Gilead Perspective and Updates

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VP, Medical Affairs
Gilead Sciences

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PrEP Indication

• Truvada is indicated in combination with safer sex practices for pre-exposure prophylaxis to reduce the risk of sexually acquired HIV-1 infection in adults at high risk

• This indication is based on clinical trials in MSM at high risk for HIV-1 infection and in heterosexual serodiscordant couples
Factors to Help Identify Individuals at High Risk

• Has a partner known to be HIV-1 infected, or
• Engages in sexual activity within a high prevalence area or social network and one or more of the following:
  – Inconsistent or no condom use
  – Diagnosis of sexually transmitted infections
  – Exchange of sex for commodities (such as money, food, shelter, or drugs)
  – Use of illicit drugs or alcohol dependence
  – Incarceration
  – Partner(s) of unknown HIV-1 status with any of the factors listed above
When Prescribing Truvada for a PrEP Indication, Healthcare Providers must:

- Prescribe Truvada as part of a comprehensive prevention strategy
- Counsel individuals to strictly adhere to a daily dosing schedule
- **Confirm a negative HIV-1 test** immediately prior to initiating PrEP
  - If clinical signs or symptoms consistent with acute viral infection are present and recent (<1 month) exposures are suspected,
    - Delay starting PrEP for at least one month and reconfirm HIV-1 status or
    - Use a test approved by the FDA as an aid in the diagnosis of HIV-1 infection, including acute or primary HIV-1 infection
- While using Truvada for PrEP, HIV-1 screening tests should be repeated at least every 3 months
  - If symptoms consistent with acute HIV-1 infection develop following a potential exposure event, PrEP should be discontinued until negative infection status is confirmed using a test approved by the FDA as an aid in the diagnosis of HIV-1, including acute or primary HIV-1 infection

Adapted from Truvada® US Prescribing Information, Gilead Sciences, Inc. July 2012
What is a REMS?

• Risk Evaluation and Mitigation Strategy
• FDA program to manage a known or potential risk associated with a drug
  – Designed to ensure the benefits of a drug outweigh its risks

• Goals of REMS for Truvada for PrEP is to educate prescribers and individuals about
  – The importance of adherence
  – The importance of regular monitoring of HIV-1 serostatus
  – Truvada for PrEP must be part of a comprehensive prevention strategy
REMMS Materials
Available at www.truvadapreprems.com

• Dear Healthcare Provider Letter
• Training Guide for Healthcare Providers
• Important Safety Information for Healthcare Providers
• Safety Information Fact Sheet
• Agreement Form
• Checklist for Prescribers
• Medication Guide
• Important Safety Information for Uninfected Individuals
• Full Prescribing Information
Additional Non-REMS Measures

- Free HIV & HBV testing for qualified individuals
- Free condoms
- Subsidized HIV-1 viral resistance testing to individuals who seroconvert
- Opt-in reminder service regarding regular testing for HIV and other STDs (to be built)
- Support for community education activities on PrEP
- Support for demonstration projects
- Truvada Medication Assistance Program for PrEP for uninfected individuals who lack insurance coverage
How will PrEP be made available in clinical practice?

♦ Drugs will be the same as for HIV treatment (Truvada (FTC/TDF), Viread (TDF), and generic versions)

♦ Guidance could be normative, regulatory (by labeling), or both. Process may vary by country.
  – CDC has issued draft guidance for PrEP for high risk MSM and serodiscordant couples in US based upon the iPrEx, Partners PrEP and other studies
  – Guidelines drafted by other groups (UK, France, WHO, etc.)

♦ Access to medication remains to be determined at the local level (same sites as for HIV treatment or other venues??) but Gilead Access Program will support both treatment and prevention. PEPFAR, Global Fund, WHO interested but decisions regarding the use of PrEP not yet established
Registration for TDF and FTC/TDF for HIV treatment in over 100 countries globally including all of Africa

Partnership with distributors to make branded Truvada and Viread available locally

Partnership with over a dozen generic manufacturers in India and Africa to make generic versions of TDF and FTC in combination with other products. Able to brand and price flexibly. Has driven the price of TDF from $1.35 per day to $0.14 per day over 5 years. Current lowest price of TVD is $0.20 per day.

Over 3 million patients in the developing world are now on a TDF containing regimen; more than 90% on generic drug
Support for ongoing research

♦ Ongoing Phase 3 studies
  – CDC Bangkok IDU study
  – IPERGAY study

♦ Phase 3 study extensions and rollovers
  – Partners PrEP
  – iPrEx OLE
  – TDF2

♦ Demonstration projects
  – CDC demonstration project in US
  – San Francisco/Miami/Washington DC demonstration project
  – PROUD study in London
Support for ongoing research

♦ Phase 1 and 2 studies of alternative dosing strategies and regimens and populations
  – Intermittent dosing
    • HPTN 066, 067 (ADAPT)
  – Alternative regimens
    • HPTN 069 (miraviroc+/− TDF or FTC)
  – Alternative populations
    • Adolescent studies in young MSM ages 15-22 (ATN)

♦ PrEPception??!!

♦ Support for microbicide gel research; vaginal, rectal, new formulations and patient populations, safety and efficacy trials

♦ New drugs; new prodrug of tenofovir GS 7340; new prevention specific ARVs?
Ongoing and Planned Phase 3/4 Research, Including Demonstration Projects

♦ Phase 3 studies are continuing to evaluate PrEP in various demographic groups
♦ Gilead is committed to post-marketing demonstration studies in the U.S. and globally
♦ Collaborators: ANRS, CDC, FHI, MRC, NIAID (DAIDS), NICHD (ATN), SFDPH, U. Washington, and Gilead Sciences

<table>
<thead>
<tr>
<th>Population</th>
<th>Studies</th>
<th>Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSM</td>
<td>17</td>
<td>13,920</td>
</tr>
<tr>
<td>Heterosexual Men &amp; Women</td>
<td>8</td>
<td>10,201</td>
</tr>
<tr>
<td>Serodiscordant Couples</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
<td>24,121</td>
</tr>
</tbody>
</table>

ANRS = French National Agency for AIDS Research; CDC = Centers for Disease Control and Prevention; FHI = Family Health International; MRC = Medical Research Council (UK); NIAID = National Institute of Allergy and Infectious Diseases; DAIDS = Division of AIDS; NICHD = National Institute of Child Health and Human Development; SFDPH = San Francisco Department of Public Health
## Phase 3/4 Research and Demonstration Projects in MSM

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Duration</th>
<th>Location</th>
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</thead>
<tbody>
<tr>
<td><strong>Ongoing Phase 3 Studies</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>IPERGAY</td>
<td>1900</td>
<td>24 months</td>
<td>France, Canada</td>
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<tr>
<td><strong>Demonstration Projects and Open-Label Extensions (planned and ongoing)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>iPrEx OLE</td>
<td>1770</td>
<td>72 weeks</td>
<td>Americas, Thailand, S. Africa</td>
</tr>
<tr>
<td>DAIDS PrEP MSM Demo</td>
<td>500</td>
<td>12 months</td>
<td>U.S.</td>
</tr>
<tr>
<td>CDC PrEP Demo*</td>
<td>600</td>
<td>12 months</td>
<td>U.S.</td>
</tr>
<tr>
<td>PROUD</td>
<td>5000 (500 as pilot)</td>
<td>12 months on tx, 12 month follow-up</td>
<td>U.K.</td>
</tr>
<tr>
<td>Project PrEPare 110</td>
<td>200</td>
<td>48 weeks</td>
<td>U.S.</td>
</tr>
<tr>
<td>SFDPH EPIC PrEP</td>
<td>300</td>
<td>12 months</td>
<td>U.S.</td>
</tr>
<tr>
<td>ALERT</td>
<td>400</td>
<td>12 months+</td>
<td>U.S.</td>
</tr>
<tr>
<td>Los Angeles PATH</td>
<td>300</td>
<td>48 weeks</td>
<td>U.S.</td>
</tr>
<tr>
<td>Seattle PrEP</td>
<td>300</td>
<td>48 weeks</td>
<td>U.S.</td>
</tr>
<tr>
<td>NYC PrEP</td>
<td>200</td>
<td>12 months</td>
<td>U.S.</td>
</tr>
<tr>
<td>Brazilian PrEP</td>
<td>400</td>
<td>12 months</td>
<td>Brazil</td>
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<tr>
<td>Rio PrEP</td>
<td>65</td>
<td>12 months</td>
<td>Brazil</td>
</tr>
<tr>
<td>HPTN 073</td>
<td>225</td>
<td>12 months</td>
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<tr>
<td>HPTN 069**</td>
<td>400</td>
<td>48 weeks</td>
<td>U.S.</td>
</tr>
<tr>
<td>HPTN 067**</td>
<td>360</td>
<td>34 weeks</td>
<td>U.S., Thailand, S. Africa</td>
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<tr>
<td>HVTN 505</td>
<td>1000</td>
<td>5 years</td>
<td>U.S.</td>
</tr>
<tr>
<td><strong>TOTAL: 17</strong></td>
<td></td>
<td></td>
<td>13,920</td>
</tr>
</tbody>
</table>

*CDC PrEP Demo includes both MSM and heterosexual men and women (1200 participants total)
**Includes both MSM and heterosexual women (estimated 50% MSM, 50% heterosexual women)*
## Phase 3/4 Research and Demonstration Projects in Heterosexual Women and Men

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Duration</th>
<th>Location</th>
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</thead>
<tbody>
<tr>
<td><strong>Ongoing Phase 3 Studies</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Partners PrEP (discordant couples)</td>
<td>4758</td>
<td>12 month extension</td>
<td>Kenya, Uganda</td>
</tr>
<tr>
<td>CDC Bangkok TDF (IVDU)</td>
<td>2413</td>
<td>Endpoint driven</td>
<td>Thailand</td>
</tr>
<tr>
<td><strong>Demonstration Projects and Open-Label Extensions (planned and ongoing)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDC PrEP Demo* (men and women)</td>
<td>600</td>
<td>12 months</td>
<td>U.S.</td>
</tr>
<tr>
<td>HPTN 069**</td>
<td>200</td>
<td>48 weeks</td>
<td>U.S.</td>
</tr>
<tr>
<td>HPTN 067**</td>
<td>~180</td>
<td>34 weeks</td>
<td>U.S., Thailand, S. Africa</td>
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<tr>
<td>TDF2 Open-Label Extension (men and women)</td>
<td>900</td>
<td>12 months</td>
<td>Botswana</td>
</tr>
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<td>CHAMPS (men and women)</td>
<td>150</td>
<td>12 months</td>
<td>South Africa</td>
</tr>
<tr>
<td>UW Partners PrEP Demo (discordant couples)</td>
<td>1000</td>
<td>24 months</td>
<td>Kenya, Uganda</td>
</tr>
<tr>
<td><strong>TOTAL: 8</strong></td>
<td><strong>10,201+</strong></td>
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</tr>
</tbody>
</table>

*CDC PrEP Demo includes both MSM and heterosexual men and women (1200 participants total)

**Includes both MSM and heterosexual women (estimated 50% MSM, 50% heterosexual women)

*Excluding rollover participants
Challenges for Regulators, the Community and Gilead

♦ Intervention may be less effective in real world vs. clinical trial setting, particularly when used intermittently

♦ Potential for behavioral impact (disinhibition)

♦ Risk of resistance development in HIV+ individuals

♦ Risk of hepatic flares in HBV-infected individuals

♦ High cost relative to other prevention interventions; potential reimbursement barriers?

♦ Challenge of delivering appropriate education to healthcare providers and target populations

♦ Need to ensure no impact on ease of access to medication for HIV+ individuals
Challenges to Implementation of PrEP in the US

♦ Initial uptake of PrEP in the US has been slow but is increasing

♦ Limited provider experience. Small number of patients enrolled in clinical trials in US (only 3 US sites and < 1000 subjects out of ~10,000 in pivotal studies).

♦ New strategy with no clear template for administration (many practical questions re implementation) and no PrEP “protocol” in place. Many (most?) LGBT centers in the US do not yet have an active PrEP program in place

♦ Separation of HIV prevention and treatment services in the US
Challenges to Implementation of PrEP in the US

♦ Reimbursement for drug and services not clear
♦ Low level of awareness amongst subjects and providers
♦ Eligible subjects not clearly defined
♦ Good news: many of the above issues can be addressed with additional experience/data
Conclusions

♦ Truvada has been approved for a pre-exposure prophylaxis indication in the US

♦ A REMS program is in place to ensure the safe and appropriate use of PrEP
  – Educate healthcare providers and uninfected individuals
  – REMS materials are available at www.truvadapreprems.com

♦ Ongoing demonstration projects will yield important information on the use of TVD for PrEP when given in an open label fashion
Conclusions

♦ Gilead is committed to supporting a comprehensive prevention program via education but is not actively promoting the indication

♦ TVD for PrEP is now being implemented in the US. Initial uptake has been slow but should improve with additional experience in the field and data from ongoing demonstration projects.
  – Similar to a product launch but is a “new strategy” launch
  – Will take 5-10 years to realize the potential of the strategy

♦ Phase 3b/4 studies are ongoing evaluating TVD, TDF, various dosing strategies, and other ARV combinations for prevention of HIV infection