



# 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

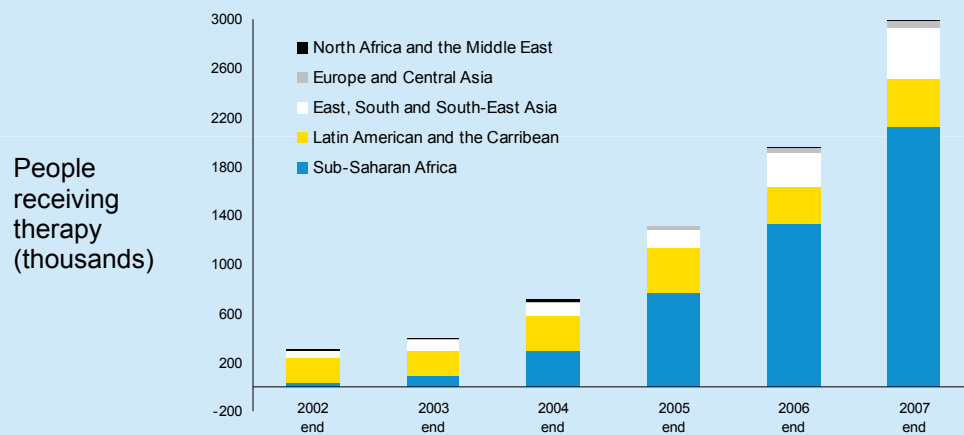
Pediatric HIV and support for orphans and vulnerable children

Strengthening of health systems

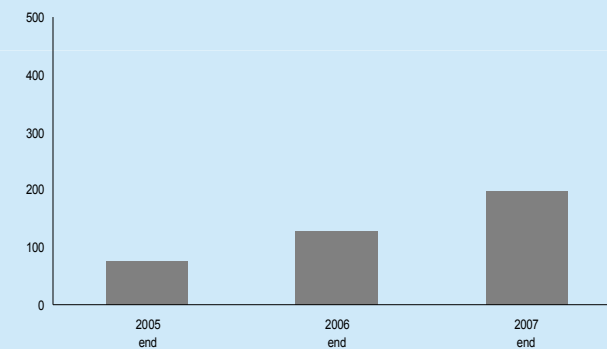
Access to Abbott's HIV tests and medicines

# 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



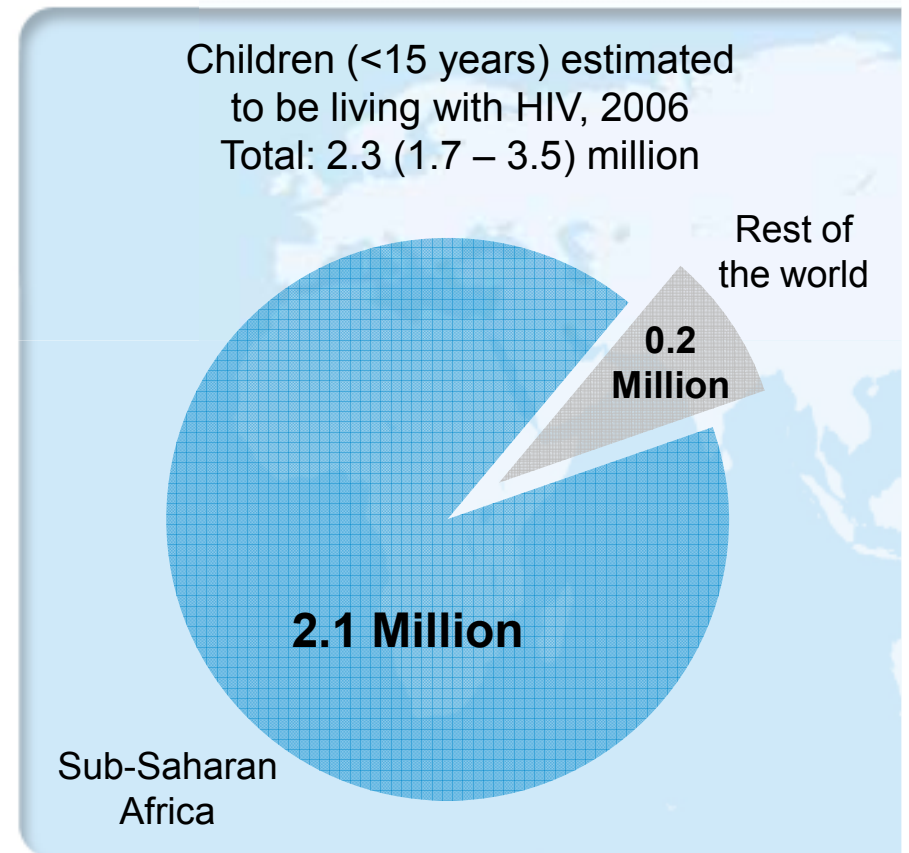
SOURCE: 2002-2005 data: WHO/UNAIDS (2005). Progress on global access to HIV antiretroviral therapy: An Update on "3 by 5". 2006 DATA: WHO/UNAIDS: "TOWARDS UNIVERSAL ACCESS: Scaling up priority HIV/AIDS interventions in the health sector" Progress Report, April 2007. 2007 DATA : WHO/UNAIDS: "TOWARDS UNIVERSAL ACCESS: Scaling up priority HIV/AIDS interventions in the health sector" Progress Report, 2008

## 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



SOURCE: WHO/UNAIDS: "AIDS Epidemic Update," December 2006 – Fact sheets – Slides and graphs Available at:  
[http://www.who.int/hiv/mediacentre/Epicore2006\\_27Oct06\\_en.pdf](http://www.who.int/hiv/mediacentre/Epicore2006_27Oct06_en.pdf)

## Pediatric HIV is an epidemic centered primarily on Africa

- 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
- 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

Broad registration

Building ongoing, quality supply

Offering tiered, affordable prices

Continued innovation

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

First-line regimen at failure	Preferred second-line regimen	
	RTI components (NRTI/NNRTI) <sup>5</sup>	PI component <sup>1</sup>
2 NRTI + 1 NNRTI AZT- or d4T-containing	ddl <sup>6</sup> + ABC <sup>7</sup>	plus LPV/r <sup>2</sup> or SQV/r <sup>3</sup> or NFV <sup>4</sup>
ABC-containing	ddl <sup>6</sup> + AZT	
Triple NRTI	ddl <sup>6</sup> + EFV <sup>8</sup> or NVP	

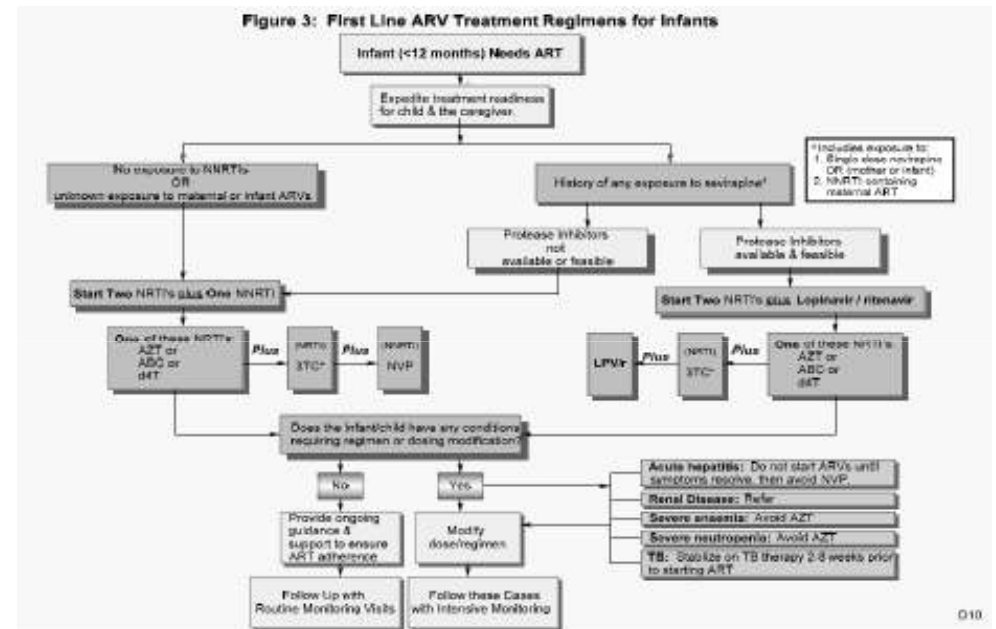
- 1 PI components are listed in order of potency/acceptability.
- 2 LPV/r is available coformulated as solid and liquid.
- 3 SQV/r should not be used in children or adolescents weighing less than 25kg.
- 4 Unboosted NFV may need to be used where no cold chain is in place for liquid LPV/r or SQV/r; it 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 Ddl 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.

SOURCE: WHO: "Antiretroviral Therapy of HIV Infection In Infants and Children: Towards Universal Access: Recommendations for a public health approach"

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

Guidelines recommend LPV/r as 1<sup>st</sup>-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:

WHO, Report of the WHO Technical Reference Group, Paediatric HIV/ART Care Guideline Group Meeting, WHO Headquarters, Geneva, Switzerland, 10-11 April 2008

WHO/UNAIDS: "TOWARDS UNIVERSAL ACCESS: Scaling up priority HIV/AIDS interventions in the health sector" Progress Report, 2008

## 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<sup>nd</sup> 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.



## A Unique Approach to Meeting the Needs of the Developing World

Developing formulations suitable for pediatric patients

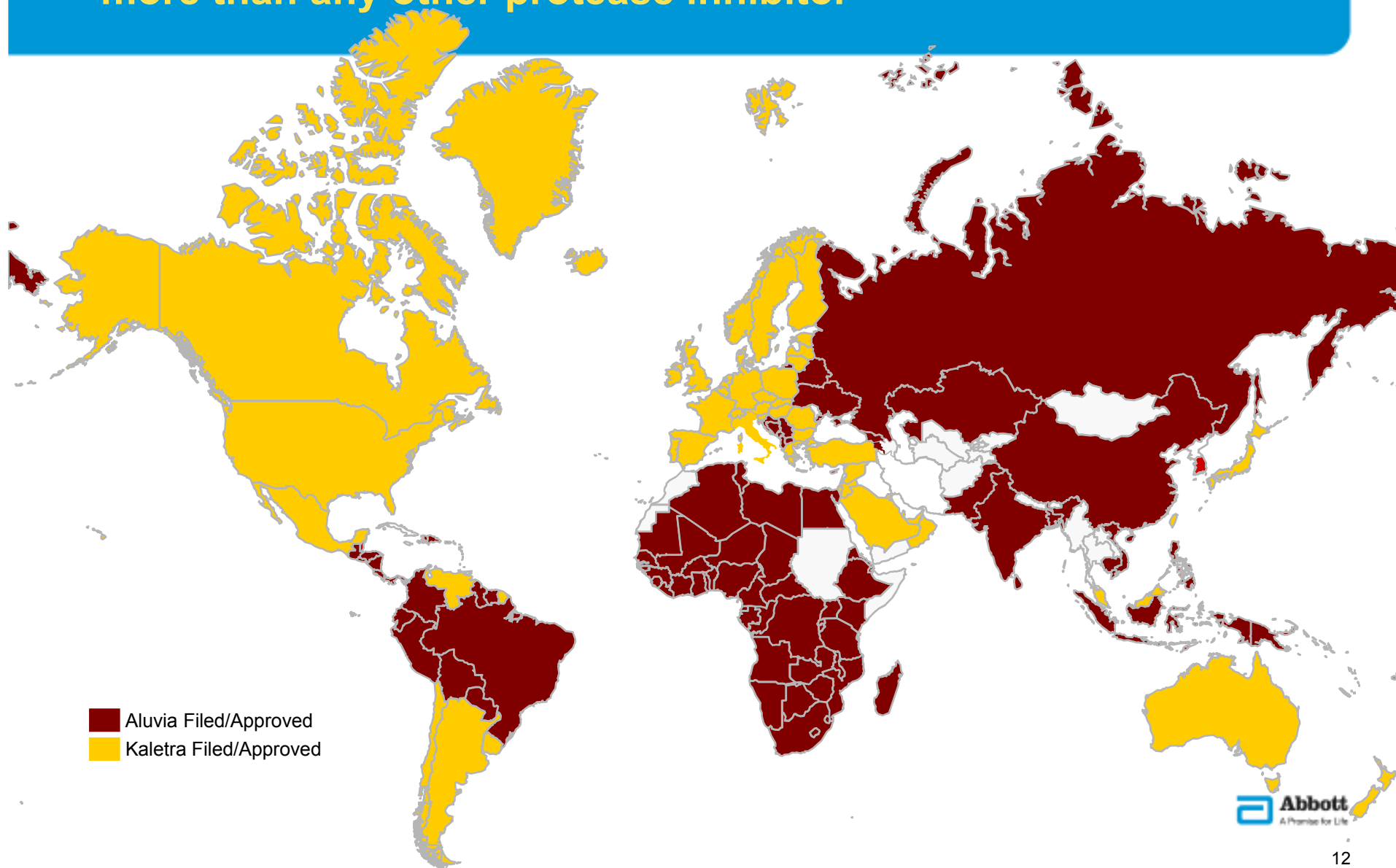
### Broad registration

Building ongoing, quality supply

Offering tiered, affordable prices

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

Number of Countries	
Filed (not yet approved)	42
Approvals	115
Total	157



## Commitment to Broad Registration: Half strength tablet will quickly be filed as broadly

Number of Countries	
Filed (not yet approved)	30
Approvals	60
Total	90



## A Unique Approach to Meeting the Needs of the Developing World

Developing formulations suitable for pediatric patients

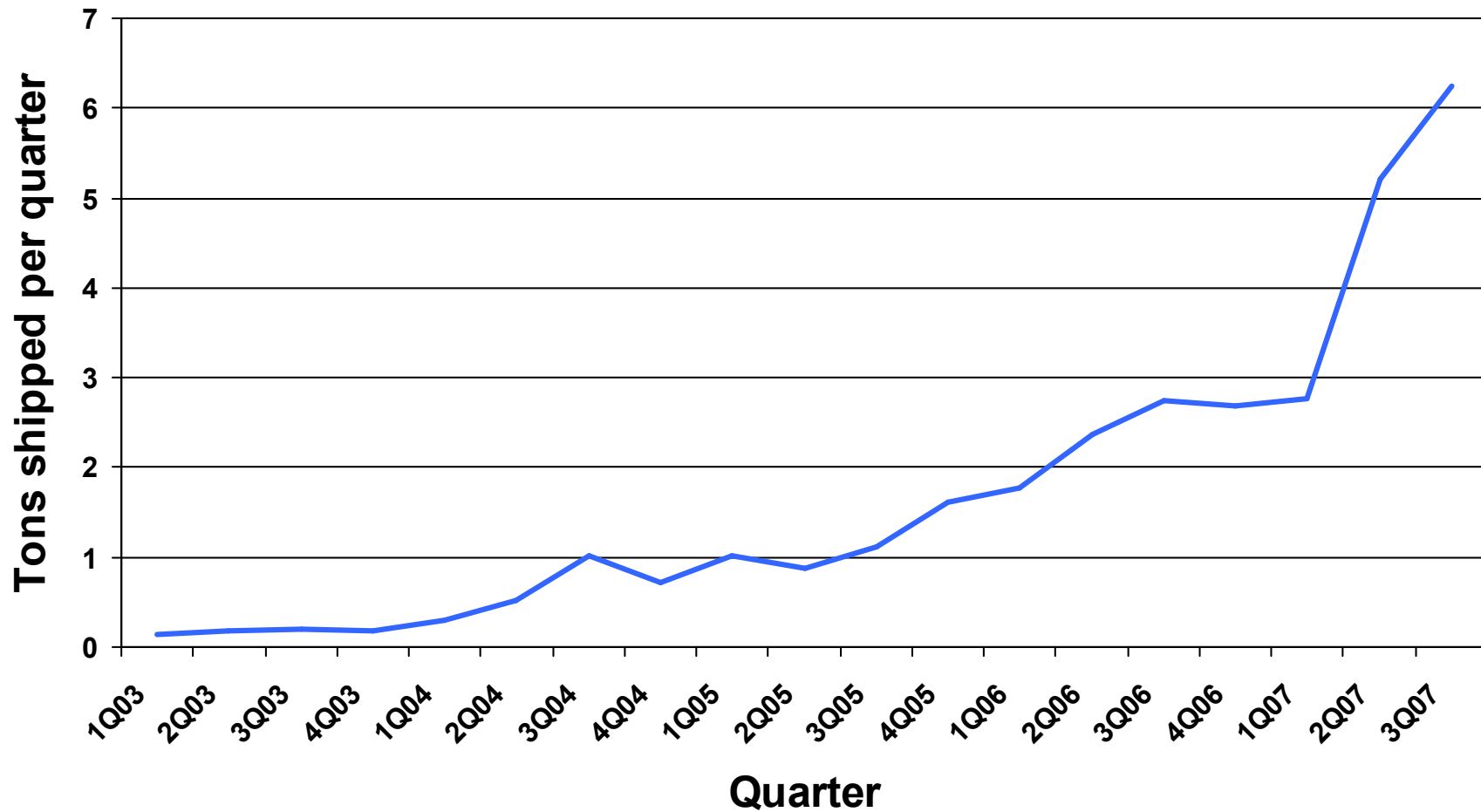
Broad registration

**Building ongoing, quality supply**

Offering tiered, affordable prices

Continued innovation

# 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

## A Unique Approach to Meeting the Needs of the Developing World

Developing formulations suitable for pediatric patients

Broad registration

Building ongoing, quality supply

Offering tiered, affordable prices

Continued innovation

# Abbott's Tiered Pricing Plan



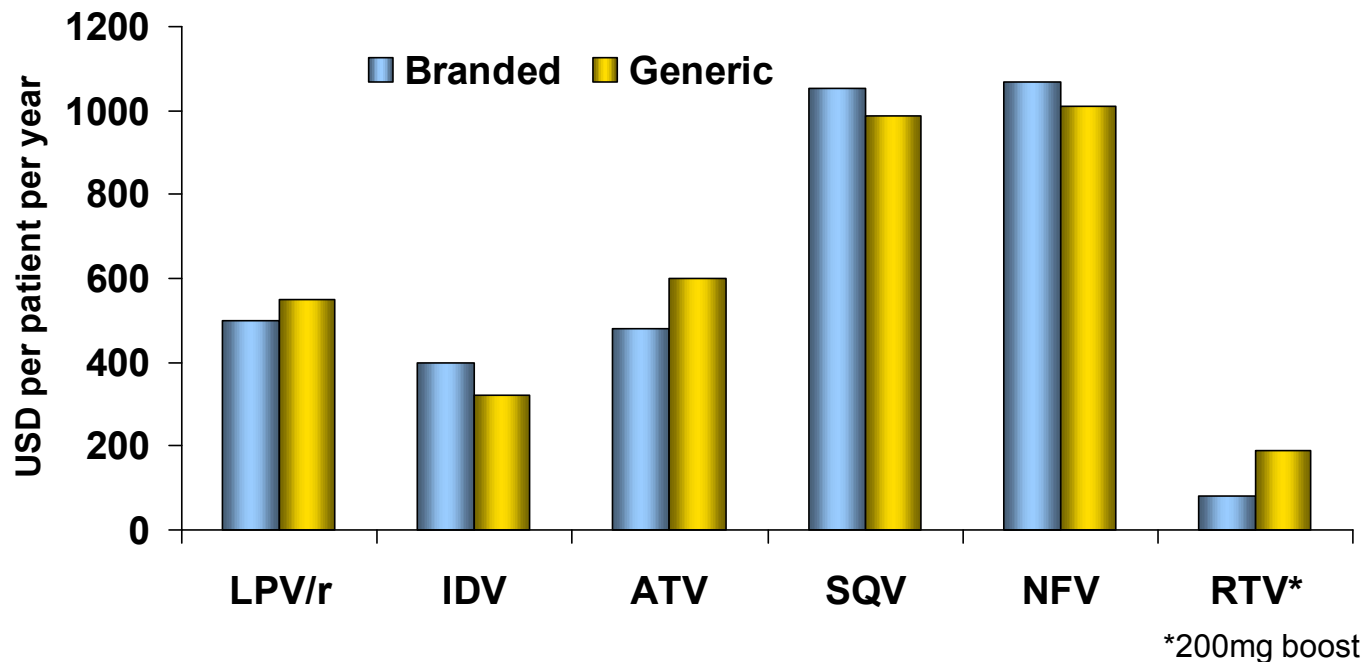
■ Africa and Least Developed Countries  
\$500 Per Patient/Year

■ Low and Low-middle Income Countries  
\$1000 Per Patient/Year

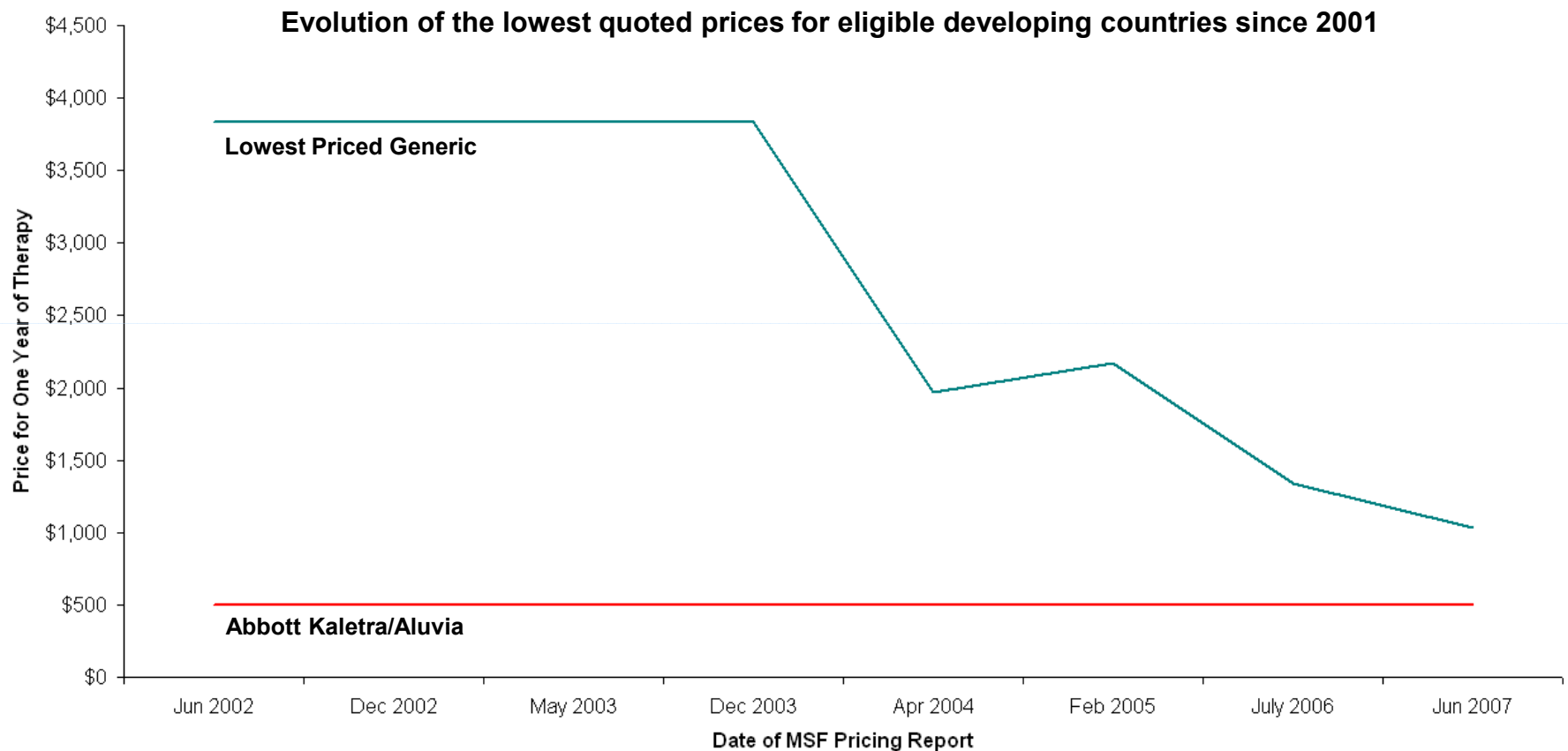
□ Upper Middle Income and Developed Country Prices

## 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

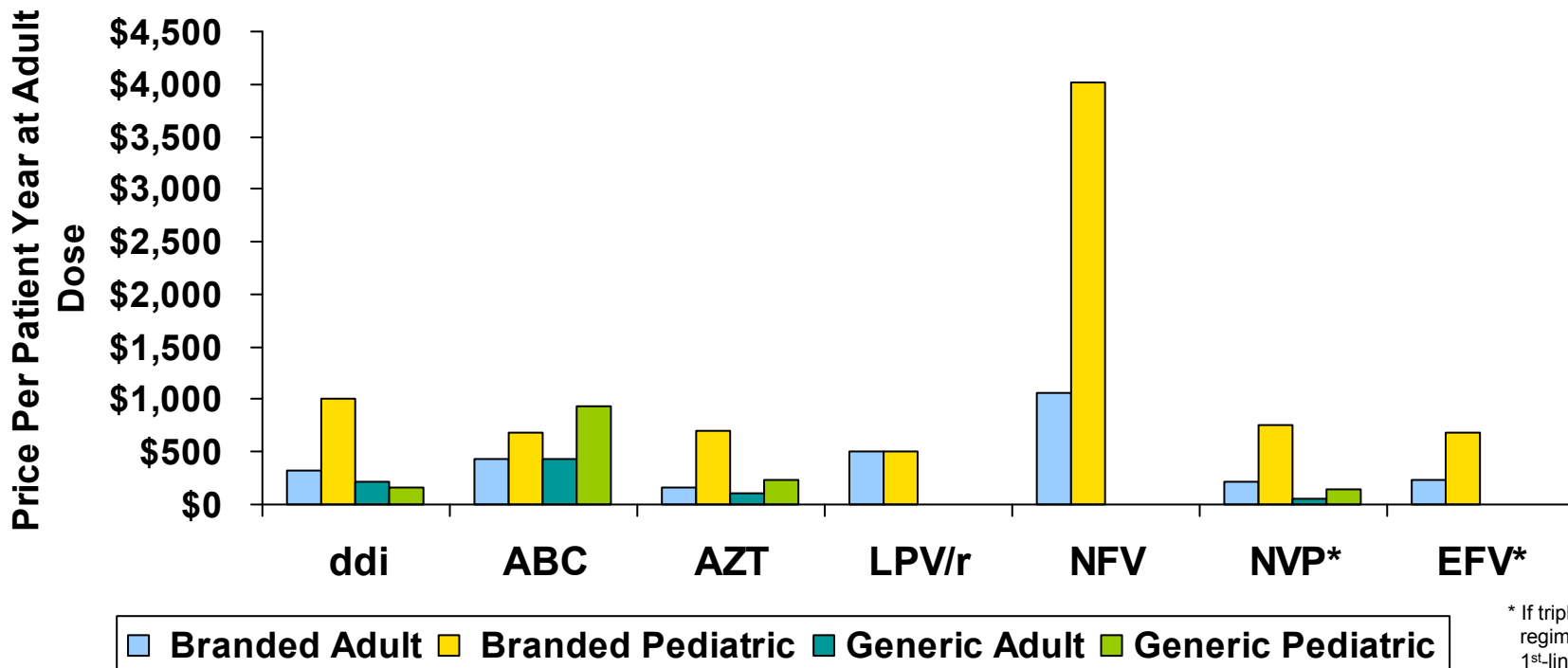


As of July 2008, there was no WHO pre-qualified or US FDA approved generic LPV/r. The lowest generic price is included in the graph.

Source: MSF Untangling the Web of Price Reductions, 5<sup>th</sup> – 10<sup>th</sup> editions, 2002-2007

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

Comparison of Adult and Pediatric Formulation Prices for WHO 2nd Line Pediatric ARVs



\* If triple NRTI regimen used in 1st-line

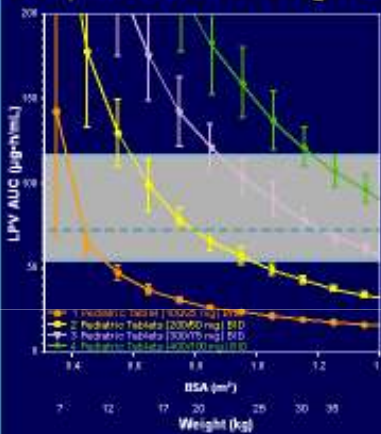
Source: MSF Untangling the Web of Price Reductions, 10<sup>th</sup> Edition, June 2007; Feb 2008 Update; March 2008 Update  
 Note: Only WHO Pre-qualified or FDA Tentatively Approved generic formulations included.



# Three formulations provide dosing options

## Price parity across formulations makes pediatric therapy more affordable

Predicted LPV AUC in Pediatric Patients Following Administration of 1 to 4 LPV/r 100/25 mg Tablets Compared to 230/57.5 mg/m<sup>2</sup> as the Oral Solution



- Symbols represent the predicted mean LPV AUC, error bars represent the predicted SD
- The dashed line represents the mean AUC seen in a previous study<sup>1</sup> for subjects receiving LPV/r 230/57.5 mg/m<sup>2</sup> oral solution BID without nevirapine
- The lower edge of the grey box represents 20% lower exposure than observed for subjects receiving LPV/r 230/57.5 mg/m<sup>2</sup> oral solution BID without nevirapine and the upper edge of the grey box represents exposure at the higher dose, LPV/r 300/75 mg/m<sup>2</sup> without nevirapine

1. Liu W et al. HIVB, Glasgow 2005, #366

Klein C et al., 17<sup>th</sup> EACS, Madrid, October 2007, #P4.1.01



## A Unique Approach to Meeting the Needs of the Developing World

Developing formulations suitable for pediatric patients

Broad registration

Building ongoing, quality supply

Offering tiered, affordable prices

Continued innovation

# Continued Innovation with the Developing World Patient in Mind

## Norvir Tablet

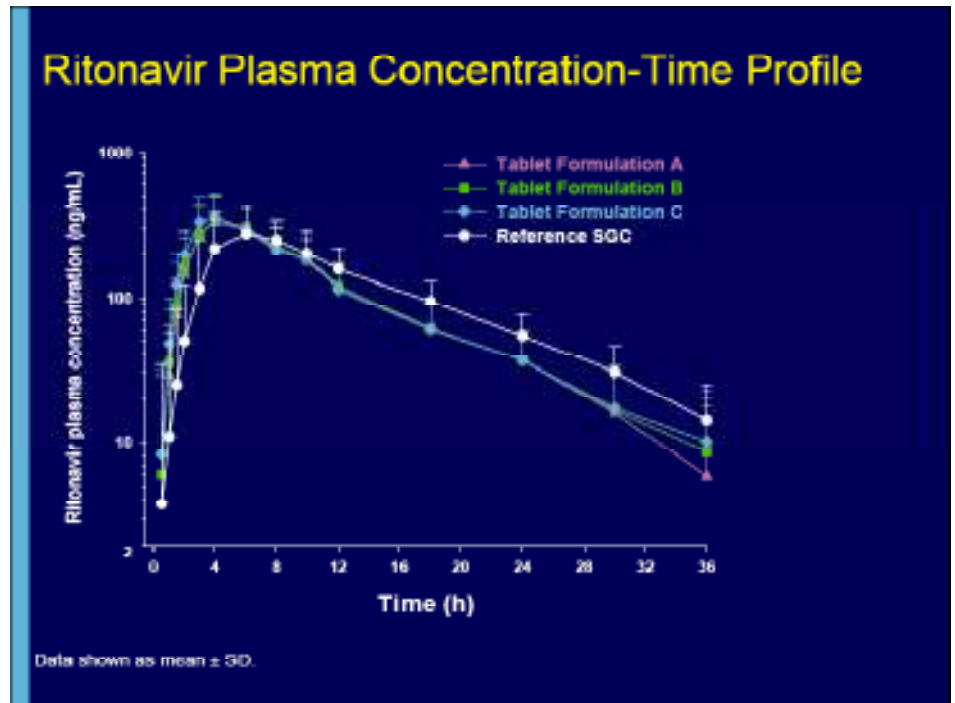
Progress in developing a heat-stable tablet formulation of ritonavir

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



Case Discussion

**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
- You diagnose bacterial pneumonia with septicemia and begin intravenous antibiotics and order an HIV test
- The patient does well, and a few days later the HIV antibody test returns positive

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/ $\mu$ L, followed for 24 months

SUPPRESSION (COPIES/ML)	% ACHIEVED OR ? CD4 (95% CI)	24 MONTHS SINCE ART INITIATION N=482
Full (< 400)	% achieved ? CD4	74.5 (70.3-78.3) 306 (287-325)
Partial (401-100,000)	% achieved ? CD4	3.9 (2.4-6.1) 186 (122-250)
Not suppressed (> 100,000)	% achieved ? CD4	21.6 (18.0-25.5) 7 (55-69)

Loima, et al. 15th CROI 2008, Boston, # 823

- 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 1<sup>st</sup>-line Failure

Module 2 – Pediatrics & Pregnancy

## Summary: A Unique Approach to Meet Needs of the Developing World

### Goal

Make our HIV therapies among the most widely available ARVs globally

Ensure high quality, timely availability, and adequate supply

Maximize affordability

Provide new solutions

### Outcome

Filed in >150 countries, Kaletra & Aluvia Tablets are the most broadly filed ARV;  
Pediatric tablet filed in 90 countries

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

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

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!

