Annual Performance Report, Year 1

Advancing the Microbicide Pipeline

30 September 2013 – 30 September 2014

Cooperative Agreement No. AID-OAA-A-13-00096

Office of HIV/AIDS

Submitted 27 October 2014

International Partnership for Microbicides
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A. EXECUTIVE SUMMARY

IPM’s product development program aims to progress a diverse portfolio of microbicide products based on a range of promising antiretroviral (ARV) drugs and dosage forms through preclinical and early-/mid-stage clinical testing. The need to continue advancing the microbicide pipeline is twofold: (1) multiple product options need to be developed to enable women to choose which one(s) best fit their needs and preferences; and (2) the HIV prevention field cannot afford to wait until drug resistance occurs to begin developing additional HIV prevention drugs. While promising candidates are currently in Phase III testing, IPM will continue advancing highly potent ARV drugs, including those not currently used for HIV treatment and those that can be combined with other ARVs, through the pipeline. As such, this Cooperative Agreement comprises the following activities: (1) advancing a candidate based on DS003 (a gp120-binding entry inhibitor not currently used in HIV prevention or treatment) through early clinical trials; (2) advancing a combination-ARV vaginal ring through formulation and preclinical development; and (3) identifying and evaluating new and early development ARV compounds with alternative mechanisms of action for pipeline progression.

Progress and Achievements: Year 1

In the first year of this award (30 September 2013 – 30 September 2014), IPM has:

- Selected Aptuit Verona as the manufacturer for DS003 tablet under Good Manufacturing Practice (GMP) and initiated technology transfer activities
- Selected Huntingdon Life Sciences as the preclinical partner for the DS003 rabbit vaginal irritation study and reproductive toxicology program and conducted pre-study preparation activities
- Selected PRA as the bioanalytical development partner to support the DS003 toxicology program
- Conducted a pre-IND (Investigational New Drug) consultation with the FDA for DS003 development; IPM’s product development plans to advance a DS003 tablet to Phase I evaluation were supported
- Completed re-testing of maraviroc plasma samples from the Phase I maraviroc-based ring trial (MTN-013/IPM 026) to inform product development plans for maraviroc
- Collected multiple proposals from potential development partners for formulation optimization of the dapivirine-maraviroc combination ring and initiated a technical review
- Selected Queens University Belfast as the development partner for DS003-based vaginal rings and initiated prototype formulation activities
- Continued discussions with pharmaceutical company partners regarding access to new ARV compounds
- Synthesized and released 2 batches of DS003 drug substance under GMP (non-USAID funding)
- Defined the formulation and completed 6 months of stability assessments of a single-use DS003 vaginal tablet developed at the University of South Australia (non-USAID funding)
- Completed in vitro pharmacokinetic (PK) assessments of DS003 (non-USAID funding)
- Filed an IND for maraviroc gel to support the upcoming CHARM-03 clinical trial of maraviroc gel (tested rectally and vaginally) and maraviroc pill tested orally (non-USAID funding)

Advancing the Microbicide Pipeline: Workplan Timeline, Year 1

<table>
<thead>
<tr>
<th>Activity 1: DS003-based Tablet</th>
<th>2013</th>
<th>2014</th>
<th>Year 1 STATUS OVERVIEW</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q4</td>
<td>Q1</td>
<td>Q2</td>
<td>Q3</td>
</tr>
<tr>
<td>Contract Manufacturing Organization (CMO) evaluation and selection</td>
<td>✓</td>
<td></td>
<td>Achieved: Q1 2014</td>
</tr>
<tr>
<td>Technology transfer to CMO</td>
<td></td>
<td>✓</td>
<td>Achieved: Q3 2014</td>
</tr>
<tr>
<td>Non-GMP production</td>
<td></td>
<td></td>
<td>Delayed to Year 2</td>
</tr>
<tr>
<td>Analytical method development/validation</td>
<td></td>
<td></td>
<td>Delayed to Year 2</td>
</tr>
<tr>
<td>Initiation of stability testing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rabbit vaginal irritation study</td>
<td>✓</td>
<td>✓</td>
<td>Ongoing</td>
</tr>
<tr>
<td>Reproductive toxicity studies</td>
<td></td>
<td>✓</td>
<td>Ongoing</td>
</tr>
<tr>
<td>Pre-IND consultation with FDA</td>
<td>✓</td>
<td></td>
<td>Achieved: Q1 2014</td>
</tr>
<tr>
<td>Efforts to access additional entry inhibitor compounds</td>
<td></td>
<td>✓</td>
<td>Completed: Q2 2014</td>
</tr>
</tbody>
</table>
Activity 2: Combination-ARV Rings

<table>
<thead>
<tr>
<th>Activity</th>
<th>Status</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Re-analysis of MTN-013/IPM 026 clinical samples (new activity)</td>
<td>✔ Achieved: Q2 2014</td>
<td></td>
</tr>
<tr>
<td>Vendor identification and contracting</td>
<td>✔ Achieved: Q1 2014 (DS003 ring)</td>
<td></td>
</tr>
<tr>
<td>Active Pharmaceutical Ingredient (API) interaction studies</td>
<td></td>
<td>On Hold</td>
</tr>
<tr>
<td>API combination + polymer system interaction studies</td>
<td></td>
<td>On Hold</td>
</tr>
<tr>
<td>Analytical method adaptation/validation</td>
<td></td>
<td>On Hold</td>
</tr>
<tr>
<td>Development of prototype rings</td>
<td></td>
<td>On Hold</td>
</tr>
<tr>
<td>Initiation of non-GMP stability assessment</td>
<td></td>
<td>On Hold</td>
</tr>
<tr>
<td>Initiation of preclinical evaluations</td>
<td></td>
<td>On Hold</td>
</tr>
</tbody>
</table>

Activity 3: Investigation of New ARV Compounds for Development

<table>
<thead>
<tr>
<th>Activity</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Field survey and discussions ongoing</td>
<td>Ongoing</td>
</tr>
</tbody>
</table>

Obstacles and Challenges: Year 1

In Year 1, IPM encountered obstacles and challenges as described below.

Activity 1: Before filing an IND for the DS003 tablet, a set of preclinical toxicology studies (reproductive toxicology in rats and rabbits, and vaginal irritation in rabbits) must be completed. IPM selected HLS as the partner for these studies and it took a substantial amount of time to negotiate the contract and gain HLS’s acceptance and understanding of all of the USAID flow down provisions. After agreement was reached, and while the procurement package for the reproductive toxicology studies were in USAID review, IPM made the decision to let the pre-ordered rabbits and rats for the studies be re-directed to another client at HLS, to avoid the risk that the animals would age beyond the acceptable range for these studies before USAID approval was received. Sourcing of new animals for the studies has resulted in a 2-3 month delay in the original program timeline to reach Phase I. IPM is working to understand and adhere to the USAID procurement guidelines and process required for making sub-awards to contractors. IPM is now allowing for additional time needed to complete the elements of the procurement package and USAID approval process to minimize any delays in implementing project activities.

In addition, in Q1 2014, DAIDS/NIAID/NIH agreed to conduct a macaque study of DS003, to compare PK across various dosage forms (tablet, gel, and ring). IPM was subsequently notified in Q3 that funding on the applicable contract mechanism would no longer be able to support this activity fully. IPM and DAIDS are exploring the option to delay the study to 2015, when additional funding might be available. This impacts the timing of the macaque efficacy study, but does not impact the start of the Phase I clinical study. IPM will continue discussions about the timing for the macaque PK and efficacy studies throughout Year 2 of the program.

Activity 2: PK data from the MTN-013/IPM 026 trial prompted additional analyses of the clinical samples which was important to conduct before continuing development work on maraviroc-based rings, as initially described in the Year 1 Workplan. USAID approved the re-directing of funds for this purpose and these analyses were completed, informing the ongoing competitive bidding evaluation for the next phase of the ring program. IPM is also supporting the implementation of a Phase I rectal and vaginal maraviroc gel trial (to be conducted under the NIH/NIAID funded CHARM U19 grant to the University of Pittsburgh) which will offer key data on vaginal use of maraviroc which will inform future development efforts. IPM filed an IND for the maraviroc gel product in Q3 2014, and the trial is targeted for initiation in Q4 2014 (non-USAID funding).
B. ACTIVITY SUMMARY: YEAR 1 PROGRESS AND PLANS GOING FORWARD

This section describes progress made in meeting Year 1 objectives during the performance period (30 September 2013 – 30 September 2014), with an overview of planned activities for the next performance period (01 October 2014 – 30 September 2015).

Activity 1: DS003-based Tablet

Primary Countries of Activity: United States, Italy, UK  
Period: 2006–2018

Technical Coordinator: Bríd Devlin, Exec. Vice President, Product Development

Implementers: IPM; Aptuit, Huntingdon Life Sciences (HLS), Particle Sciences Inc (PSI), PRA Health Sciences

Objective: The primary objective of this activity is to determine the safety, tolerability and acceptability of DS003 administered vaginally to healthy, HIV-negative women by advancing a DS003-based tablet through first-in-human Phase I clinical evaluation. A single-use tablet will allow for a small, stepwise dose-escalation evaluation which will support and inform other DS003-based formulation efforts such as a vaginal ring. In parallel with the preclinical development of DS003, IPM will attempt to gain access to and evaluate other promising gp120 entry inhibitor compounds currently in development.

Activity Description: DS003 is a small molecule compound originally developed by Bristol Myers-Squibb (BMS) that was licensed to IPM in 2005, with worldwide rights, for development as a microbicide product. This class of compounds (gp120-binding entry inhibitors) has been shown to have potent inhibitory effects on HIV-1. DS003 is an important microbicidal candidate for several reasons: (1) it acts early in the HIV lifecycle, potentially increasing the chances of protection; (2) the target is the virus itself rather than the host cell, reducing the likelihood of unwanted secondary effects; (3) this mechanism of action is not in use for HIV treatment or prevention, which means that (a) if resistance to DS003 were to occur in an infected individual unaware of their status and using a DS003-based microbicide, it is unlikely to compromise current treatment options, and (b) the increasing use of ARVs for treatment of HIV/AIDS in developing countries is unlikely to result in HIV strains that are resistant to DS003; and (4) as a small molecule ARV, DS003 can be developed as a microbicide, either alone or combined with other ARVs. It is anticipated that the DS003-alone tablet formulation will be the subject of the initial DS003 IND filing and first-in-human clinical trial. Future development of DS003 will likely be in combination with other ARVs given the advantages of combining two APIs and the fact that DS003 has reduced activity against subtype AE viruses.

Sub-Activity 1: Formulation, Manufacturing and Analytical Development. Implementation of the current tablet production process at a GMP manufacturer will be necessary to provide materials for the proposed Phase I clinical trial. Analytical testing to support formulation, process implementation and drug product stability will also be performed, as well as clinical packaging and labeling work necessary for the Phase I trial.

Sub-Activity 2: Preclinical Development. Several preclinical and toxicology studies are planned and underway, including Segment I and II reproductive toxicology studies and a 14-day rabbit vaginal irritation (RVI) study with the tablet. IPM will also test various formulations of DS003 (ring, tablet and gel) in macaque PK and efficacy studies.

Sub-Activity 3: Regulatory and Other Exploratory Efforts. In Q1 2014, IPM submitted a pre-IND request and questions which covered the toxicology program as well as the preliminary Phase I trial design, to support the first-in-human DS003 tablet trial. Written responses were provided by the FDA supporting IPM’s continued development of the DS003 tablet for clinical evaluation. Also as part of this program, IPM will explore the possibility of performing a comparative analysis between DS003; the small-molecule inhibitor BMS-626529; BMS-663068 (a prodrug for BMS-626529 with the same mechanism of action as DS003, currently in Phase II clinical testing for HIV treatment); and any other promising gp120 inhibitor compounds available from BMS.

Progress in Past 12 Months: During the performance period (30 September 2013 – 30 September 2014), IPM made progress toward the Year 1 expected results for this activity, as summarized below.

- Sub-Activity 1: Formulation, Manufacturing and Analytical Development. IPM selected Aptuit (Verona, Italy) as the DS003 tablet GMP manufacturer, and developed a plan for technology transfer and manufacture/testing of technical and GMP batches. The contract was signed in Q3 2014 and technology transfer has been initiated. Non-GMP
manufacture and analytical method development/validation were delayed but will be completed by Q1 2015. Due to other study delays, manufacture of the Phase I materials will not impact the timeline for the Phase I study.

- **Sub-Activity 2: Preclinical Development.** Protocols were finalized for reproductive toxicology studies and the RVI study (the remaining studies needed to support the DS003 IND filing). As described in the Obstacles and Challenges section above, the original schedule for the studies had to be revised due to delays associated with the finalization of the contracts. The schedule for these studies is now as follows:
  - RVI: treatment initiates 07 November 2014; draft report 09 March 2014
  - Preliminary rat Segment I: treatment initiates 05 November 2014; draft report 23 January 2015
  - Rat Segment I: treatment initiates 07 January 2015; draft report 16 April 2015
  - Rabbit Segment II: treatment initiates 08 January 2015; draft report 26 June 2015

IPM has recently received USAID approval to contract with PRA for bioanalytical support for these studies which is needed to analyze the preclinical toxicokinetic samples.

IPM continued discussions with the DAIDS group at NIAID/NIH and received agreement from them to conduct a macaque PK study comparing DS003 gels, tablets, and rings through a DAIDS funded contract mechanism. However, as explained in the Obstacles and Challenges section above, due to budget constraints at DAIDS, this study will likely be delayed until 2015. Discussions with DAIDS are ongoing to confirm what will be feasible.

- **Sub-Activity 3: Regulatory and Other Exploratory Efforts.** IPM’s expectation is that since DS003 has never been administered to humans before, regulatory agencies will require a cautious approach for the initial Phase I trial involving administration of a single dose followed by a safety review and possibly PK data review before proceeding to the next dose level. Therefore, a dosage form that is suitable for this kind of approach will be necessary, i.e. something via which a single bolus can be administered, such as a single use vaginal tablet. IPM submitted to the FDA a pre-IND briefing package and questions which covered the toxicology program as well as the preliminary Phase I trial design in January 2014. Written responses were provided by the FDA in February 2014 and no significant concerns were raised. IPM also received feedback from the NIH funded Microbicides Trial Network that conducting the DS003 tablet clinical trial was not likely in their current planning scenario. Therefore, IPM discussed with USAID the possibility of using funds from this grant to support the trial which was approved as part of the Year 2 work plan. IPM plans to submit an IND to the FDA to support the Phase I trial in July 2015, after completion of planned preclinical toxicology studies described above.

In a discussion with BMS held in April 2014, BMS explained that they had made DS003 available to IPM based on the specific characteristics that would be favorable for microbicide development (spectrum of activity, bioavailability, potency, solubility). The other compounds in development at BMS as oral therapy have characteristics that would make them favorable orally (and not vaginally), and would likely be inferior for microbicide development, even if further along in clinical development as therapeutics. BMS would not share written technical details nor expand on what they told IPM verbally due to confidentiality but did provide assurance that DS003 is the optimum gp120 binding candidate that they have available for microbicide development. Therefore, access to additional BMS entry inhibitors will not be further pursued.
## Activity 1: DS003 Tablet
### Year 1 Workplan Expected Results

<table>
<thead>
<tr>
<th>Activity Description</th>
<th>2013</th>
<th>2014</th>
<th>Status as of 30 September 2014 (Major Milestones)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SUB-ACTIVITY 1: Formulation, Manufacturing, Analytical Dev.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CMO evaluation and selection</td>
<td></td>
<td></td>
<td>Achieved: Q1 2014 (GMP tablet manufacturer selected: Aptuit Verona, Italy) Contract awarded</td>
</tr>
<tr>
<td>Technology transfer to CMO</td>
<td></td>
<td></td>
<td>Achieved: Q3 2014 Technology transfer in process; to remain ongoing through non-GMP production</td>
</tr>
<tr>
<td>Non-GMP production</td>
<td></td>
<td></td>
<td>Delayed to Year 2</td>
</tr>
<tr>
<td>Analytical method development/validation</td>
<td></td>
<td></td>
<td>Delayed to Year 2</td>
</tr>
<tr>
<td>Initiation of stability testing</td>
<td></td>
<td></td>
<td>Delayed to Year 2</td>
</tr>
<tr>
<td>SUB-ACTIVITY 2: Preclinical Development</td>
<td></td>
<td></td>
<td>Ongoing</td>
</tr>
<tr>
<td>Rabbit vaginal irritation study</td>
<td></td>
<td></td>
<td>Study protocol outlined, vendor selected, contract awarded and study scheduled. Dosing to be initiated in Q4 2014</td>
</tr>
<tr>
<td>Reproductive toxicity studies</td>
<td></td>
<td></td>
<td>Ongoing</td>
</tr>
<tr>
<td>SUB-ACTIVITY 3: Regulatory and Other Exploratory Efforts</td>
<td></td>
<td></td>
<td>Achieved: Q1 2014 (pre-IND package to FDA Jan-14; written responses received Feb-14 supporting IPM’s DS003 product dev. plans)</td>
</tr>
<tr>
<td>Pre-IND consultation with FDA</td>
<td></td>
<td></td>
<td>Completed</td>
</tr>
<tr>
<td>Efforts to access additional entry inhibitor compounds</td>
<td></td>
<td></td>
<td>Completed</td>
</tr>
</tbody>
</table>

### Planned Activities for Next 12 Months:
- Completion of non-GMP and GMP tablet production, testing, and clinical packaging for Phase I trial
- Completion of RVI and reproductive toxicity studies and associated bioanalytical analyses
- Conduct of a macaque PK study (via NIH contract)
- Planning for initiation of a macaque efficacy study
- Finalization of clinical protocol and regulatory dossier submitted for Phase I tablet trial
- Initiation of Phase I tablet trial

## Timeline of Activities for Proposed Year 2 Work Plan

<table>
<thead>
<tr>
<th>Activity Description</th>
<th>2014</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-GMP tablet production and testing</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>GMP tablet production, testing, and packaging for Phase I trial</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>RVI and reproductive toxicity studies</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Macaque PK study</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Initiation of macaque efficacy study</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Regulatory dossier submitted for Phase I tablet trial</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Initiation of Phase I tablet trial</td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>
Activity 2: Advancing the Microbicide Pipeline – Combination rings (dapivirine, maraviroc, DS003)

Primary Countries of Activity: United States, TBD in Europe  
Period: 2006–2018  
Technical Coordinator: Brid Devlin, Exec. Vice President, Product Development  
Implementers: IPM; Tandem Labs, Inc.; QUB; contractors TBD

Objective: The main objective of this activity is to advance combination microbicide vaginal rings containing dapivirine, maraviroc and DS003 through formulation and preclinical development. Dapivirine is a non-nucleoside reverse transcriptase inhibitor (NNRTI), and maraviroc and DS003 are both viral entry inhibitors although they act on different targets (host cell CCR5 co-receptor and viral gp120, respectively). A multi-ARV microbicide ring product is a priority for IPM and the wider microbicide field because (1) the use of multiple APIs with varying mechanisms of action is likely to provide greater (possibly synergistic) inhibitory activity against HIV; and (2) a microbicide containing a combination of ARVs is likely to maintain efficacy even if an individual is exposed to viral strains with mutations conferring resistance to one of the active ingredients, because the other ARV will act as a ‘safety net.’ Thus, there is a strong scientific rationale for exploring combinations of dapivirine, maraviroc and DS003 in a microbicide product, and a ring dosage form is being pursued due to the reduced burden of compliance with this type of product.

Activity Description: In the development of a multi-ARV product, it is important to assess the potential efficacy and risks around the individual components. IPM has already completed varying degrees of development on vaginal microbicide rings containing dapivirine alone; dapivirine and DS003; maraviroc alone; and dapivirine and maraviroc (summarized below). All of this past work will serve as a platform upon which to develop a combination-ARV ring for clinical evaluation.

Dapivirine: IPM has developed a silicone-based vaginal ring delivering dapivirine over 28 days that is currently being assessed in two parallel Phase III trials (IPM 027 and MTN-020), and thus there is substantial preclinical and clinical data to support the incorporation of dapivirine in a new ring. IPM has also worked with partner Particle Sciences, Inc. (PSI) to develop prototype rings combining dapivirine and DS003 in an ethyl vinyl acetate (EVA)-based polymer.

Maraviroc: This CCR5 antagonist was licensed to IPM in 2008 from Pfizer (now Viiv Healthcare) and has a large volume of safety and efficacy data available from currently marketed HIV treatments (Selzentry/Celsentri®). In addition, information from an initial Phase I study of a dapivirine-maraviroc vaginal ring (MTN-013/IPM 026) provides key PK and pharmacodynamic (PD) data to inform the design of future maraviroc-based rings.

DS003: As described in Activity 1 above, IPM is progressing a DS003-only vaginal tablet program in order to collect necessary preclinical information on DS003, with the goal of assessing its safety and tolerability when administered vaginally to women in a Phase I study. As such, it is anticipated that there will be sufficient safety information available for DS003 in advance of any regulatory submissions or clinical study initiation with a combination ring containing this compound.

Initial activities for this program will focus on formulation and defining the Target Product Profile (TPP) and lead ring design. Preliminary work has shown that all three agents are compatible with EVA and this will be used as a starting point for formulation design; other thermoplastic polymers (e.g., polyurethane) will be explored if needed. Parallel development of rings containing each single agent will also likely be part of this program, in order to demonstrate to regulators that the benefit of the combination outweighs the individual drugs. IPM will maintain ongoing dialogue with regulatory authorities to clarify the optimum pathway forward for a combination product.

Progress in Past 12 Months: During the performance period (30 September 2013 – 30 September 2014), IPM made progress toward the Year 1 expected results for this activity, as summarized below.

- Maraviroc-based ring development: In 2013, data emerged from the MTN-013/IPM 026 clinical trial of maraviroc based rings. The method used originally for the analysis of maraviroc in plasma samples from the trial was relatively insensitive with a lower limit of quantification (LLOQ) of 0.5 ng/mL (for comparison, the LLOQ for dapivirine was 20 pg/mL), and no maraviroc was detected in any of the trial samples. IPM felt there would be value in reanalyzing these samples using a more sensitive assay, and requested USAID support under this Activity for this purpose. IPM re-analyzed clinical plasma samples from the MTN-013/IPM 026 Phase I trial of maraviroc-based rings using a more sensitive assay (LLOQ of 6 pg/mL). These data showed that low levels of
maraviroc were detectable on Day 1 but not 28, and suggest that greater release of maraviroc from the ring will be necessary. An extensive request for proposal (RFP) process is underway for the optimization of the dapivirine-maraviroc ring formulation. IPM is also providing support (with non-USAID funds) for the NIH-funded CHARM-03 maraviroc rectal gel trial; the trial will include a vaginal arm for gel use, which will provide additional data on vaginal PK and safety of maraviroc. IPM provided CMC and Quality Assurance oversight for the gel manufacturing, and also filed the IND for the product. The trial is scheduled to initiate in Q4 2014.

- **DS003-based ring development:** IPM identified Queens University Belfast (QUB) as its partner for DS003-based ring development, and a set of studies has been defined to develop a formulation as well as production of DS003 rings for use in the macaque PK study described in the Activity 1 description. A contract was awarded to QUB following USAID approval, and ring formulation trials using three different EVA grades have commenced.

### Activity 2: Combination-ARV Rings

#### Year 1 Workplan Expected Results

<table>
<thead>
<tr>
<th>Activity Description</th>
<th>2013</th>
<th>2014</th>
<th>Status as of 30 September 2014 (Major Milestones)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Re-analysis of MTN-013/IPM 026 clinical samples (new milestone)</td>
<td>Q4</td>
<td>Q1</td>
<td>Achieved: Q2 2014</td>
</tr>
<tr>
<td>Vendor identification and contracting</td>
<td>Q2</td>
<td>Q3</td>
<td>Achieved: Q1 2014 (DS003-based ring development partner selected: Queens University Belfast, UK). Contract approved and awarded in Q3 2014; RFP process ongoing in Q3 2014 for dapivirine-maraviroc ring; Partner selection targeted for Q4 2014</td>
</tr>
<tr>
<td>API interaction studies</td>
<td></td>
<td></td>
<td>On hold* IPM will be developing DS003 alone rings first, and this program is now underway. DS003 combination ring work is included in the Year 2 work plan. The dapivirine-maraviroc program is targeted for initiation in Q4 2014.</td>
</tr>
<tr>
<td>API combination + polymer system interaction studies</td>
<td>Q3</td>
<td></td>
<td>*see above</td>
</tr>
<tr>
<td>Analytical method adaptation/validation</td>
<td>Q1</td>
<td></td>
<td>*see above</td>
</tr>
<tr>
<td>Development of prototype rings</td>
<td>Q1</td>
<td></td>
<td>*see above</td>
</tr>
<tr>
<td>Initiation of non-GMP stability assessment</td>
<td>Q3</td>
<td></td>
<td>*see above</td>
</tr>
<tr>
<td>Initiation of preclinical evaluations</td>
<td></td>
<td></td>
<td>*see above</td>
</tr>
</tbody>
</table>

#### Planned Activities for Next 12 Months:

Development of single agent and combination rings will continue in Year 2. Specifically, IPM aims to achieve the following expected results during the October 1, 2014 – September 30, 2015 program period:

- Maraviroc-based ring reformulation efforts initiated and prototypes developed, with plans for continued product advancement to be informed by CHARM-03 data, available in late 2015
  - Go/No-Go criteria identified for maraviroc-based ring development based on amount of maraviroc drug release achieved *in vitro* from optimized prototypes, and PK/PD data resulting from CHARM-03
- Conduct PK evaluation of reformulated maraviroc-based ring in a sheep model
- DS003 EVA ring prototype developed; API combinations explored
  - Go/No-Go criteria established for DS003 rings based on drug release achieved *in vitro* and preclinical and clinical PK data from the planned macaque study and DS003 tablet Phase I trial. After single agent rings are formulated, IPM will explore development of combination rings containing DS003 (e.g. with dapivirine, maraviroc, darunavir and other available APIs)
- GMP production of DS003 API to support continued DS003-based ring development activities; a 5kg batch will be produced using the established synthetic process
Timeline of Activities for Year 2

<table>
<thead>
<tr>
<th>Activity</th>
<th>2014</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maraviroc-based ring reformulation plans identified</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Maraviroc-based prototype rings developed and on stability</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Maraviroc-based ring PK evaluation in sheep</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>DS003 EVA ring prototypes developed and available for macaque study</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>DS003 combination ring development initiated</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>GMP production of DS003 API</td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

**Activity 3: Advancing the Microbicide Pipeline – New and early development ARV compounds**

**Primary Countries of Activity:** United States, TBD  
**Period:** 2013–2018  
**Technical Coordinator:** Bríd Devlin, Exec. Vice President, Product Development  
**Implementers:** IPM

**Objective:** The main objective of this activity is to identify and evaluate new and promising microbicide candidates with alternative mechanisms of action for development by working in collaboration with global partners.

**Activity Description:** IPM will continue to survey the field and consult with partners and pharmaceutical companies to identify new and promising ARV compounds for microbicide development. Of particular interest are compounds that target the HIV protease and integrase enzymes which have not previously been tested as microbicides in humans and may have important benefits for HIV prevention, as well as alternative entry inhibitors.

*Darunavir:* This compound works by blocking the HIV enzyme protease, which prevents the host cell from producing new viruses. As a marketed product for HIV treatment (PREZISTA®), it has robust preclinical and clinical packages of data available which will streamline the microbicide development pathway. Additionally, IPM has successfully partnered with Janssen R&D Ireland (formerly Tibotec) on its dapivirine program since 2004, providing a strong relationship and a solid starting point for license agreement negotiations.

*GSK1265744:* ViiV Healthcare’s promising candidate acts by blocking the HIV enzyme integrase, preventing the viral DNA from being integrated into the host cell genome. It is currently in development as a long-acting injectable, both for HIV treatment and prevention, and is also being considered for development as a vaginal microbicide. This compound represents a promising integrase inhibitor to add to the microbicide pipeline given its novel mechanism of action (from a prevention perspective) and its potential as a long-acting product because of its demonstrated PK properties. IPM also has a strong partnership with ViiV Healthcare, as the provider of IPM’s maraviroc license (since it was transferred from Pfizer in 2010).

If IPM is successful in securing access to these compounds, they will be evaluated for formulation and cost feasibility, and early safety and anti-HIV activity assessments will be performed. If promising, IPM will attempt to negotiate license agreements that support IPM’s charitable mission, and these promising candidate(s) will be progressed through an evidence-based early development program toward a defined TPP. This will include early formulation and analytical development activities as well as preclinical studies, and establishing a formal cross-functional Product Development Team, TPP and Development Plan.

**Progress in Past 12 Months:** During the performance period (30 September 2013 – 30 September 2014), IPM and Janssen have made progress on licensing discussions for darunavir. IPM staff continue to survey the field, attend conferences, and engage in discussions to identify additional pipeline compounds of interest.

<table>
<thead>
<tr>
<th>Activity 3: New ARV Compounds Year 1 Workplan Expected Results</th>
<th>2013</th>
<th>2014</th>
<th>Status as of 30 September 2014 (Major Milestones)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year 1 Workplan Expected Results</td>
<td>Q4</td>
<td>Q1</td>
<td>Q2</td>
</tr>
<tr>
<td>Field survey and discussions ongoing</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

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IPM also continued to provide support (with non-USAID funds) to the EC-funded CHAARM Consortium in the development of dapivirine-darunavir gels and rings. The combination gel is targeted to enter a Phase I clinical trial in Q4 2014.

**Planned Activities for Year 2:** Efforts currently underway to obtain licenses for additional compounds, will continue in Year 2. Specifically, IPM aims to achieve the following expected results during the October 1, 2014 – September 30, 2015 program period:

- Continued development of dapivirine-darunavir gel and rings with CHAARM Consortium (IPM supporting with non-USAID funds)
- License obtained from Janssen R&D Ireland to develop darunavir as microbicide candidate, supported by data from combination dapivirine-darunavir gel trial
- Continued discussion with pharmaceutical partners on access to additional compounds of interest

### Timeline of Activities for Proposed Year 2 Work Plan

<table>
<thead>
<tr>
<th>Activity</th>
<th>2014</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continued development of dapivirine-darunavir gel and rings with CHAARM</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Consortium</td>
<td>X</td>
<td>Q2</td>
</tr>
<tr>
<td>License for darunavir obtained from Janssen R&amp;D Ireland</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Continued discussion with pharmaceutical partners on access to additional</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>compounds of interest</td>
<td>X</td>
<td>Q3</td>
</tr>
</tbody>
</table>

### C. GENDER

IPM is working to develop female-initiated HIV prevention products specifically because of the disproportionate impact this virus has on women in the developing world, particularly in sub-Saharan Africa. All of IPM’s work stems from the recognition that there are currently no tools women can use to discreetly protect themselves from HIV infection, and the social context within which many African women live constricts their ability to use the most effective HIV prevention methods without the active participation of a male partner (i.e., abstinence, condom use, mutual monogamy, male circumcision). It is hoped that the monthly dapivirine vaginal ring meets women’s expressed interest in a convenient HIV prevention method that would not require negotiation with a male partner.

IPM is committed not only to understanding the influence of gender roles on project objectives, but also to the ultimate goal of promoting gender equality. To this end, the organization recognizes that gender considerations must be integrated into the product development pathway for microbicides. Consistent with USAID expectations, IPM utilizes gender analyses to guide development activities as well as long-term planning. Each of the areas described below demonstrates a specific example of IPM’s dedication to ensuring gender equality through integrating and understanding of the impact of gender issues on organizational goals.

**Clinical Programs:** To better understand how to mitigate potential barriers to microbicide use, IPM collects social and behavioral data from women enrolled in its trials as well as a subset of participants’ male partners. These data focus on trial-related product use as well as the broader social, cultural and gender norms that might influence sexual behavior. Male partner interviews focus on gender roles and norms that may facilitate or impede adherence to product use in current and future IPM trials, and foreshadow male partner influence on microbicide uptake and correct, consistent and continued use. For example, in IPM 011, a safety and acceptability study of a placebo vaginal ring in two sub-Saharan African countries, data was gathered from some study participants with regard to using a vaginal ring to prevent HIV infection without disclosing use to their partners. Data indicated that although women may value having the choice of disclosing ring use to their partner, whether they can actually exercise that choice will depend on specific aspects of their relationship as well as social and cultural norms. Although 65% of trial participants said they would use the ring without telling their partner, 63% said their partner might become angry if he was not told, and 13% of these respondents further indicated that their partner might become violent. These social and behavioral data serve the secondary clinical trial objectives of assessing acceptability and adherence, as well as the goal of developing a database to inform future microbicide research and introduction efforts.
Assessment of Gender-Based Violence: It is inconclusive whether or how the availability of vaginal microbicides might exacerbate the problem of gender-based violence, given that some men may oppose their use. IPM recognizes that its local partners may need to address this issue as part of the larger women’s health and empowerment movement salient to their communities. Thus far, there has been no general social movement against microbicide trial participants. To the contrary, community support for HIV prevention efforts in general, and for microbicides in particular, remains strong. IPM trials routinely monitor and collect data on social harms, which include physical, emotional and financial harms experienced by participants during the trial. Collaborating research centers have strategies and referral resources in place to mitigate the effects of such harms, and there have been no significant findings to suggest that an increased incidence of social harms to study participants have occurred as a result of their participation in IPM clinical trials.

Community Relationships: Where IPM conducts its clinical trials, the RCs have established Community Advisory Groups (CAGs), which routinely include representation from groups working on gender issues. This has become common practice for HIV prevention research and facilitates inclusive community participation. The most notable risk of exacerbating inequalities is partnering with community groups that, inadvertently or otherwise, maintain an inequitable status quo. IPM will continue to engage with communities for microbicide introduction efforts, and it will be necessary to extend to groups outside of the clinical research setting. At this point, another round of assessments will be needed to systematically identify additional effective and appropriate community groups with which to partner.

D. HUMAN SUBJECTS PROTECTION

IPM holds a Federal Wide Assurance, which attests to IPM’s intent and ability to conduct Human Subjects Research according to guidelines required by the US Government. IPM’s FWA number is FWA00018657 and is currently valid through 13 March 2019. IPM conducts research in full compliance with internationally recognized guidelines for GMP, Good Clinical Practice (GCP) and Good Clinical Laboratory Practice (GCLP), in accordance with the Council for International Organizations of Medical Sciences (CIOMS). For all IPM clinical trials, participants are asked to sign an informed consent form in advance of any study procedure. Informed consent information sheets/forms are approved by the institutional review boards/independent ethics committees and regulatory authorities (if applicable) responsible for approving research conducted at each research center.

E. ENVIRONMENTAL COMPLIANCE

The investigational vaginal products for the proposed activities will be prepared for research and clinical trial purposes only. The manufacturing steps involved in the preparation of the clinical material will be carried out in accordance with applicable environmental regulations, including disposal or destruction of waste materials. Vaginal products used by participants in clinical trials during development are either collected for potential post-use evaluation, or disposed of as biohazard clinical waste per study protocol. In this regard, the activities conducted as part of this award are consistent with the exclusions described in Federal Regulations 22 CFR 216.2(c)(2), and will not require an Initial Environmental Examination, Environmental Assessment and Environmental Impact Statement.

F. SUCCESS STORIES

IPM expects that Phase I readiness of one or more new microbicide candidates will be the greatest success generated by the activities implemented under this Cooperative Agreement. However, IPM does not have documented success stories to share as of yet, although rapid progress is being made toward the first in human evaluation of an ARV microbicide with a novel mechanism of action, DS003. Organizational successes achieved during calendar year 2013 have been described in IPM’s Annual Report, which was made available in August 2014.

G. PRESS & MEDIA

Descriptions of all media coverage that appeared during the performance period (30 September 2013 – 31 March 2014) are provided below; clippings and additional information are included in this report as an appendix.

Summary of IPM Public Statements and Messages

IPM Receives 2 Awards from USAID through PEPFAR to Advance HIV Prevention Technologies for Women (21 Oct 2013)

• Picked up by UNAIDS Daily News Clips (24 October 2013) and PEPFAR Daily News Clips (14 November 2013)

The Promise of Progress in 2014 (1 January 2014)

IPM Announces Dr. James McIntyre as Board Chair, New Board Members Ms. Heidemarie Wieczorek-Zeul and Mr. Michael Stevens (24 January 2014)

Two Studies Advance HIV Prevention Options for Women (4 March 2014)
  • Cross posted on Armenian Medical Network, eWallstreeter, Infection Control Today, Science Codex, Science Newsline, allAfrica and News Medical

International Women's Day: Inspiring Ideas for Women's Health (8 March 2014)

IPM Receives Worldwide Rights to HIV Prevention Medicine (May 8, 2014)
  • Reposted by EurekAlert!, Biotechnology Forums, Kontactor, News Locker, Phys, EATG, Health Medicinet, News Medical, Women Deliver

IPM Welcomes Executive Vice President, Global Product Access Lynn Bodarky and Chief Financial Officer Mike Goldrich (September 10, 2014)

Congressional Briefing, 22 October 2013

Dr. Zeda Rosenberg participated in the Congressional briefing, “Saving lives through research: USAID’s role in creating breakthrough global health products,” hosted by Global Health Technologies Coalition (GHTC) and PATH. The event aimed to encourage continued investment in research for and development of new and innovative global health products, and the media coverage reflected this overarching objective.

Print/Digital Media
  • GHTC Breakthroughs Blog: No more business as usual: USAID’s important role in global health R&D highlighted at Capitol Hill briefing
  • Science Speaks Blog: Supporting Global Health Technologies Act, speakers warn: time is running out on tools for infectious diseases

Social Media
  • IPM live-tweeted during the briefing; GHTC and PATH retweeted IPM throughout the event

New USAID Grants (4 November 2013)

A piece on the Science Speaks Blog highlighted IPM’s recent grants from USAID and discussed how they have helped to generate new, critical momentum for women’s HIV prevention research. It specifically focused on IPM’s most advanced product – the dapivirine ring – and the challenges and obstacles that IPM overcame to develop it.

Print/Digital Media
  • Science Speaks Blog: Can a vaginal ring be part of HIV prevention arsenal by 2016?

Social Media
  • IPM, other leading women’s health and HIV/AIDS groups (e.g. Women Deliver, IAVI) tweeted about the piece

World AIDS Day (27 November 2013; 1 December 2013)

To mark World AIDS Day, Dr. Zeda Rosenberg authored an op-ed published on Devex highlighting the role of innovation in achieving an AIDS-free generation. She emphasized the need for female-initiated health technologies and a robust pipeline of products that meet individuals’ preferences and help offset the risk of the virus’ resistance. On December 1, IPM released the third and final installment of its Real Voices videos, which featured scientists, clinicians, advocates and community members discussing the potential impact of an effective microbicide.

Print/Digital Media
  • Devex: How innovations will pave the way to an AIDS-free generation

Social Media
  • IPM and a number of organizations, including AIDS-Fondet and Sex og Politikk, tweeted about the Devex op-ed
  • AVAC and Sex og Politikk tweeted about the Real Voices video
2014 Conference on Retroviruses and Opportunistic Infections (4 March 2014)
The Microbicide Trials Network published a press release about new data on the combination dapivirine-maraviroc ring, announced at the 2014 Conference on Retroviruses and Opportunistic Infections (CROI). The press release highlighted the combination ring’s safety but noted that additional research was needed to improve maraviroc’s absorption into tissues. IPM published its own press release on the data (included in the “IPM Public Statements and Messages” document). Media coverage of the data focused on the results of the study and the product’s potential, noting that while it is still in the early stages of development, the combination ring could eventually expand the range of HIV prevention options for women.

Print/Digital Media
- Microbicide Trials Network: First Trial of Combination ARV Vaginal Ring for HIV Prevention Finds Ring Safe but One ARV Carrying the Weight; cross posted on eWallstreeter, First Word MedTech, First Word Pharma, Medical Xpress, Science Codex, Science Daily and Science Newsline
- Fierce Drug Delivery: Study: In two-drug, HIV-preventing vaginal ring, only one drug does the job
- Healio Infectious Disease News: Dapivirine vaginal ring blocked HIV infection in cervical tissue
- UAB News: New method for women’s HIV prevention found to be safe for use

Social Media
- IPM and partners, including AVAC, tweeted about the CROI announcement

58th Session of the UN Commission on the Status of Women (21 March 2014)
IPM launched a new infographic highlighting how women’s HIV prevention and sexual and reproductive health impacts broader global development to mark the final day of the 58th session of the UN Commission on the Status of Women.

Social Media
- IPM promoted the infographic on Twitter, and it was subsequently shared by a number of organizations, including Women Deliver, CAMI and AIDS-Fondet, among others

Worldwide Rights Agreement with Janssen R&D Ireland (May 8, 2014)
IPM received exclusive worldwide rights to dapivirine from Janssen R&D Ireland, one of the Janssen Pharmaceutical Companies of Johnson & Johnson. The agreement expands on IPM’s existing rights to develop, manufacture and commercialize dapivirine-based products for use by women in developing countries and gives women in developed countries access to future dapivirine-based products, such as a dual-purpose HIV prevention-contraceptive ring.

The agreement generated original articles in well-known outlets, including Bloomberg and Devex, among others. Dr. Zeda Rosenberg and Dr. Paul Stoffels, Chief Scientific Officer and Worldwide Chairman of Janssen Pharmaceutical Companies, co-authored an op-ed about the agreement that was published by Global Post.

Print/Digital Media
- Bloomberg: J&J Gives AIDS Drug Rights to Charity for Vaginal Ring (May 8)
- Global Health Technologies Coalition: IPM Receives Worldwide Rights to HIV Prevention Medicine (May 8)
- Science Speaks Blog: International Partnership for Microbicides, pharmaceutical company agreement sets path for woman-controlled HIV prevention (May 8)
- Crazy Joys: Healthcare most Active Stocks: Johnson & Johnson, Bristol-Myers Squibb, Mylan Inc, Arena Pharmaceuticals, Ariad Pharmaceuticals (May 12)
- Gaining Green: Drug Manufacturer Most Active: Pfizer Inc., Merck & Co., Inc., Bristol-Myers Squibb Co, Johnson & Johnson (May 13)
- Pharmaceutical Online: Janssen and IPM Expand Public-Private Collaboration for HIV Drugs (May 13)
- ZENOPA: Janssen and IPM to develop preventative HIV therapy (May 15)
- Devex: Institutions lean on creative financing, partnerships to further disease research (May 30)
  - Included in Kaiser Daily Global Health Policy Report (June 3)

Op-Ed
- Global Post: Partnering to protect women from HIV (15 May)
Included in Kaiser Daily Global Health Policy Report (16 May) and Global Health Technology Coalition’s Weekly Information Update (19 May)

**Social Media**

IPM also developed an infographic about the announcement that was shared on Twitter by organizations such as Women Deliver, GlobalHealth.ie and Sex og Politikk.


IPM hosted a one-hour Twitter Chat on women and HIV/AIDS ahead of the 20th International AIDS Conference. Co-hosts included Women Deliver, the International HIV/AIDS Alliance, the International Center for Research on Women, AVAC and CONRAD. According to TweetReach, over 350 individuals and global health and US health organizations posted more than 2,200 tweets to the chat’s hashtag, #StepUp4Women, over the course of the day. The chat generated 5.8 million impressions—the number of times that a tweet could be seen by registered Twitter users—that reached 501,600 unique Twitter users. The chat hashtag continued to be used throughout AIDS 2014 by individuals and organizations highlighting issues related to HIV and women.

**Social Media**

- *Selected Partner Tweets and Retweets:* Johnson & Johnson, Global Fund, USAID Global Health, Elizabeth Glaser Pediatric AIDS Foundation, mothers2mothers, Global Health Technologies Coalition (GHTC), Francoise Girard, Serra Sippel
- *Most Retweeted Answer Tweets from Other Participants:* EngenderHealth, International Rectal Microbicide Advocates, Women Deliver, USAID Global Health, Pathfinder International

**The 20th International AIDS Conference in Melbourne, Australia (July 20-25, 2014)**

Dr. Zeda Rosenberg attended AIDS 2014, which was themed “Stepping Up the Pace.” The conference aimed to assess progress toward ending the HIV/AIDS epidemic, evaluate recent scientific developments and lessons learned, and collectively chart a course forward. At the conference, Dr. Rosenberg participated in FHI360’s AIDS 2014 Live video interview series, highlighting the burden of HIV/AIDS on young women in Africa and microbicides’ promise for advancing HIV prevention. IPM was also an AIDS 2014 Live coverage partner, working with FHI360 to shape the content of and disseminate daily digital recaps.

**Print/Digital Media**

- *FHI360 Video:* Hope in microbicides for young women in sub-Saharan Africa

**Social Media**

- *AIDS 2014 Live Daily Delivery (July 24, 2014):* Hope in microbicides for young women in sub-Saharan Africa

**Daily Twitter Activity (October 1, 2013 – September 10, 2014)**

IPM posts an average one to three tweets per day on issues related to women and girls, HIV/AIDS, sexual and reproductive health, research and development, technology and innovation, gender equality and international development. Since October 1, 2013, IPM has gained nearly 200 new followers. IPM has become increasingly visible on Twitter, hosting and participating in and Twitter chats (see above) and engaging in hashtag campaigns such as #MDGmomentum. IPM has been retweeted by individuals and organizations such as USAID, Raj Shah, PEPFAR and Girl Rising.

**Social Media**

- *Selected Retweets:* USAID, Raj Shah, PEPFAR, Girl Rising

**H. BEST PRACTICES**

IPM conducts its research and product development activities in full compliance with regulations as put forth by the US FDA and the European Medicines Agency (EMA), as well as internationally recognized guidelines for GMP, GCP and GCLP, in accordance with the CIOMS. IPM’s research involving animals is contracted to research organizations with laboratories that can provide assurance of compliance with the highest standards for animal care and welfare. IPM contributes to and informs best practices for the field by publishing and presenting its findings in highly-regarded venues (i.e., peer-reviewed journals, international conferences).
Congressional Briefing (October 22, 2013)

GHTC Breakthroughs Blog: No more business as usual: USAID’s important role in global health R&D highlighted at Capitol Hill briefing
October 22, 2013
By Nick Taylor

“You’re in a position to make such a difference and to be innovative with your thinking,” Margaret McCluskey, senior technical advisor at the US Agency for International Development (USAID), said to an audience of Congressional staffers at a briefing yesterday on Capitol Hill. The briefing, co-hosted by GHTC and PATH, focused on the critical role USAID plays in supporting lifesaving global health research and development (R&D) for new health tools. Panelists also stressed the need for policymakers in Congress and across the US government to support the development of new and innovative health products.

All of the panelists at yesterday’s briefing called on the US government to continue its strong investment in global health research. Rep. Albio Sires (D-NJ)—lead co-sponsor of the 21st Century Global Health Technology Act, a bill that would strengthen health R&D and product development at USAID—spoke at the briefing and reiterated this important message. “New vaccines, drugs, and tests are desperately needed, but progress cannot be sustained without R&D,” he said, adding that the United States has a legacy of supporting global health R&D and that health R&D is a smart economic investment.

Much progress in global health R&D has been made over the years, and USAID has unquestionably supported many of today’s success stories—including new tools for malaria, HIV/AIDS, child health, family planning, and reproductive health. Several panelists stressed that product development for global health tools doesn’t happen overnight, and that USAID’s sustained commitment to research has been a crucial element of these health R&D success stories. Dr. Zeda Rosenberg, CEO of the International Partnership for Microbicides, stressed that R&D can take many years, and thanked USAID for its support for microbicide research—as well as for providing dedicated resources and long-term investments in global health product development.

Panelists also emphasized that despite this progress, there is still a need for sustained investment in R&D today to ensure that there are appropriate tools for diseases of poverty tomorrow. Rosenberg warned that complacency with today’s current tools is the wrong mindset, saying, “As soon as you think you’ve got [a health issue] under control, you’ve lost.” Kari Stoever, vice president of external affairs at Aeras, noted that investing now in tuberculosis (TB) vaccine research will save billions of dollars in future
spending for TB treatment programs in low- and middle-income countries, which currently costs $8-10 billion per year. She added, “Without an effective vaccine, many lives are at risk.” USAID does not currently fund TB vaccine R&D.

Additionally, USAID’s partnerships with the private and nongovernmental sectors have been key to its success in developing effective public health tools. One particularly effective partnership is USAID’s support for nonprofit product developers (NPPDs). These organizations combine the resources of governments, the experience of the private sector, and the know-how of nonprofit groups. PATH is one such NPPD that, with USAID support, partnered with Becton, Dickenson and Company (BD) to develop the SoloShot™ syringe and Uniject™ system. Both devices are designed specifically for use in low- and middle-income countries. “Though BD is a for-profit company, we share a common goal of providing access to important devices where they are needed most,” said Renuka Gadde, vice president of Global Health at BD. She added at none of these successes would have happened without government agencies like USAID looking at complex global health problems and spurring various sectors to become involved through programs like the Saving Lives at Birth Grand Challenge.

While USAID is a key player in global health R&D, coordination between the other US agencies involved in this work—such as the Centers for Disease Control and Prevention, the Department of Defense, the US Food and Drug Administration, and the National Institutes of Health (NIH)—is crucial. The 21st Century Global Health Technology Act requests that USAID work to align its health-related research strategy with similar strategies at other agencies, with the goal of creating a whole-of-government approach to global health R&D. Greater coordination among US agencies can hold lead to more efficient health R&D—for example, Rosenberg noted at the briefing that both USAID and NIH are supporting the organization’s microbicide clinical trials.

We are at a critical juncture in much of the global health R&D currently underway, and USAID will be instrumental in ensuring these technologies come to fruition. As McCluskey said at the end of the briefing, “Don’t be business as usual with infectious diseases.” Dr. Joanne Carter—executive director of RESULTS/RESULTS Educational Fund and moderator of the briefing—summed it up nicely: “Investments in R&D are what’s needed to take us to the next level in global health.”

Social Media (selected coverage)

**GHTC @GHTCoalition **· Oct 21
10/22 GHTC and @PATHAdvocacy host a congressional briefing about #RandD4Health. Panelists: @aeraglobaltb @IPMicrobicides @BDGlobalHealth

**PATH Advocacy **retweeted you
Oct 22: Kari Stoever @aeraglobaltb: Public sector funding for a TB vaccine is catalytic for leveraging private sector investment. #RandD4Health

**USAID Global Health @USAIDGH **· Oct 22
. @IPMicrobicides receives 2 5yr awards worth $40m from @USAID to advance #HIV prevention tech. for women ow.ly/q4Jpt #GHMatters
Science Speaks Blog: Supporting Global Health Technologies Act, speakers warn: time is running out on tools for infectious diseases

October 24, 2013
By Rabita Aziz

Science Speaks: HIV & TB News

A PROJECT OF THE CENTER FOR GLOBAL HEALTH POLICY

When Rep. Albio Sires toured rural South American villages a while back the lasting memory he carried with him was not what he saw but what he didn’t see: safe, appropriate tools to diagnose and treat diseases.

That, he told a packed room on Capitol Hill Tuesday, is why he joined with Rep. Mario Diaz-Balart (R-FL) to cosponsor the 21st Century Global Health Technologies Act (H.R. 1515), which would authorize a long-term program coordinated by USAID to advance affordable, easy-to-use technologies such as safe injection devices, rapid diagnostics, and other innovative health solutions.

At the congressional briefing on Tuesday, Sires (D-NJ) spoke first, saying he has seen first hand the desperate need for new healthcare technologies. Progress, he added, won’t come without sustained investments by the U.S. government.

“This is something close to my heart,” he said.

USAID is well positioned to help develop those new tools, Dr. Zeda Rosenberg, chief executive officer of the International Partnership for Microbicides said. The agency not only helps in the development of new technologies, Rosenberg said, it has experience getting products out to the people who need them.
most, and strengthens health care systems everywhere it operates, by supporting clinics and labs, training staff, and generally building medical capacity in resource limited settings.

Long-term investments and dedicated resources from USAID are crucial in fighting infectious diseases, she said, because without working to develop the right products now, they won’t be available ten to fifteen years down the line when they are needed.

More than 40 percent of the women who showed up to enroll in microbicide clinical trials in KwaZulu-Natal in South Africa were already infected with HIV but didn’t even know it, she said, adding that women who bear the brunt of the HIV epidemic globally need prevention tools that are under their initiation. USAID has made significant contributions to developing those tools, including the tenofovir topical gel and the dapivirine vaginal ring, she said.

Whenever we think we have an infectious disease under control, Rosenberg said, we’ve already lost because with infectious diseases, you have to be one step ahead.

Needed tools include new drugs to counteract growing drug resistance for infectious diseases, and a new vaccine for tuberculosis, event moderator Joanne Carter of RESULTS said.

In spite of extraordinary progress in global health technologies development over the last decade, she added, much of the world still relies on outdated and ineffective methods to combat the world’s deadliest diseases, which leads to drug resistance.

Global resources to fight tuberculosis provide a case in point, she said. Although TB claims the lives of 1.3 million every year, most of the world still diagnoses TB using a 100-year-old method which is time consuming and doesn’t reveal if the disease has become resistant to drugs. Even the treatment options for tuberculosis can lead to further drug resistance, as the 6-9 month regimen poses challenges to patients struggling to make their livings and provide for their families.

H.R. 1515 would formalize USAID’s role in developing health technologies, Carter said.

Margaret McCluskey, senior technical advisor with USAID agreed. She recalled a walk through a graveyard in her Tenleytown neighborhood, when she saw dozens of small graves of children. “That’s the world before vaccines,” she said. “Don’t have business as usual when it comes to this bill and infectious diseases.”
**New USAID Grants** (November 4, 2013)

Science Speaks Blog: Can a vaginal ring be part of HIV prevention arsenal by 2016?
November 4, 2013
By Antigone Barton

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**Science Speaks: HIV & TB News**

_A Project of the Center for Global Health Policy_

*With up to $40 million in two five-year USAID grants, HIV prevention for women gathers speed . . .*

A little more than 10 years ago, a New York Times reporter interviewing International Partnership for Microbicides chief executive Zeda Rosenberg pointed to estimates putting the earliest possible marketing of topical product women could use and control to protect themselves from HIV about seven years away and asked if women at greatest risk for infection had seven years to wait.

No they don’t, Rosenberg replied, adding that all the same, testing the safety and effectiveness of the most promising product would take at least that long. Developments and setbacks in the microbicide field during the years since have only underscored the combination of patience, persistence and urgency that have characterized the quest for biomedical tools that can put the barriers to HIV transmission into the hands of people who need them most. Most recently, they have included the CAPRISA trial that provided proof that topical application of an HIV-fighting drug could prevent transmission, and the results of the VOICE trial, which indicated that possible barriers for some women using such a product remained unidentified. In the course of both of those developments the potential for a microbicide containing vaginal ring that could remain in place for a month gained prominence as a promising next step.

Now two grants from USAID totaling as much as $40 million puts completed development of a vaginal ring releasing the antiretroviral dapivirine as near as three years away, with distribution following swiftly, and new product in the pipeline, word from IPM says.

The time between now and 2016 will be spent completing phase III trials on the dapivirine ring, moving toward the regulatory approval that will be needed to distribute the product, and working to make it widely and affordably available, Rosenberg told Science Speaks last week.

Rosenberg evinces optimism fueled in part by setbacks — the current product represents the fourth attempt to make an effective ring, each an improvement over the previous version. “Now it is a highly stable ring,” she says, pointing to a potential four-year shelf life, important to developing country settings. And, of course, replaced monthly, that is will not be “what used to be called coitally dependent,” (and now Rosenberg adds, is called on demand), addresses a major issue driving vaginal microbicide research: “The reality of many women’s lives is they don’t plan for sex,” Rosenberg notes.
So, with the problems it has been developed to address, and the high hopes that it will, how do researchers prepare for the possibility of disappointment?

“I’m not sure you can ever be prepared for it,” Rosenberg said. Researchers will know more than they do now, she added. In addition, they will know, in the course of the trial whether the product was used as intended — used rings will provide that indication. She notes the inarguable point that has to be the mantra of anyone invested in outcomes that must be demonstrated through clinical trial research:

“There’s no such thing as failure, because what you learn takes you to the next step,” she says. But, she adds, as time passes between each step, women continue to be infected.

“That’s the hard part,” she says. “But do I think we will get there? Yes. I just hope it’s not too many more steps.”

Social Media (selected coverage)
The fight against HIV and AIDS stands at a crossroads.

Worldwide, new infections have fallen by one-third since 2001, and AIDS-related deaths have decreased by 30 percent since their peak in 2005, largely due to the availability of antiretrovirals for treatment. Our arsenal of prevention and treatment tools is stronger than ever, with strategies ranging from male circumcision, pre-exposure prophylaxis and treatment-as-prevention to female condoms and voluntary counseling and testing.

Yet, on World AIDS Day, we must acknowledge the profound challenges we still face. The epidemic continues to disproportionately overwhelm certain populations, and some regions of the world are seeing the problem worsen. Our work is far from over. Business as usual will not get us anywhere near the goal of zero new cases — we need game-changing solutions.

There is no question that a highly effective vaccine would be the holy grail of HIV prevention that other tools will complement. Many organizations are working to make one a reality as soon as possible, but it’s safe to say that a HIV vaccine could be 10 years away, and no vaccine will be 100 percent effective or appropriate for everyone.

To bring an AIDS-free generation within reach, we need additional options and continued investments in other innovative prevention technologies, especially those that prioritize women. They bear the greatest burden of HIV and AIDS globally despite the rollout of existing, effective interventions. AIDS is the leading cause of death among women of reproductive age globally. In parts of sub-Saharan Africa, young women are three times more likely to become infected than men, and approximately 40 percent of young women are already infected with HIV in some regions of South Africa.

New female-initiated health technologies have the power to reverse this unacceptable inequity by giving women — who have been left behind by global progress — products they can use to protect themselves. Vaginal microbicides are one such innovation in development. These products contain the same types of ARV drugs that are already being used successfully to treat HIV-positive individuals and to prevent mother-to-child transmission. Discreet and self-initiated, microbicides could put HIV prevention directly in the hands of women.
Right now, the HIV prevention community is eagerly awaiting the results of two late-stage microbicide trials evaluating products that could revolutionize the way women protect themselves against HIV. Tenofovir vaginal gel, developed by Gilead Sciences and used around the time of sex, previously demonstrated the ability to reduce HIV transmission to women by 39 percent. It is now in a confirmatory trial, with results expected in 2014. The monthly vaginal dapivirine ring, developed by the International Partnership for Microbicides, could offer women a long-acting prevention option that may encourage consistent use. It is now in two parallel third-phase trials, with results expected in 2015. Rectal microbicide gels for both men and women are in earlier stages of development as well.

But any product, no matter how technically effective it may be at preventing HIV, will not work unless women find it easy to incorporate into their everyday lives. Therefore, we need new and complementary tools that fit women’s needs to ensure they will be widely used and ultimately increase the real-world effectiveness of the broader HIV prevention toolkit.

We must also recognize that women’s HIV prevention needs do not exist in isolation of their sexual and reproductive health, and that we need to take a holistic approach to have maximum impact against the disease. In response, IPM, CONRAD, Population Council and others are also developing multipurpose prevention technologies, or MPTs, and other tools designed for women that could deliver simultaneous protection against unintended pregnancy, HIV, and in some cases, other sexually transmitted infections. Because women’s perceived risk of HIV is low compared to their perceived risk for pregnancy, combined technologies may also be widely used. Together, microbicides and MPTs will be critical to closing the HIV and AIDS gap for women everywhere.

In addition, a robust pipeline of new drugs and optimized formulations for both women and men will be required to build upon current successes and stay one step ahead of the virus. HIV is extraordinarily adaptable, so the emergence of drug resistance is a serious concern. This is compounded by the fact that HIV treatment is lifelong, which increases the potential for resistance to develop to products over time.

Because it takes more than a decade for most prevention products to go through clinical trials and reach regulatory approval, we cannot wait until we need a new product to begin developing it. When it comes to HIV, the luxury of time is not an option, so research and development on additional prevention drugs must happen now.

That is why organizations, including nonprofit product developers like IPM, are working on a variety of microbicides, MPTs and other products that use new and different types of ARVs — alone and in combination — that may be more likely to prevent HIV over time.

AIDS is an incredibly complex, opportunistic disease, and we need equally creative and bold solutions to beat it. The global community must continue to invest in breakthrough and complementary global health technologies like vaccines, microbicides, MPTs and pre-exposure prophylaxis that hold immense promise. Innovation will broaden the prevention options available to everyone, and help offset the risk of the virus’ resistance — two factors that will make or break our ability to change the course of the epidemic.
This work should be motivated by the simple recognition that global health research and development for HIV prevention is not secondary to the global development agenda, but integral to it. It is an investment in a healthy, productive future for women, families and communities everywhere.

**Social Media (selected coverage)**

**DeveX Op-ed**

IPM @IPMicrobicides · Nov 30
Our CEO Z. Rosenberg on innovations, especially for women, that could bring an #AIDS-free generation bit.ly/1cR8D4p @devex #WAD2013

IPM @IPMicrobicides · Nov 29
To beat #AIDS, "business as usual" not enough. "Need game-changing solutions," Z. Rosenberg, our CEO bit.ly/1cR8D4p @devex #WAD2013

Sex og Politikk and AIDS-Fondet retweeted you · Dec 1
Nov 29: To beat #AIDS, "business as usual" not enough. "Need game-changing solutions," Z. Rosenberg, our CEO bit.ly/1cR8D4p @devex #WAD2013

**Real Voices Video**

IPM @IPMicrobicides · Dec 2
What do people want for their communities? New Real Voices video shares their hopes for #AIDS-free world bit.ly/1cN5dQu #HIV

AVAC retweeted you · Dec 2
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Dec 2: What do people want for their communities? New Real Voices video shares their hopes for #AIDS-free world bit.ly/1cN5dQu #HIV
2014 Conference on Retroviruses and Opportunistic Infections
(March 4, 2014)

Microbicide Trials Network: First Trial of Combination ARV Vaginal Ring for HIV Prevention Finds Ring Safe but One ARV Carrying the Weight
March 4, 2014

Phase I study indicates more work needed to develop maraviroc, the first entry inhibitor tested as a microbicide; Results are a positive for dapivirine ring, already in Phase III trials

BOSTON, Ma. (March 4, 2014) – An early phase clinical trial of a vaginal ring containing the antiretroviral (ARV) drugs dapivirine and maraviroc found the ring was safe in women who wore it for 28 days and evidence of dapivirine in cervical tissue and blood. In addition, laboratory tests of tissue samples showed that dapivirine was able to block HIV infection, though levels of maraviroc were not sufficient to have a similar effect, reported researchers from the National Institutes of Health-funded Microbicide Trials Network (MTN) today at the 21st Conference on Retroviruses and Opportunistic Infections (CROI) in Boston.

The Phase I trial, known as MTN-013/IPM 026, was the first clinical study of a vaginal microbicide with two ARV drugs, and with the inclusion of maraviroc, the first involving an ARV belonging to a class of anti-HIV drugs called entry inhibitors. Microbicides are products applied inside the vagina or rectum to prevent the sexual transmission of HIV. Vaginal microbicides are being designed in many forms, including gels, films and rings that, once inserted into the vagina, release the active ingredient gradually over time.

“It’s encouraging that both drugs were safe, and that most women didn’t mind wearing the ring. However, we found maraviroc wasn’t getting absorbed in tissue like dapivirine was and it didn’t work as well as dapivirine in our laboratory studies looking at activity against HIV,” explained Beatrice A. Chen, M.D., M.P.H., of the University of Pittsburgh School of Medicine and Magee-Womens Hospital of UPMC, who as protocol chair of MTN-013/IPM 026, presented the results on behalf of the study team.

Though the findings indicate that further work is needed on the development of the combination ring, they bode well for the dapivirine ring, which is currently being evaluated in two ongoing Phase III effectiveness trials in Africa: the ASPIRE trial led by MTN and The Ring Study led by the nonprofit International Partnership for Microbicides (IPM). IPM developed both the dapivirine ring and the combination dapivirine-maraviroc ring.
MTN-013/IPM 026 was designed to evaluate the safety, acceptability and drug absorption qualities of the dapivirine-maraviroc ring when worn by women for 28 days. It enrolled 48 HIV-negative women ages 18 to 40 at the University of Pittsburgh, The Fenway Institute in Boston, and the University of Alabama at Birmingham (UAB) and was conducted between September 2011 and September 2012. Women were randomly assigned to use either the combination dapivirine-maraviroc ring, a ring containing maraviroc alone, a ring containing dapivirine alone, or one with no active product. The rings are made of a silicone elastomer, each measuring 56mm (about 2 ¼ inches) in diameter and 7.7mm thick (¼ inch).

Of the few side effects experienced by women, most were considered mild in nature and not thought to be associated with use of the ring. Women also found the ring generally acceptable, although 17 percent of the women said they preferred not wearing the ring during menstruation. Of the 48 women in the trial, 45 of them kept the ring in place at all times throughout the 28 days.

“The vast majority of women said they had no discomfort wearing the ring, though some had some concerns about this. Most women said they forgot it was in place,” said Lori Panter, M.D., M.P.H., of The Fenway Institute and Harvard University, who is the MTN-013/IPM 026 protocol co-chair. “The rings are quite similar to the vaginal ring currently approved for contraception.”

Researchers collected samples of blood, vaginal fluid and cervical tissue at different time points during the four weeks that women wore the ring, as well as after it was removed, in order to assess how much of each drug was being absorbed. Dapivirine was detected in all three types of samples. Laboratory tests of cervical tissue biopsies from women using either the dapivirine-only ring or the combination dapivirine-maraviroc ring also showed that dapivirine protected the tissue against HIV infection. In addition, researchers noted a direct correlation between drug concentration levels and protection against HIV for both rings containing dapivirine in the lab tests.

Biopsies from women using the maraviroc-only ring did not show protection against HIV in the laboratory model and maraviroc was not detected in blood. Only 4 of 24 women using either the combination ring or the maraviroc-only ring had detectable levels of the drug in cervical tissue. Additional testing of blood is ongoing to determine whether the drug can be detected using more sensitive methods.

“As an entry inhibitor, maraviroc is a promising candidate for development as a microbicide for HIV prevention because it acts at a different step in the infectious process from other HIV prevention drugs” said Zeda F. Rosenberg, Sc.D., chief executive officer of IPM, a nonprofit organization developing HIV prevention tools and other sexual and reproductive health technologies for women. “IPM is conducting additional development work to increase the amount of maraviroc that gets into cervical tissue in order to best harness the drug’s potential in the combination ring, and we are planning a second safety study for 2015.”

IPM is developing maraviroc as a microbicide through a royalty-free licensing agreement with ViiV Healthcare. Maraviroc is approved for use in the treatment of HIV in combination with other ARVs and is marketed under the trade names Selzentry® in the United States and Celsentri® in Europe. Dapivirine, also known as TMC-120, is being developed as a monthly microbicide ring and in other formulations by IPM through a royalty-free licensing agreement with Janssen R&D Ireland.
The two drugs work against HIV in different ways. As an entry inhibitor, maraviroc is designed to block HIV from getting inside target cells, while dapivirine belongs to a class of ARVs called non-nucleoside reverse transcriptase inhibitors (NNRTIs) that prevent HIV from making copies of itself. Prior to MTN-013/IPM 026, clinical trials of ARV-based microbicides were only of products containing an NNRTI or nucleoside reverse transcriptase inhibitors (NRTIs). Tenofovir, for example, is an NRTI being tested in both vaginal and rectal microbicide gel formulations.

In addition to Drs. Chen and Panther, other authors of the MTN-013/IPM 026 study were Craig Hoesley, M.D. (UAB); Craig Hendrix, M.D. (Johns Hopkins University); Ariane van der Straten, Ph.D., M.P.H. (RTI International/Women’s Global Health Imperative); Marla Husnik, M.S., (Statistical Center for HIV/AIDS Research and Prevention); Lydia Soto-Torres, M.D., M.P.H., (Division of AIDS, National Institute of Allergy and Infectious Diseases); Annalene Nel, M.D., Ph.D. (IPM); Sherri Johnson, M.P.H. (FHI 360); and Charlene Dezzutti, Ph.D. (University of Pittsburgh and Magee-Womens Research Institute).

MTN-013/IPM 026 was funded by the National Institute of Allergy and Infectious Diseases (NIAID) and the National Institute of Mental Health (NIMH), components of the U.S. National Institutes of Health (NIH). IPM provided the active and placebo rings that were tested in the study.

Fierce Drug Delivery: Study: In two-drug, HIV-preventing vaginal ring, only one drug does the job
March 5, 2014
By Michael Gibney

FierceDrugDelivery

The National Institutes of Health has shown that a study of its vaginal ring for the prevention of HIV came back with mixed results. The ring, which delivers two drugs, was safe for 28 days, but only one of the antiretroviral drugs was effective in protecting against the virus.

The Phase I study, performed by the Microbicide Trials Network, who announced the results at the 21st Conference on Retroviruses and Opportunistic Infections this week in Boston, was the first study to examine the delivery of two different drugs as a measure against HIV.

The microbicides used in the vaginal ring are dapivirine, which demonstrated effectiveness by appearing in cervical tissue and blood, and maraviroc, which didn't have the same effect.

"It's encouraging that both drugs were safe, and that most women didn't mind wearing the ring," said presenter Beatrice Chen of the University of Pittsburgh in a statement. "However, we found maraviroc wasn't getting absorbed in tissue like dapivirine was and it didn't work as well as dapivirine in our laboratory studies looking at activity against HIV."

Dapivirine alone is undergoing two Phase III trials in Africa. But with the combination trial, which in theory would provide more protection because the drugs act in different ways to prevent HIV, there's more work to do to make it effective.

The combination ring was worn by HIV-negative women between the ages of 18 and 40 for 28 days in the trial. The silicone elastomer rings, which are similar to those used for contraception, caused only
mild side effects and were deemed comfortable. The women either wore the ring with the combination of drugs, one with either one of the drugs or one with no active substance.

The researchers collected samples of tissue during the trial, exposing them to the virus in the lab, noting that dapivirine protected the samples against infection. Tissue from women who wore only the maraviroc ring, however, showed very little of the drug and wasn’t protected against HIV.

The nonprofit organization IPM is working with Viiv Healthcare to develop maraviroc, which has been approved for use in HIV treatment with other antiretroviral drugs. Dapivirine is being developed by IPM with Janssen R&D Ireland.

"As an entry inhibitor, maraviroc is a promising candidate for development as a microbicide for HIV prevention because it acts at a different step in the infectious process from other HIV prevention drugs," IPM CEO Zeda Rosenberg said in a statement. "IPM is conducting additional development work to increase the amount of maraviroc that gets into cervical tissue in order to best harness the drug’s potential in the combination ring, and we are planning a second safety study for 2015."

Healio Infectious Disease News: Dapivirine vaginal ring blocked HIV infection in cervical tissue
March 5, 2014

BOSTON — A dapivirine vaginal ring was effective for 28 days at blocking HIV infection in cervical tissue, according to data from a first-in-human trial presented here at the 2014 Conference on Retroviruses and Opportunistic Infections.

“What’s very exciting is that the levels of dapivirine found in the cervical tissue were high enough to block HIV infection in the laboratory, with higher levels associated with better protection against HIV,” Beatrice Chen, MD, MPH, assistant professor of obstetrics, gynecology and reproductive sciences at the University of Pittsburgh, said during her presentation. “Unfortunately maraviroc did not have similar success in our trial. However, maraviroc is still a promising drug for a microbicide, if we can develop a ring that produces higher levels of the drug that is better absorbed into the body.”

Chen and colleagues conducted a double-blind, randomized, placebo-controlled trial among 48 sexually abstinent women to evaluate three different vaginal rings containing microbicides: one with dapivirine (International Partnership for Microbicides) only; one with maraviroc (Selzentry, ViiV) only; and one with both dapivirine and maraviroc. The rings included 25 mg dapivirine and/or 100 mg maraviroc. The rings were left in for 28 days and the women underwent cervical biopsies when the rings were removed to determine drug levels and for an HIV explants challenge. The drug levels were also quantified in plasma and vaginal fluid. This study was the first in-human study of a vaginal ring containing maraviroc alone, as well as the first study of a vaginal ring containing two different microbicides.
“We found that the rings were safe in women who used them for 28 days and that women almost always kept them in place throughout the study,” Chen said. “Dapivirine was absorbed well enough among those who had the dapivirine-alone ring, as well as those who had the combination ring.”

Plasma dapivirine levels were similar among women on the dapivirine ring and the combination ring. On day 28, the mean vaginal fluid levels of dapivirine were 14.9 mcg/mL for the dapivirine ring and 10 mcg/mL for the combination ring. The day-28 mean tissue levels of dapivirine were 0.6 mcg/mL for the dapivirine ring and 1.6 mcg/mL for the combination ring.

For maraviroc, the plasma concentrations were below limits of quantification. The day-28 mean maraviroc vaginal fluid levels were 6.7 mcg/mL for the maraviroc ring and 1.1 mcg/mL for the combination ring. Only four women among the maraviroc ring group and the combination ring group had tissue levels of maraviroc above levels of quantification.

“There are currently two very large studies underway in Africa looking at the efficacy of the dapivirine vaginal ring, and our study gives us hope that the ring may be able to prevent HIV infection in these studies,” Chen said.

**UAB News: New method for women’s HIV prevention found to be safe for use**
March 6, 2014
By Nicole Wyatt

Findings of an early phase clinical trial at the University of Alabama at Birmingham suggest that a possible new method of protecting women from the transmission of HIV is safe.

The Phase I trial by the Microbicide Trials Network, known as MTN-013/IPM 026, was designed to evaluate the safety, acceptability and drug absorption qualities of an intravaginal ring containing two anti-HIV medications, dapivirine and maraviroc, when worn by women for 28 days.

Forty-eight HIV-negative women ages 18 to 40 enrolled at UAB, as well as at the University of Pittsburgh and the Fenway Institute. Women were randomly assigned to use either the combination dapivirine-maraviroc ring, a ring containing maraviroc alone, a ring containing dapivirine alone, or one with no active product. The study was conducted between September 2011 and September 2012.

Until now, clinical trials for HIV prevention for women have been focused on vaginal gels. The MTN believes a ring, which would be used monthly, rather than the daily use of a gel, would have better chances of being used by women. There are about 34 million people worldwide living with HIV, and half of those are women, according to the MTN.

“We need effective methods to prevent sexual HIV transmission besides condoms,” said Craig Hoesley, M.D., professor of medicine, who oversaw the Phase I clinical trial at UAB. “In addition, we need prevention methods which can be controlled by women, and a ring would fulfill that need.”
The study found that the ring was safe; that women using the ring found it acceptable; that the dapivirine component of the ring was detected in blood and in tissue, but maraviroc levels were not readily detected; and that laboratory tests of cervical tissue biopsies from women using either the dapivirine-only ring or the combination dapivirine-maraviroc ring also showed that dapivirine protected the tissue against HIV infection. Results were presented in March at the 21st Conference on Retroviruses and Opportunistic Infections in Boston.

“This was the first study to assess a combination of anti-HIV drugs in an intravaginal ring,” Hoesley said. “But it is a Phase I study, so we did not measure the effectiveness of the ring in preventing the sexual transmission of HIV.”

Hoesley says their results were not surprising, but it was disappointing that the maraviroc element of the ring was not readily detected. Still, there is more work to be done to determine whether the ring can become a preventive measure for women.

“Ongoing and future studies will study the effectiveness of the ring to prevent HIV infection in women,” Hoesley said. “One large study, ASPIRE, is currently enrolling women in Africa to assess the efficacy of the dapivirine-only intravaginal ring.”

This trial was funded by the National Institute of Allergy and Infectious Diseases and the National Institute of Mental Health, both of the U.S. National Institutes of Health.

Social Media (selected coverage)
58th Session of the UN Commission on the Status of Women (March 21, 2014)

Infographic: Why Is Women's Sexual and Reproductive Health Integral to Global Development?

Learn about how HIV prevention for women supports global development goals in health, poverty, education and gender equality.

Social Media (selected coverage)

IPM @IPMicrobicides · Mar 21
Women’s #HIV prevention & #SRHR are critical to global development. Check out our new infographic to learn more: bit.ly/1pivACY
Expanding view

**AIDS-Fondet** @AIDSFondet · Mar 24
Hvorfør kvinders seksuelle sundhed skal være en cel af #post2015 agendaen #CSW58 @IPMicrobicides #SRHR #dkaid pic.twitter.com/3Rwk8BNnwK

**Women Deliver** @WomenDeliver · Mar 21
As #CSW58 wraps up, an infographic from @IPMicrobicides on why women’s #SRHR must be part of #post2015 agenda bit.ly/1gGBngq

**CAMI** @CAMIhealth · Mar 21
How does women’s #SRHR impact global development? Check out this brand new infographic from @IPMicrobicides bit.ly/1gGBngq #CSW58

**Women Deliver** @WomenDeliver · Mar 21
How does women’s #SRHR +#HIV prevention impact global development? Check out brand new infographic re: @IPMicrobicides bit.ly/1gGBngq

**Global Health Strat.** @GHS · Mar 21
How does women’s #SRHR impact global development? Check out this brand new infographic from @IPMicrobicides bit.ly/1pivACY #CSW58
IPM Worldwide Rights Agreement with Janssen R&D Ireland (May 8, 2014)

Johnson & Johnson (JNJ) gave the rights to an experimental AIDS drug to a charity that’s testing the medicine in a vaginal ring to prevent HIV infection.

J&J gave the global rights to develop and market dapivirine to the International Partnership for Microbicides, a Silver Spring, Maryland-based organization that works on developing HIV prevention tools for women, IPM said today in a statement.

The agreement expands a previous partnership in which IPM held the drug rights for developing nations. The group is testing dapivirine in a vaginal ring in two late-stage studies in Africa and may in the future combine the drug with contraceptives.

“Women are in a race against time for new HIV prevention methods and they need innovative tools to protect themselves,” Zeda Rosenberg, IPM’s chief executive officer, said in the statement.

GHTC member the International Partnership for Microbicides (IPM) announced today that is has received the exclusive worldwide rights to dapivirine—a promising HIV prevention medicine—from Janssen R&D Ireland, one of the Janssen Pharmaceutical Companies of Johnson & Johnson. This represents an expansion of IPM’s existing rights to develop, manufacture, and bring to market dapivirine-based products for women in resource-poor countries.

This agreement will allow IPM to make dapivirine-based products—such as its vaginal ring which combines dapivirine with contraceptives, and is now completing a Phase III clinical trial—available to women everywhere. Future sales of these products will also lead to a sustainable funding stream to finance the research, development, and market affordability of other health tools in IPM’s pipeline.

Janssen originally licensed dapivirine to IPM under a royalty-free agreement in 2004 to develop the antiretroviral (ARV) medicine as a microbicide for women in resource-poor countries. The expansion of this rights agreement to the worldwide level demonstrates the promise of dapivirine’s potential as an HIV prevention tool. Dapivirine is a type of ARV that works by preventing HIV from making copies of itself.
“Our worldwide rights agreement with Janssen is a powerful example of how public-private partnerships can accelerate access to urgently needed, affordable health products,” said Dr. Zeda F. Rosenberg, chief executive officer of IPM. “By pooling the expertise of partners across sectors, we can more effectively help women at risk for HIV and, ultimately, end the spread of HIV/AIDS altogether.”

Science Speaks Blog: International Partnership for Microbicides, pharmaceutical company agreement sets path for woman-controlled HIV prevention
May 8, 2014
By Antigone Barton

Science Speaks: HIV & TB News

The announcement today that Janssen R&D Ireland pharmaceutical company will give the nonprofit International Partnership for Microbicides exclusive worldwide rights to develop, make and market sexual and reproductive health products with the antiretroviral dapivirine was heralded by both organizations as a stride for global public health in general, and HIV prevention for women in particular.

The catch? The first product to be covered by the agreement is still being tested for proof that it will work, in trials not due to yield results until late 2015.

So why the excitement? On the obstacle-strewn path towards an HIV prevention method that can be controlled by women, the agreement addresses two of the challenges: wide-scale distribution of products to the women who need them most, and funding to continue to develop products that address the greatest threats to women’s health. It will speed availability of a product that has been more than a decade in development, and, in the event that the first product is effective, will ease development of more.

The agreement will cover a vaginal ring containing the antiretroviral dapivirine now in trials across Africa to determine if it can prevent HIV acquisition, and it will cover multi-purpose products, including a vaginal ring combining dapivirine and a contraceptive.

While progress in HIV prevention and treatment efforts have seen infections drop across many of the hardest hit countries, HIV, pregnancy and childbirth remain the leading causes of death among women of reproductive-age worldwide. The quest for products that help women to protect themselves from HIV and unintended pregnancy is “a race against time,” IPM chief executive Zeda Rosenberg says in the announcement.

“The ability to prepare for access is accelerated quite a bit by this agreement,” AVAC director Mitchell Warren said today. “Further down the road it allows IPM to build a wider pipeline.”

It is a pipeline that will benefit women outside of the highest burden countries, he added. “A combination ring would have benefit all over the world.”
A vaginal ring that can stay in place for a month at a time would be one answer to the results of the VOICE — Vaginal and Oral Interventions to Control the Epidemic trial — which found low adherence to products requiring daily use. Researchers are still interpreting the results of the trial.

In addition, Warren said, the agreement sets an example.

“No one can do this alone,” he said. “It’s time to figure out how to provide products in the field. We hope that other companies will be just as engaged.”

Crazy Joys: Healthcare most Active Stocks: Johnson & Johnson, Bristol-Myers Squibb, Mylan Inc, Arena Pharmaceuticals, Ariad Pharmaceuticals
May 12, 2014
By Erin Rice

Johnson & Johnson (NYSE:JNJ) gave the rights to an experimental AIDS drug to a charity that’s testing the medicine in a vaginal ring to prevent HIV infection. J&J gave the global rights to develop and market dapivirine to the International Partnership for Microbicides, a Silver Spring, Maryland-based organization that works on developing HIV prevention tools for women, IPM said today in a statement. Johnson & Johnson (NYSE:JNJ)’s stock on May 9, 2014 reported an increase of 0.41% to the closing price of $100.91. Its fifty two weeks range was $82.12-$101.98. The overall volume in the last trading session was 5.69 million shares. In its share capital, company has 2.83 billion outstanding shares.

Bristol-Myers Squibb Co (NYSE:BMY) announced that Brian Daniels, senior vice president, Global Development and Medical Affairs, will be retiring from the company, effective July 1, 2014. Bristol-Myers Squibb Co (NYSE:BMY)’s stock traded beginning with a price of $50.90 and throughout the trading session climbed at a high of $51.39 and later when day-trade ended the stock finally advanced 0.87% to end at $51.18.

Mylan Inc (NASDAQ:MYL) announced that the company will present at the UBS Global Healthcare Conference on Tuesday, May 20, 2014, in New York. The presentation is scheduled to begin at 10:30 a.m. ET. Mylan Inc (NASDAQ:MYL)’s stock in last trading day held volume of 8.77 million shares as compared to its average volume of 7.12 million shares. Shares after opening at $46.87 attained maximum price of $46.97 and then ended up on $46.14 by decreasing -2.51%.

Arena Pharmaceuticals, Inc.(NASDAQ:ARNA) reported that Eisai plans to add more than 200 new contract sales representatives to its Metabolic Business Unit, increasing the sales force for BELVIQ® by 50% to approximately 600, triple the size from the commercial launch of BELVIQ in June 2013. Eisai expects this expansion of the sales force will become effective on July 1, 2014, and enable them to reach approximately 90,000 physicians in the United States. Arena Pharmaceuticals, Inc.(NASDAQ:ARNA)’s stock traded beginning with a price of $7.00 and throughout the trading session climbed at a high of $7.22 and later when day-trade ended the stock finally advanced 3.01% to end at $7.19.
Ariad Pharmaceuticals, Inc. (NASDAQ:ARIA) fell despite the company’s first-quarter results that beat analysts’ expectations. The company reported net loss of $49.8 million, or 27 cents a share, compared to $64.7 million, or 36 cents a share, in the same period one year earlier. Revenue rose 81.5% year over year to $11.8 million for the quarter. These figures beat the Capital IQ consensus estimate of a loss of 32 cents a share on revenue of $10.41 million. Ariad Pharmaceuticals, Inc. (NASDAQ:ARIA)’s stock traded beginning with a price of $6.63 and throughout the trading session climbed at a high of $6.68 and later when day-trade ended the stock finally ended at $6.67.

**Gaining Green: Drug Manufacturer Most Active: Pfizer Inc., Merck & Co., Inc., Bristol-Myers Squibb Co, Johnson & Johnson**

*May 13, 2014*

*By Carmen Gutierrez*

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**GainingGreen**

Helping To Make Your Portfolio Ever Green

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Pfizer Inc. (NYSE:PFE) and its advisers are crafting a new offer that would increase the value modestly above the current 50 pounds-a-share (about $84) level while bumping the cash portion, said two of the people, who asked not to be identified discussing private information. Pfizer will probably wait until after U.K. government hearings to raise its bid, they said. Pfizer Inc. (NYSE:PFE) net profit margin is 81.20% and weekly performance is -1.92%. On last trading day company shares ended up $29.13. Analysts mean target price for the company is $33.97. Pfizer Inc. (NYSE:PFE) distance from 50-day simple moving average (SMA50) is -6.14%.

Merck & Co., Inc. (NYSE:MRK) known as MSD outside the United States and Canada, announced that it signed an agreement for Santen Pharmaceutical Co., Ltd. (Santen) to purchase Merck’s ophthalmology products, COSOPT® (dorzolamide hydrochloride – timolol maleate ophthalmic solution), COSOPT PF® (dorzolamide hydrochloride-timolol maleate ophthalmic solution) 2%/0.5%, TRUSOPT® (dorzolamide hydrochloride ophthalmic solution) sterile ophthalmic solution 2%, ect. Merck & Co., Inc. (NYSE:MRK) shares advanced 0.14% in last trading session and ended the day on $55.29. MRK Gross Margin is 61.30% and its return on assets is 5.70%. Merck & Co., Inc. (NYSE:MRK) quarterly performance is 1.52%.

Bristol-Myers Squibb Company (NYSE:BMY) has been reiterated by The Street Ratings as a buy with a ratings score of B+. According to The Street Ratings team: The company’s strengths can be seen in multiple areas, such as its impressive record of earnings per share growth, compelling growth in net income, good cash flow from operations, solid stock price performance and notable return on equity. Bristol-Myers Squibb Co (NYSE:BMY) shares moved up 1.62% in last trading session and was closed at $52.01, while trading in range of $51.35 – $52.31. Bristol-Myers Squibb Co (NYSE:BMY) year to date (YTD) performance is -1.46%.

Johnson & Johnson (NYSE:JNJ) gave the rights to an experimental AIDS drug to a charity that’s testing the medicine in a vaginal ring to prevent HIV infection. J&J gave the global rights to develop and market dapivirine to the International Partnership for Microbicides, a Silver Spring, Maryland-based
organization that works on developing HIV prevention tools for women, IPM said in a statement.

Johnson & Johnson (NYSE:JNJ)'s stock on May 9, 2014 reported an increase of 0.41% to the closing price of $100.91. Johnson & Johnson (NYSE:JNJ) ended the last trading day at $100.52. Company weekly volatility is calculated as 0.92% and price to cash ratio as 9.74. Johnson & Johnson (NYSE:JNJ) showed a positive weekly performance of 0.52%.

Pharmaceutical Online: Janssen and IPM Expand Public-Private Collaboration for HIV Drugs
May 13, 2014
By Estel Grace Masangkay

Janssen R&D Ireland and the International Partnership for Microbicides (IPM) announced that the two partners have expanded their public-private collaboration to develop and deliver dapivirine (TMC120) products for the prevention of HIV. IPM is a non-profit organization focused on developing HIV prevention technologies for women.

The two organizations created one of the first public-private partnerships in the microbicide field in 2004. The initial partnership was focused on manufacturing and marketing dapivirine in resource-poor countries. Under the terms of the expanded agreement, IPM gains exclusive global rights for the development and commercialization of the drug for the prevention of sexually transmitted HIV alone or combined with either microbicidal antiretroviral medicines and/or in combination with contraceptives.

Adrian Thomas, VP of global market access, global commercial strategy operations, and global public health at IPM said that the expanded agreement stands on the companies’ vision of a zero-HIV transmission world. “Our goal is to contribute significantly towards the development and delivery of an effective product that directly addresses a huge unmet public health need, and could help in the fight against one of our time’s most devastating diseases,” VP Thomas said.

Microbicides are a novel prevention tool being investigated in different forms, such as sustained-release vaginal rings, to prevent sexual transmission of the disease. Two parallel efficacy trials are evaluating IPM’s monthly vaginal microbicidal rings with dapivirine across sites in African countries. Results of the trials are expected in late 2015.

The non-profit organization will establish a program ensuring women in lower income communities have access to any of its products, specifically those it may commercialize in developed nations via affordable pricing strategies. The IPM program will build on the access rights gained within the previous agreement to keep dapivirine-based products affordable for its intended patient population.

Wim Parys, head of R&D, Janssen Global Public Health, said that Janssen will continue to seek new solutions to stop the spread of HIV and help women affected by the disease. “We hope that now even more at-risk women around the world may benefit from this important collaboration by having affordable access to new prevention technologies in the future,” he said.

Aside from the dapivirine product, IPM is also developing a 90-day ring containing a combination of the drug and a contraceptive, expected to enter clinical testing next year.
Janssen has announced a new collaborative project with the International Partnership for Microbicides (IPM), centering on the creation of a new preventative therapy for HIV.

The company has expanded its existing relationship with IPM to encompass the development and delivery of dapivirine - also known as TMC120 - for the prevention of sexually-transmitted HIV.

Under this agreement, IPM now has exclusive worldwide rights to commercialise dapivirine for the prevention of sexual transmission of HIV, alone or in combination with either microbicidal antiretroviral medicines and/or in combination with contraceptives.

This would include a programme to ensure that women in lower-income communities have access to any product that IPM may choose to make available in developed countries through affordable pricing strategies.

Dr Wim Parys, head of research and development at Janssen Global Public Health, said: "We hope that now even more at-risk women around the world may benefit from this important collaboration by having affordable access to new prevention technologies in the future."

This comes after the firm announced a new agreement with the Stop TB Partnership to facilitate access to tuberculosis therapies in developing countries last month.

**Devex: Institutions lean on creative financing, partnerships to further disease research**

**May 30, 2014**

By Adva Saldinger

In a time when funding is harder to secure — especially for what are neglected diseases that disproportionately affect those in developing countries — the research institutions working on solutions are finding creative ways to finance progress.

Lately the news has been dotted with announcements of nonprofits licensing products to pharmaceutical companies in order to use the profit from commercialization to fund research; other examples include companies giving drug rights to nonprofit research organizations to pursue and monetize.
These announcements point toward a shift to more creativity when it comes to developing sustainable funding sources for typically under-resourced disease research.

“We try to diversify both the source and the nature of funding so we don’t become reliant on any particular source,” said Erik Iverson, the president of business and operations at the Infectious Disease Research Institute. IDRI ensures that those agreements stay true to serving the organization’s values by building in requirements for benefits to developing countries, which can include pricing and availability assurances.

While these mechanisms of sponsored research, licensing products to private companies and spinning off for-profit entities are not new, the difference is that global health organizations are beginning to use them, Iverson said.

This begs the question, why now? The huge influx of private money, from the likes of the Gates Foundation, has allowed the industry to mature and create the product platform and technology to grow to a point where these options are feasible, he said.

**Leveraging discoveries to fund future work**

Earlier this year, the TB Alliance, an international nonprofit drug development organization, assigned several patents to TenNor Therapeutics, a Chinese biotech company – it’s first transaction of that type. TB funding is not keeping pace with inflation or the magnitude of the disease, and the science necessary to research it and many other diseases is difficult and expensive, while those using the medications are often poor and lack the ability to pay much, if anything, for the product. As a result, researchers are unlikely to recoup their investment, which makes it a hard sell to pharmaceutical companies who need a financial return.

But in the course of researching tuberculosis treatments, the Alliance discovered a compound that could instead be used for bacterial infections. It then set about finding a way to use that intellectual property to bring resources back to the organization to further its research.

The agreement it struck with TenNor is similar to those that academic institutions often carry out, said Mel Spigelman, director of research and development at the TB Alliance. While confidentiality agreements prevent him from disclosing details of the deal, there are standard arrangements in similar situations that often include upfront payments, milestone payments and royalties.

“This is a very logical outgrowth,” he said. “The real difference is I don’t think that many people associate organizations like the TB Alliance with technology and discoveries...people haven’t recognized the work public-private partnerships have done in coming up with discoveries.”

But one of the challenges is that as promising drugs get further down the development pipeline, each step becomes more expensive. At the TB Alliance, a new drug regimen is scheduled to go into phase three trials, the last stage before licensing, but the $65 million price tag to complete that step poses a significant hurdle.

“The amount of financing that’s available on a global basis for neglected diseases is just so woefully insufficient for the magnitude of the problem,” he said. “We all have to be on the lookout for innovative ways [to fund research].”
Private sector partnerships

Pharmaceutical companies, too, are increasingly open to addressing urgent health needs that may not have a strong profit motive — and have the assets necessary to do so. In fact, a pharmaceutical company might give the rights to a drug to a nonprofit organization, as in the case of a recent announcement by Janssen Pharmaceuticals and the International Partnership for Microbicides. Janssen, a Johnson & Johnson pharmaceutical company, gave the IPM exclusive rights to develop and manufacture products containing the company’s antiretroviral dapivirine, the active ingredient in IPM’s vaginal HIV prevention ring.

The agreement deepened a collaboration between the nonprofit product development organization and the pharmaceutical company by allowing IPM to commercialize dapivirine products everywhere. Development and sales of products, including a birth control and HIV-prevention vaginal ring IPM is developing, could be sold in the developed world to help finance continued research and distribution in the developing world.

There is more of a willingness from organizations like IPM to engage with the private sector, said IPM CEO Zeda Rosenberg.

“I think it’s going to be seen a lot more and I think it is because product development costs a lot of money and there is so much need out there for our products,” she said.

Janssen’s appetite to bring company expertise to bear on these diseases is increasing, said Wim Parys, global head of research and development for Janssen’s global public health division.

“We internally are very committed to these type of collaborations where we don’t have a for-profit market but there is a huge need,” Parys said. “If we have an innovation, it should be made available to address the needs that exist. We do feel that we have a social responsibility there.”

The company’s global public health division has more flexibility than other parts of Janssen, can partner more easily with organizations like IPM or the TB Alliance and can seek additional grant funding to further research. They are currently researching treatments for HIV, Hepatitis, multidrug resistant tuberculosis, river blindness and modifying existing products, like a de-worming medication that would be usable without water if safe water is not available.

In order to make these partnerships and research sustainable, it’s important to establish new ways to work with governments and other pharmaceuticals, he said. One example of programs that help support the global health group’s work is a special U.S. Food and Drug Administration voucher that allows a drug with high medical need and no return on investment to get accelerated to priority review.

The trend of companies investing in some of this research and providing rights to nonprofits or partnering with them in other ways is growing slowly, Parys said. There is potential for more companies to get involved and build on progress, but it’s essential to think constantly about how to reduce the burden due to a company’s obligation to shareholders, he said.

B.T. Slingsby, the executive director of the Global Health Innovation and Technology Fund, concurred in a recent Devex interview, noting that pharmaceuticals alone cannot invest all of the money needed for
research and development because it’s critical that their contributions do not threaten the company’s stability.

More than just helping to provide financing, private sector expertise is critical in funding and developing treatments or preventative drugs for these diseases. Janssen will often contribute technical knowledge and advise nonprofit partners on the trial process, Parys said. 

The business case and market strategies

Research and development commitments for neglected diseases may have positive reputational impacts for pharmaceuticals looking ahead to emerging middle income countries and developing countries as future markets.

Increasingly, emerging middle income countries are presenting market opportunities — so vaccines for dengue fever may have some financial returns in places like Brazil, even if they do not have a European or American market, said Robert Hecht, managing director at Results for Development, where he focuses on health financing.

Companies are exploring multiple ways of tackling these issues, including having both commercial and philanthropic arms, where revenues from one side of the business can help support the less lucrative but significant public health aspect of their work, he said.

Despite some potential openness to increased investments from the private sector, traditional streams of funding from government and foundations will continue to be essential as financial disincentives remain for companies that have to be sure they meet the bottom line.

While middle income countries — and the developing countries that will rise to that level in the coming years — present interesting market opportunities, they also represent critical challenges for developing and distributing drugs and treatment.

Instead of more cut and dry systems in which organizations can structure tiered pricing at the country level, it will be increasingly necessary to explore steps for ensuring access for the poor in countries where there are growing populations that can afford to pay for the treatment or preventative care.

Some companies are also licensing technology to drug companies in countries like India and South Africa so that manufacturers can produce cheaper generic drugs and sell them in developing markets while the parent company markets them and earns royalties from sales in the developing world, Hecht said.

“The smart pharmaceutical companies realize it’s good corporate relations, good politics and good business for them” to sell products in lower income countries at just above cost and charge those who can pay more higher prices, he said.

The challenges go beyond tiered pricing, extending to how to deal with packaging, naming and avoiding counterfeit or “grey market” products, Iverson said.

It’s a complex set of issues to navigate, but organizations like the GAVI Alliance, UNICEF, The Global Fund to fight AIDS, Tuberculosis and Malaria and The Gates Foundation are all working to identify market and distribution mechanisms and tiered pricing, which is helping the system mature, he said.
As more clarity develops and markets in the developing world gain a stronger appeal, there may well be more partnerships, deals and creative funding mechanisms that emerge. For critical diseases like TB, AIDS, malaria and those that are even less frequently discussed such as elephantiasis or river blindness, all sources of funding are critical to find treatments and preventative medications that have the potential to transform lives, communities and countries.

**Global Post: Partnering to protect women from HIV**  
May 15, 2014  
By Zeda Rosenberg and Paul Stoffels

The world is making tremendous progress to curb the course of the global HIV/AIDS epidemic. Since peaking in 2005, AIDS-related deaths have decreased by nearly one-third, and new HIV infections in children have fallen by more than half since 2001.

But not everyone is benefitting equally from these advances. Women and girls continue to bear a disproportionate and unacceptable burden of the disease. A new public-private partnership agreement announced last week between our organizations – the International Partnership for Microbicides (IPM), a nonprofit product developer, and the Janssen Pharmaceutical Companies of Johnson & Johnson, a major research-based pharmaceutical company – could help address this and ensure women have the tools to protect themselves from infection.

The agreement expands IPM’s existing rights to develop and deliver products containing a promising HIV prevention medicine called dapivirine. It also marks the latest step in a longstanding partnership between our organizations and opens the door to women’s future access to prevention products in all countries. Through our collaboration, IPM serves as a bridge, uniting public sector financial support from its government and foundation donors with Janssen’s private sector expertise to accelerate the progress women urgently need.

In sub-Saharan Africa, the region most seriously affected by AIDS, women make up nearly 60 percent of people infected with HIV. The problem is expected to grow worse in the coming years. The recently published 2012 South African National HIV Prevalence, Incidence and Behaviour Survey found that teenage girls in South Africa are at least four times more likely to become infected than teenage boys.

When HIV affects women, it tears at the fabric of families and communities and perpetuates a cycle of poverty in poor countries.

Women are particularly susceptible to HIV because they lack a practical prevention toolkit that meets their needs. Existing preventative options are effective but not always realistic since they primarily depend on partners’ consent. Widespread gender inequality often keeps women from accessing and
acting on prevention information. They need products they can use easily and, when necessary, independently in their daily lives.

Working in silos has only gotten us so far. We have the know-how to develop new prevention methods, but this research takes time, money, and successes and setbacks. Creating HIV prevention tools for women in the world’s poorest countries is particularly daunting because they face significant sociocultural barriers and have limited ability to pay. Partnerships like ours are powerful solutions to the challenges of developing health products for women.

One of the most closely-watched products in women’s HIV prevention – the dapivirine vaginal ring – is the result of an early public-private partnership in the microbicide field. Microbicides deliver the same antiretroviral medicines successfully being used to treat HIV-infected individuals through new mechanisms, such as vaginal rings, films and gels. Building on Janssen’s initial work with dapivirine, IPM began formulating the antiretroviral as a microbicide in 2004. The dapivirine vaginal ring, which could protect against HIV for a month before a woman needs to replace it, is now in final clinical trials in Africa, with results expected next year.

The new agreement deepens our partnership in important ways. IPM can now make future dapivirine-based products, such as a contraceptive-dapivirine ring in development, available to women in developed in addition to developing countries.

Under the agreement, IPM is exploring multiple financing strategies in line with its nonprofit status that could support its mission and help ensure product affordability. For instance, one option may be to sublicense the contraceptive-dapivirine ring – once it is shown to be safe and effective – to a third partner to market in developed countries. This could help fund IPM’s ongoing development of new prevention technologies and offset the costs of its products for women in resource-poor settings globally.

What this means in practice is that, down the road, a woman in South Africa or Uganda may be better able to access a product she wants to use to protect herself because it is affordably priced.

This sort of creative financing can complement donor and government investments in global health.

In a time of limited resources for competing priorities, the best investments are those that can be sustained for the long-term. With the worldwide rights agreement, IPM and Janssen have created a model for research, development and delivery that could be self-perpetuating.
Social Media

On 8 May 2014, Janssen Global Public Health group* and the International Partnership for Microbicides (IPM) expanded their collaboration for the development and delivery of sexual and reproductive health products containing the antiretroviral drug dapivirine for the prevention of HIV.

**TOP THREE REASONS**

**Why this agreement is important for women:**

1. Supports expanded access to future products containing dapivirine, such as a contraceptive-dapivirine ring

2. Helps ensure future products containing dapivirine will be affordable in developing countries and low-income communities in developed countries

3. Creates a funding stream to sustain essential research for new women’s sexual and reproductive health products

And, it serves as a model for how public-private partnerships can improve the health and well-being of people everywhere.

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**Women Deliver** @WomenDeliver - May 8
3 reasons why new agreement b/wn @IPMicrobicides & @JNJGlobalHealth is important for women’s #HIV prevention & #SRHR ow.ly/v5ve78

**Sex og Politikk** @Saxogpolitikk - May 9
3 reasons why new agreement b/wn @IPMicrobicides & @JNJGlobalHealth is important for women’s #HIV prevention & #SRHR pic.twitter.com/wiGIVcv81s

**GlobalHealth.ie** @globalhealth
RT @IPMicrobicides: Check this out: 3 reasons why our new agreement w @JNJGlobalHealth is a boost for #women and #globalhealth http://t.co/...

Social Media

Selected Partner Tweets and Retweets

<table>
<thead>
<tr>
<th>IMPRESSIONS</th>
<th>Tweet</th>
</tr>
</thead>
<tbody>
<tr>
<td>22.3k</td>
<td>JNJGlobalHealth: A14: Work together! Researchers, faith leaders, nonprofit advocates, private sector leaders etc. must #StepUp4Women to make HIV history! Tweeted to 3,414 people about 1 month ago with 7 retweets and 1 reply</td>
</tr>
<tr>
<td>92.5k</td>
<td>GlobalFund: RT @Nkandu005: A8: By bring services closer to the community and breaking the barriers to access #StepUp4Women #AIDSchat @theaidsalliance Retweeted Nkandu005 to 92,491 people at 2014-07-16 10:36:23 -0400</td>
</tr>
<tr>
<td>73.4k</td>
<td>USAIDGH: A20: #post2015 progress for #women and #HIV will involve more options for protection &amp; female-initiated #HIVPrevention #StepUp4Women Tweeted to 94,483 people at 2014-07-16 10:55:12 -0400 with 16 retweets and 1 reply</td>
</tr>
<tr>
<td>26.6k</td>
<td>EGFPAF: A7: Integrated treatment campaigns for #HIV/AIDS &amp; other #globalhealth issues will build #MDGmomentum! #StepUp4Women #AIDS2014 Tweeted to 8,000 people 2 months ago with 7 retweets</td>
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<tr>
<td>17.6k</td>
<td>m2mtweets: A1: 700 babies are born with #HIV every day. We need to #StepUp4Women and their babies to reach an #AIDSFreeGen in our lifetime! Tweeted to 3,488 people 2 months ago with 7 retweets and 2 replies</td>
</tr>
<tr>
<td>6.7k</td>
<td>GHTCoalition: Breakthrough multipurpose prevention technologies could result in significant health gains for #women #StepUp4Women bit.ly/1VQlJSQ Tweeted to 3,323 people 2 months ago with 3 retweets</td>
</tr>
</tbody>
</table>

Retweeted by Françoise Girard

EngenderHealth @EngenderHealth Jul 16

Did u know? #HIV is the top cause of death for women of reproductive age. @UNAIDS #StepUp4Women #AIDS2014

Retweeted by Serra Sippel

CHANGE @genderhealth Jul 16

A1: Women are >50% of all ppl living w/ HIV/AIDS globally. AIDS-free generation? Not without #women! #StepUp4Women

AIDS free generation?
Not without women.

www.genderhealth.org
**IPM Tweets with the Most Impressions**

<table>
<thead>
<tr>
<th>IMPRESSIONS</th>
<th>Tweet</th>
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<tbody>
<tr>
<td>35k</td>
<td>IPMicrobicidies: Q12 We can’t carry out #HIV prevention or #SRH integration without community leadership. Agreed. #StepUp4Women #AIDSchat Tweeted to 553 people 2 months ago with 10 retweets and 3 replies</td>
</tr>
<tr>
<td>29.8k</td>
<td>IPMicrobicidies: @WHERWeb: Great point - men’s involvement is also a factor in supporting women’s HIV prevention &amp; treatment #StepUp4Women Replied to WHERWeb 2 months ago with 4 retweets</td>
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<tr>
<td>24.7k</td>
<td>IPMicrobicidies: Welcome to the #StepUp4Women #AIDS2014 chat &amp; to @MPTANCHIV @HIVresearch @WomenDeliver @CRW &amp; @theaidsalliance as we discuss women &amp; HIV Tweeted to 545 people 2 months ago with 5 retweets and 2 replies</td>
</tr>
<tr>
<td>23.7k</td>
<td>IPMicrobicidies: A7 Women &amp; girls face multiple health risks, including #HIV. Effective solutions must be multi-faceted too. #StepUp4Women #AIDScorner #SRH Tweeted to 551 people 2 months ago with 8 retweets</td>
</tr>
<tr>
<td>19.4k</td>
<td>IPMicrobicidies: HIV prevention is a key component of sexual and reproductive health. Let’s now discuss #HIV and #SRH. #StepUp4Women #AIDSchat Tweeted to 249 people 2 months ago with 5 retweets</td>
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<tr>
<td>18.9k</td>
<td>IPMicrobicidies: A17 Women have been largely left behind by global #HIV progress. In #post2015, women’s #SRH must be top priority. #StepUp4Women #AIDSchat Tweeted to 333 people 2 months ago with 10 retweets</td>
</tr>
</tbody>
</table>

**Most Retweeted Answer Tweets from Other Participants**

<table>
<thead>
<tr>
<th>RETWEETS</th>
<th>Tweet</th>
</tr>
</thead>
<tbody>
<tr>
<td>42</td>
<td>EngenderHealth: Did u know? #HIV is the top cause of death for women of reproductive age. @UNAIDS #StepUp4Women #AIDS2014 pic.twitter.com/sjNO6sZEUc Tweeted to 14,510 people at 2014-07-16 10:24:56 -0400 w 11 13 retweets and 2 replies</td>
</tr>
<tr>
<td>18</td>
<td>RectalMicro: Let’s not forget about the needs of #TRANSGENDER WOMEN. They are too often neglected, but - and they are our SISTERS #StepUp4Women Tweeted to 2,202 people at 2014-07-16 10:23:43 -0400 w 16 retweets and 1 reply</td>
</tr>
<tr>
<td>16</td>
<td>WomenDeliver: A8: HIV is a sexual &amp; #reprohealth issue, therefore, must be integrated to improve the health &amp; lives of girls &amp; women. #StepUp4Women Tweeted to 15,094 people at 2014-07-16 10:23:54 -0400 w 6th 16 retweets</td>
</tr>
<tr>
<td>16</td>
<td>USAIDGHI: A20: #post2015 progress for #women and #HIV will involve more options for protection &amp; female-initiated #HIVPrevention #StepUp4Women Tweeted to 54,460 people at 2014-07-16 10:55:12 -0400 w 16th 16 retweets and 1 reply</td>
</tr>
<tr>
<td>14</td>
<td>Pathfinder: Major key to #HIVprevention in women: providing them with CHOICE - where they decide if, when, &amp; how often to have children! #StepUp4Women Tweeted to 8,168 people at 2014-07-16 10:31:34 -0400 w 14th 14 retweets</td>
</tr>
</tbody>
</table>
The 20th International AIDS Conference in Melbourne, Australia (July 20-25, 2014)

Print/Digital Media

FHI360 Video: Hope in microbicides for young women in sub-Saharan Africa

VIDEO: Hope in microbicides for young women in sub-Saharan Africa

Social Media

AIDS 2014 Live Daily Delivery
Daily Twitter Activity (October 1, 2013 – September 10, 2014)

Social Media

Selected Retweets

**399.8k**  
**USAID:** RT @IPMmicrobicides: How have the #MDGs changed the world? 8 leaders share examples w/ @guardian impact hub: theguardian.com/global-develop... @rash...  
Retweeted **IPMmicrobicides** to 306,705 people 24 days ago

**49k**  
**rashah:** RT @IPMmicrobicides: How have the #MDGs changed the world? 8 leaders share examples w/ @guardian impact hub: theguardian.com/global-develop... @rash...  
Retweeted **IPMmicrobicides** to 40,028 people 24 days ago

**30.9k**  
**PEPFAR:** RT @IPMmicrobicides: How @PEPFAR and @USAIDGHD are contributing to #MDGsmomentum: ow.ly/AuxUQ & ow.ly/AsFQ5 @HIV #MDGs  
Retweeted **IPMmicrobicides** to 30,680 people 21 days ago

**30.8k**  
**PEPFAR:** RT @IPMmicrobicides: Need a 3-minute break? #AmbBinx outlines 3 key priorities as @PEPFAR works toward an #AIDSfree generation: http://t.co/... @  
Retweeted **IPMmicrobicides** to 30,814 people 23 days ago

**30.4k**  
**PEPFAR:** RT @IPMmicrobicides: Heads of @UNAIDS, @PEPFAR, @GlobalFund in @TheLancet: Chance to make transformative difference in #HIV lies before us h...  
Retweeted **IPMmicrobicides** to 30,411 people about 1 month ago

**43.6k**  
**girlrising:** RT @IPMmicrobicides: A1 @girlrising Progress is being made - but women & girls are still disproportionately affected by #HIV. http://t.co/10... @  
Retweeted **IPMmicrobicides** to 43,038 people 10 days ago

IPM Tweets with the Most Impressions

**460.8k**  
IPMmicrobicides: How have the #MDGs changed the world? 8 leaders share examples w/ @guardian impact hub: theguardian.com/global-develop... @rashah #MDGsmomentum  
Tweeted to 534 people 27 days ago with 18 retweets and 1 reply

**34.1k**  
IPMmicrobicides: Heads of @UNAIDS, @PEPFAR, @GlobalFund in @TheLancet: Chance to make transformative difference in #HIV lies before us h...  
Tweeted to 575 people about 1 month ago with 3 retweets

**32.1k**  
IPMmicrobicides: Need a 3-minute break? #AmbBinx outlines 3 key priorities as @PEPFAR works toward an #AIDSfree generation: 1.usa.gov/1BnwWVQ @HIV  
Tweeted to 583 people about 1 month ago with 2 retweets

**31.5k**  
IPMmicrobicides: How @PEPFAR and @USAIDGHD are contributing to #MDGsmomentum: ow.ly/AuxUQ & ow.ly/AsFQ5 @HIV #MDGs  
Tweeted to 593 people 27 days ago with 1 retweet

**28.6k**  
IPMmicrobicides: So important to find new R&D models! @PATHtweets & @MRCza teaming up to speed health tech innovation in #SouthAfrica bit.ly/1oDJeWq  
Tweeted to 581 people about 1 month ago with 2 retweets