A. Research Projects that were still active at the close of 2016

1. **A5288:** Management Using Latest Technologies to Optimize Combination Therapy After Viral FailurE **(MULT-OCTAVE).** The aim is to test a strategy of using resistance testing to choose the optimal ART regimen in those failing 2nd line Therapy.

2. **A5264:** A Randomized Evaluation of Antiretroviral Therapy Alone or With Delayed Chemotherapy versus Antiretroviral Therapy With Immediate Adjunctive Chemotherapy for Treatment of Limited Stage AIDS-KS in Resource-Limited Settings (**REACT-KS**) AMC 067**.**

3. **A5243**: Plan for Obtaining Human Biological Samples at Non-U.S. Clinical Research Sites for Currently Unspecified Genetic Analyses.

4. **Strategic Timing of AntiRetroviral Treatment (START):** The main objective is to assess the development of serious illness or AIDS when ART is initiated at fairly highCD4+ Compared to waiting until the CD4+ count is at the level where there is good evidence for starting therapy.
5. **Pericardial fat, inflammation, and Structural heart disease in chronic HIV infection (K23)** The study **aims** to evaluate the sensitivity of a variety of biomarkers to detect early structural changes in left ventricular systolic and diastolic performance before symptoms develop.

6. **protocol GS-US-380-1961**: The study evaluates the efficacy of switching to an FDC of GS-9883/ F/TAF in virologically suppressed HIV-1 infected women as determined by the proportion of subjects with virologic failure at Week 48.

7. **Protocol 0106:** Pharmacokinetics, Safety, and Antiviral Activity of the Elvitegravir/Cobicistat/Emtricitabine/ Tenofovir Alafenamide (E/C/F/TAF) Single Tablet Regimen (STR) in HIV-1 Infected ART-Naive Adolescents and Virologically Suppressed Children

8. **Protocol 0160:** A Study to Evaluate Pharmacokinetics, Safety, and Antiviral Activity of Elvitegravir Administered With a PI/r Background Regimen for ARV-Experienced Pediatric Participants

9. **ODESSY (PENTA 20):** A randomized trial of Dolutegravir (DTG) based Antiretroviral Therapy vs Standard of Care (SOC) in Children with HIV infection starting First-line or Switching to Second-line ART.

10. **PEDO Study:** A Randomized Clinical Trial to Optimize efavirenz Dosing for HIV/AIDS Infected Infants and Children in Sub Saharan Africa. Funded by the Swedish government in collaboration with the Karolinska Institute, Sweden. JCRC is among the participating sites in Uganda.

11. **LIVING study:** The **primary objective** is to: Evaluate the effectiveness of LPV/r pellets in addition to AZT/3TC (or ABC/3TC) paediatric fixed dose combination (FDCs)

tablet under routine treatment conditions in HIV infected infants and young children who cannot swallow tablets – **Funded by DNDi.**

12. **ViiV Social Science study:** The study explores the challenges and factors affecting adolescents as they live and grow with HIV infection. **Funded by ViiV**

13. **Rheumatic Heart Disease (RHD) study** The study is investigating the role of HIV and auto-antibodies among patients with rheumatic heart disease in Uganda.

14. **ICARE - Development of an intervention to promote self management of HIV and related co-morbidities among Ugandan adolescents living with HIV**; The aim is to utilize community-based participatory (CBP) approaches with consumer experts (i.e. ALHIV, caregivers, healthcare providers), to develop a family-centered intervention to promote self-management of HIV illness and related challenges among Ugandan ALHIV.

15. Using **E**xclusion-Based **S**ample **P**reparation **(ESP),** and Generic reagents to Reduce HIV Viral load Assay Cost. The **overall goal** of this project is to close the gaps in technical capacity and cost by utilizing ESP, a simple and cost-effective test to measure VL – **Funded by UNCST**.

16. **PAINT**, A Study to Evaluate the Pharmacokinetics, Safety, Tolerability, and Antiviral Efficacy of TMC278 in Human Immunodeficiency Virus Infected Adolescents.

B. <u>Studies that were successfully closed in 2016:</u>

1. **WAVES**, Phase 3B Study to Evaluate the Safety and Efficacy of Elvitegravir/Cobicistat/Emtricitabine/ Tenofovir Disoproxil Fumarate Versus Ritonavir-Boosted Atazanavir Plus Emtricitabine/Tenofovir Disoproxil Fumarate in HIV-1 Infected, Antiretroviral Treatment-Naïve Women

2. **Gilead protocol 0117**, A Phase 3, Two Part Study to Evaluate the Efficacy of Tenofovir Alafenamide Versus Placebo Added to a Failing Regimen Followed by Treatment With Elvitegravir/Cobicistat/ Emtricitabine/ Tenofovir Alafenamide Plus Atazanavir in HIV-1 Positive, Antiretroviral Treatment-Experienced Adults

3. **REALITY**, A randomised controlled trial to investigate three methods to reduce early mortality in adults, adolescents and children aged 5 years or older starting antiretroviral therapy (ART) with severe immuno-deficiency. The three methods were: (i) increasing the potency of ART with a 12 week induction period using 4 antiretroviral drugs from 3 classes (ii) augmented prophylaxis against opportunistic/bacterial infections and helminths for 12 weeks (iii) macronutrient intervention using ready-to-use supplementary food for 12 weeks

4. **HIV-1 Reservour Substudy,** This was a substudy of START (Strategic Timing of Antiretroviral Treatment) The Primary objective of this Substudy was: To determine the difference between the concentration of total HIV-1 DNA in resting CD4+ T-cells

between participants after 36 to 44 months of cART in participants in one of three strata of CD4+ cell counts during screening: ≥800, 600-799, 500-599 cells/mm3.

5. **Pulmonary sub study,** The purpose of this study was to find out if starting anti-retroviral therapy (ART) at CD4 above 500 (early ART group) slows the rate of decrease in lung function over time compared to waiting to start ART until the CD4+ drops below 350 (deferred ART group)

6. **BREATHER,** The overall aim of the BREATHER trial was to evaluate the role of Short-Cycle Therapy (SCT) in the management of HIV-infected young people who have responded well to antiretroviral therapy (ART) and to determine whether young people with chronic HIV infection undergoing Short-Cycle Therapy of five days on ART and two days off maintain the same level of viral load suppression as those on continuous therapy, over 48 weeks.

7. **LABLITE**, was investigating strategies to roll out HIV treatment safely and cost-effectively in real-life settings in sub-Saharan Africa. The project worked closely with ministries of Health in 3 countries in Africa (Malawi, Zimbabwe and Uganda. It aimed to inform national and international policy on how best to use the limited funds available to increase coverage of HIV treatment.

8. **A5225,** A Phase I/II Dose-Finding Study of High-Dose Fluconazole Treatment in AIDS-Associated Cryptococcal Meningitis (CM)

9. **A5297,** An Open-Label, Proof of Concept, Randomized Trial Comparing a LPV/r-Based to an nNRTI-Based Antiretroviral Therapy Regimen for Clearance of Plasmodium Falciparum Subclinical Parasitemia in HIV-infected Adults With CD4+ Counts >200 and <350 Cells/mm3

10. **A5274,** Reducing Early Mortality and Early Morbidity by Empiric Tuberculosis Treatment Regimens (REMEMBER)

11. **A5278s**. A Multicenter Trial of the (ACTG) and AIDS Malignancy Consortium (AMC 074)- drug interaction between ART and Etoposide. It is a PK Study. Enrolled all participants from study A5264

C. <u>Studies that have so far started since the beginning of 2017</u>

1. **Gilead Protocol GS-US-380-1474:** A Phase 2/3, Open-Label Study of the Pharmacokinetics, Safety, and Antiviral Activity of the GS9883 /Emtricitabine Tenofovir Alafenamide (GS-9883/F/TAF) Fixed Dose Combination (FDC) in HIV-1 Infected Virologically Suppressed Adolescents and Children

2. **Protocol IPD/CLI/15/003 (Liposome Amphotericin B study):** A multicenter, open label, randomized, multiple dose, two treatment, two period crossover, steady state study to compare the bioequivalence of the Test product [Liposome Amphotericin B by Cipla Ltd, India] with that of the Reference product [AmBisome® (Liposome Amphotericin B) by Gilead life sciences, USA] in adult patients with fungal infections. The primary

objective is to test for non-inferiority of the generic Liposome Amphotericin B (By Cipla Ltd, India) against the Branded Liposome Amphotericin B(Gilead life Sciences, USA).

3. **MICRONUTRIENT STUDY:** The Relationship of metabolic factors, micronutrients and inflammation in HIV exposed and infected, HIV infected and HIV unexposed Uninfected Children in Uganda.

4. SMILE (PENTA 17): **S**trategy for **M**aintenance of H**I**V suppression with e**l**vitegravir + darunavir/ritonavir in childr**E**n (PENTA 17). It's a A Phase 2/3 multicentre, open-label, randomised study evaluating safety and antiviral effect of elvitegravir (EVG) administered with darunavir/ritonavir (DRV/r)compared to current standard antiretroviral therapy in HIV-1 infected, virologically suppressed paediatric participants.

D. Some of the studies expected to start in 2017

1. An EDCTP funded clinical trial aimed to assess the importance of an HIV baseline drug resistance test in HIV positive infants born to HIV positive mothers who were on ART during pregnancy. **Funded by EDCTP**

2. Gilead Phase 2 study of participants with multi class HIVDR. They will receive GS 9131, a new NRTI that is active against NRTI resistance strains with K65R and multiple TAMS. The other component is bictegravir (a second generation integrase inhibitor with similar properties to dolutegravir) and the third component will be cobi-boosted darunavir.

3. A Randomized, Double-Blind, Efficacy and Safety Study of AR 14 (AZILSARTAN MEDOXOMIL) Treatment and Withdrawal, Followed by an Open-Label Extension, in Children 6 to Less Than 18 Years of Age with Hypertension – **Sponsor by Arbor Pharmaceuticals, LLC**

4. **Cardiovascular Disease and Inflammation in Ugandan Children with HIV –** sponsored by Case School of Medicine

5. **CHAPAS 4 Study – funded by EDCTP**

6. **A5349:** TBTC S31 Rifapentine-Containing Treatment Shortening Regimens for Pulmonary Tuberculosis: A Randomized, Open-Label, Controlled Phase 3 Clinical Trial

7. **A5332:** Randomized Trial to Prevent Vascular Events in HIV – REPRIEVE

8. **A5345:**Identification of Biomarkers to Predict Time to Plasma HIV RNA Rebound and Post-Treatment Viral Control during an Intensively Monitored Antiretroviral Pause.

9. **A5354:**Effect of Antiretroviral Treatment Initiated During Acute HIV-1 Infection on Measures of HIV-1 Persistence and on HIV-1 Specific Immune Responses.

10. **The role of Iron Supplementation among HIV infected children on ART:** The Research project is investigating the role of Iron Supplementation among HIV infected children on ART. Sponsored by University of Minnesota.