</table>
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LPV/r demand has grown dramatically since the availability of the tablet formulation.
Significant Capacity Investment to Meet Anticipated Developing World Demand

Abbott’s current capacity expansion will support the needs of 1 million patients
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Abbott’s Tiered Pricing Plan

- **Africa and Least Developed Countries**: $500 Per Patient/Year
- **Low and Low-middle Income Countries**: $1000 Per Patient/Year
- **Upper Middle Income and Developed Country Prices**:

![Map showing tiered pricing](image)
Aluvia is preferred on the WHO guidelines and has been among the lowest priced protease inhibitors in Africa and LDCs for 5 years

- Abbott offers a $500 per patient per year price in Africa/LDCs.
- Abbott offers a $1000 price for mid-tier countries.
- No generic LPV/r or RTV has been WHO pre-qualified.
- Pricing announcements do not guarantee registration and availability.

Abbott’s price in Africa and the LDCs has set the standard

Evolution of the lowest quoted prices for eligible developing countries since 2001

Lowest Priced Generic

Abbott Kaletra/Aluvia

As of July 2008, there was no WHO pre-qualified or US FDA approved generic LPV/r. The lowest generic price is included in the graph.

Pediatric formulations are routinely more expensive on a per milligram basis than adult formulations.

<table>
<thead>
<tr>
<th>Dose</th>
<th>Branded Adult</th>
<th>Branded Pediatric</th>
<th>Generic Adult</th>
<th>Generic Pediatric</th>
</tr>
</thead>
<tbody>
<tr>
<td>ddi</td>
<td>$3,500</td>
<td>$4,000</td>
<td>$4,500</td>
<td></td>
</tr>
<tr>
<td>ABC</td>
<td>$0</td>
<td>$500</td>
<td>$1,000</td>
<td>$1,500</td>
</tr>
<tr>
<td>AZT</td>
<td>$2,000</td>
<td>$2,500</td>
<td>$3,000</td>
<td>$3,500</td>
</tr>
<tr>
<td>LPV/r</td>
<td>$2,000</td>
<td>$2,500</td>
<td>$3,000</td>
<td>$3,500</td>
</tr>
<tr>
<td>NFV</td>
<td>$4,000</td>
<td>$4,500</td>
<td>$5,000</td>
<td></td>
</tr>
<tr>
<td>NVP*</td>
<td>$0</td>
<td>$500</td>
<td>$1,000</td>
<td>$1,500</td>
</tr>
<tr>
<td>EFV*</td>
<td>$0</td>
<td>$500</td>
<td>$1,000</td>
<td>$1,500</td>
</tr>
</tbody>
</table>

Note: Only WHO Pre-qualified or FDA Tentatively Approved generic formulations included.
Three formulations provide dosing options. Price parity across formulations makes pediatric therapy more affordable.
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Continued Innovation with the Developing World Patient in Mind

**Norvir Tablet**

Progress in developing a heat-stable tablet formulation of ritonavir

Adult formulation to be filed by end of 2008.

Data to be presented at IAC 2008

**Challenges to Development**

- RTV has low solubility and low permeability (BCS Class 4)
- Solubility of RTV is critical for bioavailability
- Meltrex significantly improves the bioavailability of poorly soluble compounds like RTV

SOURCE for NORVIR paragraph: Cai Y et al., 14th CROI, Los Angeles, February 2007, Oral#52LB
Supporting Medical Education
Peer-to-Peer Education

PATIENT PROFILE:
- 26 year old woman presents with chest pain,
cough productive of green phlegm, shortness of
breath, fevers, chills, and rigors, and chronic
weight loss
- She states she has been treated for a similar
illness twice in the last year
- On examination, she appears lethargic, thin
- BP 80/50 mm Hg, HR 120, RR 32, T 39.8 C
- Decreased breath sounds on the right
- She diagnosed with bacterial pneumonia
- A negative HIV antibody test
- The patient lives with AIDS and a few days later the
HIV antibody test returns positive

Abbott is working with global HIV
treatment experts to develop
continuing education training modules

Focus on issues of special
interest to providers and patients
in the developing world

Peer-to-Peer training sessions are
structured to equip local providers to
provide training to their peers

Current Training Modules:
Module 1 – Diagnosis and
Management of Resistance and
1st-line Failure
Module 2 – Pediatrics & Pregnancy

Incomplete Virologic Suppression is Associated
With Less Robust Gains in CD4 Count at 24 Months

- 1667 patients in South Africa, mean CD4 count at ART initiation was
106 µL, followed for 24 months

<table>
<thead>
<tr>
<th>SUPPRESSION LEVEL</th>
<th>% ACHIEVED</th>
<th>CD4 µL (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full (≤400)</td>
<td>74.5 (70.3-78.3)</td>
<td></td>
</tr>
<tr>
<td>Partial (401-1000)</td>
<td>3.9 (2.4-6.1)</td>
<td></td>
</tr>
<tr>
<td>Not suppressed (&gt;1000)</td>
<td>21 (5.5-6.9)</td>
<td></td>
</tr>
</tbody>
</table>

Losina, et al. 15th CROI 2008, Boston, # 823
### Summary:
**A Unique Approach to Meet Needs of the Developing World**

<table>
<thead>
<tr>
<th>Goal</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Make our HIV therapies among the most widely available ARVs globally</td>
<td>Filed in &gt;150 countries, Kaletra &amp; Aluvia Tablets are the most broadly filed ARV; Pediatric tablet filed in 90 countries</td>
</tr>
<tr>
<td>Ensure high quality, timely availability, and adequate supply</td>
<td>Abbott has built capacity to support 1MM patients. Abbott currently supplies more LPV/r to Africa than to the US or Europe. Kaletra and Aluvia are the only WHO pre-qualified LPV/r</td>
</tr>
</tbody>
</table>
| Maximize affordability                                               | Tiered pricing in the developing world based on disease burden and economic conditions
Abbott’s price for LPV/r in Africa is lower than that offered by any generic manufacturer.
One price for both pediatric and adult formulations                   |
| Provide new solutions                                                 | Global regulatory filing of the LPV/r pediatric tablet formulation
Development of a heat-stable RTV tablet
Continuing medical education for HCP in the resource limited settings |
Thank You!