Clinical Research Newsletter Volume - 8, August 2016

LAMBDA

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## GLOBAL PHARMA/ RESEARCH UPDATE

### 1.1. Women with BRCA1 gene mutation at an increased risk of aggressive uterine cancer

July 01, 2016

- Women who carry the BRCA1 gene mutation that dramatically increases their risk of breast and ovarian cancers are also at higher risk for a lethal form of uterine cancer, according to a study led by a Duke Cancer Institute researcher.
- This newly defined risk - the first to show a conclusive link between the BRCA1 gene mutation and a small but significant chance of developing an aggressive uterine cancer - could become a consideration in weighing treatment options..

### 1.2. Montreal scientists discover new path for Parkinson's treatment

July 02, 2016

- Scientists at University of Montreal and at the Montreal Neurological Institute at McGill University have discovered a link between Parkinson's Disease and autoimmune diseases in hopes of paving the way for new treatments down the road.
- Parkinson's is caused by the death of dopamine-producing neurons in the brain, but why those brain cells die is not yet understood.
- The two-university team has shown that proteins produced by two genes associated with Parkinson's disease are required to prevent the cells from waving a big flag that invites the immune system to attack.
- The findings linking the Parkinson's genes to the immune system were published in the medical journal Cell last month.

### 1.3. A urine test may identify low-risk prostate tumors

July 07, 2016

- Canadian researchers have tentatively identified urine protein signatures that appear to differentiate the aggressive form of prostate tumors from the low-risk tumors. The findings were recently reported in Nature Communications.
- These were discovered from urine, that allow to identify aggressive prostate cancers prior to surgery. Targeted proteomics were being used to accurately and precisely quantify hundreds of proteins in urine samples to develop these liquid biopsy signatures which could help to personalize the treatment of prostate cancer.

### 1.4. Leukemia drug increases brain dopamine, lowers toxic proteins linked to Parkinson's or dementia

July 18, 2016

- A small phase I study provides molecular evidence that an FDA-approved drug for leukemia significantly increased brain dopamine and reduced toxic proteins linked to disease progression in patients with Parkinson's disease or dementia with Lewy bodies.
- The findings described in the Journal of Parkinson's Disease, support improved clinical outcomes observed and first reported at the Society for Neuroscience annual meeting in October 2015.
- The study tested nilotinib taken daily for six months. A much smaller dose of nilotinib (150 or 300 mg once daily) was used compared to the dose for chronic myelogenous leukemia (300-400 mg twice daily).



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## PHARMA INDIA

**2.1. Cipla to build a biosimilars plant in South Africa to serve global markets** July 13, 2016

- Cipla announced its plans to set up a biopharmaceutical manufacturing facility in South Africa, aiming to make biosimilar treatment cost-effective with wider penetration among the patients.
- The biosimilars produced at the proposed facility would be for both state and private sectors and there is also the potential to export to markets in the US, European Union and Asia..

**2.2 Sanofi-Synthelabo India launches 2 diabetes drugs** July 20, 2016

- Sanofi-Synthelabo, India, has expanded Sanofi's diabetes portfolio in the country with the launch of two drugs - Lyxumia and Zemiglo - for lowering blood sugar levels.
- While Lyxumia- lixisenatide is a once daily, non-insulin injectable drug, Zemiglo- gemigliptin is a once daily, oral tablet.

**2.3. India joins WHO's Global Injection Safety Campaign** July 30, 2016

- The Safe Point India, a frontline not-for profit society working in the field of public health and safety, has lauded and fully endorsed the WHO's and Government of India's noble initiative to eliminate viral hepatitis by 2030, by launching the Global Safe Injection Campaign.
- Safe injections can play an important role in eliminating a health scourge that claims over 3,50,000 lives each year globally and is the number two communicable disease killer of human lives after tuberculosis.
- On World Hepatitis Day, India became one of the first countries to join WHO's Safe Injection Campaign which is integral to the strategy for eliminating hepatitis by 2030.

## REGULATORY ROUNDUP

**3.1. FDA raises kidney injury warnings for some diabetes medications** July 01, 2016

- The US FDA reported a new requirement strengthening the current warning about the dangers of acute kidney injury involving certain diabetes medications. Drugs containing canagliflozin, (with trade names Invokana and Invokamet) and dapagliflozin (brand names Farxiga and Xigkuo XR) have received modifications in the drug labeling, informing consumers of acute kidney injury risks as well as recommendations to minimize this risk.
- Healthcare providers are advised to consider factors that may predispose patients to acute kidney injury prior to administering canagliflozin or dapagliflozin.

**3.2. FDA offers draft guidance on updates after reference products are withdrawn** July 06, 2016

- The US FDA has released a draft guidance describing the process for drug companies when they have to update a generic's label after the reference product (for which the generic is based) is withdrawn for reasons other than safety or effectiveness.
- This guidance focuses on a problem that has long plagued the generic industry, as generic labels are required by law to mirror their reference product counterparts at the time of approval but sometimes rely on drugs that have been withdrawn for economic reasons.

### 3.3. FDA advances Precision Medicine Initiative by issuing draft guidances on NGS-based tests

July 08, 2016

- In support of the President's Precision Medicine Initiative, the US FDA issued two draft guidances that, when finalized, will provide a flexible and streamlined approach to the oversight of tests that detect medically important differences in a person's genomic makeup.
- The first draft guidance is titled "Use of Standards in FDA's Regulatory Oversight of Next Generation Sequencing (NGS)-Based In Vitro Diagnostics (IVDs) Used for Diagnosing Germ line Diseases" .
- The second draft guidance is titled "Use of Public Human Genetic Variant Databases to Support Clinical Validity for Next Generation Sequencing (NGS)-Based In Vitro Diagnostics".

### 3.4. India revises draft biosimilar guidance

July 14, 2016

- The Central Drugs Standard Control Organization (CDSCO) of India has revised its draft biosimilar guidelines published earlier this year. While most of the document is unchanged, CDSCO has made notable amendments on how clinical trials must be run and the situations in which comparative studies of biosimilars and reference products are needed.
- The changes remove some of the flexibility offered by the earlier draft. The revised guidance still offers a way for regulators to waive the need for biosimilar developers to run comparative safety and efficacy studies, but it reduces the number of situations in which such an approach is acceptable.

### 3.5. FDA expands use of Pfizer's best-selling pneumonia vaccine

July 14, 2016

- US FDA had expanded the use of its best-selling pneumonia vaccine, Prevnar, to adults aged 18 through 49.
- The vaccine, which is already approved for use in adults aged 50 and above, and children aged 6 weeks to 17 years, prevents invasive diseases caused by 13 Streptococcus pneumoniae strains.
- The regulator's decision is based on data from a late-stage study in adults who had not been vaccinated against the disease previously.

### 3.6. The next PDUFA: New performance and procedural goals

July 18, 2016

- Exactly one year after the first round of negotiations over the sixth iteration of the Prescription Drug User Fee Act (PDUFA), the US FDA released the full details of the performance and procedural goals for fiscal years 2018 through 2022. The fifth and current iteration of PDUFA expires in September 2017.
- The 46-page document, which outlines how the agency will use the user fees provided to it from industry, breaks down not only the planned deadlines for new guidance documents and pilot projects, but also highlights recurring themes of recent importance, including the patient's input to the regulatory process, use of real-world evidence, biomarker qualification and increased pharmacovigilance.
- The new guidance covers the timing of review for NDAs, BLAs and various supplements. It also speaks about the communication between industry and the FDA, outlining ways that manufacturers will gain for increased access to meetings with the FDA.

## DRUG APPROVALS AND LAUNCHES

**4.1. Biogen & AbbVie's injectable approved in EU for treatment of MS** July 05, 2016

- The European Commission (EC) has granted marketing authorization for ZINBRYTA™ (daclizumab) for the treatment of adult patients with relapsing forms of multiple sclerosis (RMS), Biogen and AbbVie announced. ZINBRYTA is a once-monthly, self-administered, subcutaneous injection.
- The EC approval of ZINBRYTA is supported by results from two studies, including DECIDE, the largest and longest head-to-head Phase 3 study ever conducted in MS.

**4.2. J&J's insulin patch finally heading for launch** July 06, 2016

- Johnson & Johnson has finally announced a launch schedule for its One Touch Via insulin patch - some four years after it was first approved in the US.
- The patch is designed to be more discreet than injections for people taking insulin on demand - for example at mealtimes; and according to J&J that translates to higher rates of compliance with therapy and a reduction in embarrassment and discomfort for patients.

**4.3. US FDA approves Gilead's Epclusa® (sofosbuvir/velpatasvir) for the treatment of all genotypes of chronic hepatitis C** July 14, 2016

- Gilead Sciences, Inc. announced that the US FDA has approved Epclusa® (sofosbuvir 400 mg/velpatasvir 100 mg), the first all-oral, pan-genotypic, single tablet regimen for the treatment of adults with genotype 1-6 chronic hepatitis C virus (HCV) infection.
- Epclusa is also the first single tablet regimen approved for the treatment of patients with HCV genotype 2 and 3, without the need for ribavirin.

**4.4. FDA approves new medication for Dry Eye Disease** July 16, 2016

- The US FDA approved Xiidra (lifitegrast ophthalmic solution) for the treatment of signs and symptoms of dry eye disease. Xiidra is the first medication in a new class of drugs, called lymphocyte function-associated antigen 1 (LFA-1) antagonist, approved by the FDA for dry eye disease.

**4.5. AstraZeneca receives approval in the EU for Qtern in type 2 diabetes** July 21, 2016

- AstraZeneca announced that the European Commission (EC) has approved Qtern (saxagliptin/dapagliflozin) tablets for the treatment of type 2 diabetes in all 28 EU member countries plus Iceland, Liechtenstein and Norway.
- This combination is the first DPP-4i/SGLT-2i combination product to be approved in Europe.

**4.6. FDA approves treatment for opioid-induced constipation** July 22, 2016

- Valeant Pharmaceuticals International, Inc. and Progenics Pharmaceuticals, Inc. announced the FDA approval of RELISTOR® (methylnaltrexone bromide) tablets for the treatment of opioid-induced constipation (OIC) in adults with chronic non-cancer pain. RELISTOR has a unique mechanism of action that binds to mu-opioid receptors without impacting the opioid-mediated analgesic effects on the central nervous system.

## DRUG DEVELOPMENT AND CLINICAL TRIALS

### 5.1. Merck & Pfizer initiate Phase III trial for ovarian cancer treatment — July 06, 2016

- Merck and Pfizer announced the initiation of a Phase III study, JAVELIN Ovarian 100, to evaluate the efficacy and safety of avelumab in combination with, and/or as a follow-on (maintenance) treatment to, platinum-based chemotherapy in patients with locally advanced or metastatic disease (Stages III or IV) with previously untreated epithelial ovarian cancer.
- JAVELIN Ovarian 100 is the first Phase III study evaluating the addition of an immune checkpoint inhibitor to the standard-of-care first-line treatment for this aggressive disease.

### 5.2. Ablynx's vobarilizumab achieves positive top-line results as RA monotherapy — July 07, 2016

- Ablynx announced topline results showing that its experimental anti-IL-6R nanobody vobarilizumab achieved the primary endpoint of a Phase IIb study of certain patients with moderate to severe active rheumatoid arthritis (RA). Shares in Ablynx jumped more than 15 percent on the news.
- The drug, also known as ALX-0061, is being co-developed for inflammatory diseases as part of a 2013 partnership with AbbVie worth as much as $840 million.

### 5.3. Loxo Oncology receives breakthrough therapy designation from US FDA for LOXO-101 — July 13 , 2016

- Loxo Oncology, Inc., a biopharmaceutical company innovating the development of highly selective medicines for patients with genetically defined cancers, announced that the US FDA has granted breakthrough therapy designation to LOXO-101, a selective inhibitor of tropomyosin receptor kinase (TRK), “for the treatment of unresectable or metastatic solid tumors with NTRK-fusion proteins in adult and pediatric patients who require systemic therapy and who have either progressed following prior treatment or who have no acceptable alternative treatments.”
- The LOXO-101 Breakthrough Therapy Designation application included data from the ongoing Phase I dose-escalation study of LOXO-101 in adult patients with advanced solid tumors, the ongoing Phase I pediatric study of LOXO-101 in patients with advanced solid tumors or primary CNS tumors, and the ongoing Phase II basket trial of LOXO-101 in adult cancer patients whose tumors harbor TRK fusions.

### 5.4. Tagrisso met primary endpoint in Phase III 2nd-line lung cancer trial — July 21, 2016

- AstraZeneca announced that the Phase III AURA3 trial met its primary endpoint, demonstrating superior progression-free survival (PFS) compared to standard platinum-based doublet chemotherapy.
- Tagrisso demonstrated a safety profile consistent with previous trials and also demonstrated efficacy as a 2nd-line treatment in more than 400 patients with EGFR T790M mutation-positive, locally-advanced or metastatic NSCLC, whose disease had progressed following 1st-line EGFR tyrosine kinase inhibitor (TKI) therapy.
- In addition to PFS, the objective response rate (ORR), disease control rate (DCR) and duration of response (DoR) also achieved clinically meaningful improvement versus chemotherapy.

## MERGER/ ACQUISITIONS/ COLLABORATION

**6.1. AstraZeneca inks licensing deals with LEO Pharma on skin diseases** July 01, 2016

- AstraZeneca has entered a global licensing agreement with Denmark's LEO Pharma for tralokinumab, a potential new medicine for treating skin diseases.
- The agreement was subject to customary closing conditions, and the deal was expected to close in the third quarter of 2016.
- This is in line with AstraZeneca's recent strategy to focus on cancer treatments while pruning commercial and manufacturing operations.

**6.2. Sanofi Pasteur in Zika vaccine collaboration with US government lab** July 06, 2016

- Sanofi and its vaccines global business unit Sanofi Pasteur announced a Cooperative Research and Development Agreement with the Walter Reed Army Institute of Research (WRAIR) on the co-development of a Zika vaccine candidate.
- According to the terms of the agreement, WRAIR will transfer its Zika purified inactivated virus (ZPIV) vaccine technology to Sanofi Pasteur, opening the door for a broader collaboration with the US government.

**6.3 Amgen and Daiichi Sankyo announce agreement to commercialize biosimilars in Japan** July 13, 2016

- Amgen and Daiichi Sankyo announced the execution of an exclusive agreement to commercialize nine biosimilars in Japan.
- The deal includes several biosimilars in late-stage development, including biosimilars of adalimumab, bevacizumab and trastuzumab.

**6.4. Boehringer and Lilly to trial breast cancer drugs combination** July 15, 2016

- Already having an existing collaboration in diabetes, Eli Lilly and Germany's Boehringer Ingelheim have announced a new research pact, this time focused on breast cancer.
- In a statement, the two companies said they will combine two experimental meds: BI's insulin-like growth factor-1/ 2 (IGF-1/2) ligand neutralising antibody BI 836845, and Lilly's cyclin-dependent kinase (CDK) 4 and 6 inhibitor abemaciclib.

**6.5. GSK collaborates with University of Leicester in search of cancer treatments** July 24, 2016

- A collaboration between the University of Leicester and global pharmaceutical company GlaxoSmithKline (GSK) has been established to discover and develop novel medicines to treat aggressive forms of blood cancer.
- The new project is part of GSK's Discovery Partnerships with Academia (DPAc) initiative, which brings together the insight and creativity of world-leading academics with the drug discovery expertise of GSK to create new medicines and bring them to the clinic.

## PATENT (NEW APPROVAL/ LITIGATION/ SETTLEMENTS)

**7.1. Biosimilar 'Patent Dance': Federal circuit rules 180-day notice is mandatory** July 05, 2016

- The US Court of Appeals for the Federal Circuit affirmed a district court's ruling that a biosimilar applicant must provide a reference product sponsor with 180 days' notice, before commercial marketing of a biosimilar begins, regardless of whether the applicant provided notice of US FDA review.
- The ruling has major implications for when biosimilars can be launched and it follows the US Supreme Court's request in late June that the solicitor general provide more information on whether the highest court in the US should review the terms of this so-called "patent dance," the rules of which govern how biosimilar and reference product manufacturers must work out their patent issues as established by the Biologics Price Competition and Innovation Act of 2009 (BPCIA).

**7.2. Patent litigation resolved over Sandoz version of AstraZeneca's Faslodex** July 13, 2016

- AstraZeneca announced that it has entered into an agreement with Sandoz, Inc. and affiliates ("Sandoz") to resolve Faslodex (fulvestrant) patent litigation in the US relating to Sandoz's generic fulvestrant product, for which it is seeking FDA approval.
- Fulvestrant is a type of hormonal therapy drug used to treat breast cancer.
- The US Faslodex patents in question are due to expire in January 2021, with paediatric exclusivity continuing until July 2021.

**7.3. New patent for Microbiome technology to combat drug-resistant bacteria and suppress body odour** July 14, 2016

- Pharmaceutical Ortek Therapeutics, Inc., a global leader in oral care innovations and microbiome technology, announced that the US Patent and Trademark Office has awarded a patent for new methods to use new compositions to prevent or treat drug-resistant bacteria and suppress body odour.
- US Patent 9,370,476, was issued to The Research Foundation of State University of New York (Albany, NY), an Ortek licensing partner, and is directed at the topical application of a zinc and arginine-based composition.

## TECHNOLOGY/ DISCOVERY

**8.1 FDA approves first absorbable stent for coronary artery disease** July 05, 2016

- The US FDA approved the first fully absorbable stent to treat coronary artery disease. The Absorb GT1 Bioresorbable Vascular Scaffold System (BVS), which releases the drug everolimus to limit the growth of scar tissue, is gradually absorbed by the body in approximately three years.
- The Absorb GT1 BVS is manufactured from a biodegradable polymer called poly (L-lactide), which is similar to materials used in other types of absorbable medical devices, such as sutures.
- The Absorb GT1 BVS is manufactured by Abbott Vascular in Santa Clara, California.

**8.2. FDA approves single monthly injection for a PCSK9 inhibitor** July 11, 2016

- Amgen has announced that the US FDA has approved the Repatha (evolocumab) PushtronexT system (on-body infusor with prefilled cartridge), a new, monthly single-dose administration option.
- The Pushtronex system is a hands-free device designed to provide 420 mg of Repatha in a single dose. Repatha is a human monoclonal antibody that blocks a protein called proprotein convertase subtilisin/kexin type 9 (PCSK9), which inhibits the body's natural system for eliminating "bad" cholesterol (low-density lipoprotein cholesterol or LDL-C) from the blood.
- Repatha is the first and only PCSK9 inhibitor to offer a monthly single-dose delivery option.

**8.3. FDA approved BELVIQ XR® (lorcaserin HCl) extended-release tablets** July 19, 2016

- Eisai Inc. and Arena Pharmaceuticals, Inc. announced that the US FDA has approved the New Drug Application (NDA) for BELVIQ XR® (lorcaserin HCl) CIV extended-release 20 mg tablets.
- The new formulation of lorcaserin will offer patients, a once-a-day dosing option that may help them achieve and maintain weight loss.
- BELVIQ XR is proven to be slowly absorbed in the body and lasts throughout the day.

**8.4. New technology stores vaccines for 35 days without electricity** July 22, 2016

- Scientists and engineers from the UK have developed a cost-effective vaccine storage device which perfectly preserves vaccines for 35 days using 30 liters of ice and without needing electricity.
- Research engineers from the Sure Chill Company, based in Cardiff, conceived a way to use their patented Sure Chill technology to keep vaccine cool for a month or more at tropical temperatures without the need for any power supply.
- Sure Chill's patented technology which cocoons the vaccine chamber in water at 4°C with super-efficient vacuum insulation panels to keep the surrounding heat at bay. These panels are the best solid insulation currently available and are many times more effective than conventional refrigeration materials.