Clinical Research Newsletter Volume - 9, September 2016

LAMBDA

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GLOBAL PHARMA/ RESEARCH UPDATE

1.1. FDA Begins Intercenter Pilot Project on combination products

August 01, 2016

- The US FDA has started the pilot phase of its new intercenter consult request (ICCR) process, designed to streamline submissions and reviews of combination products, (drugs, medical devices and/or biologics).
- The agency expects full implementation to finish by the end of second quarter, 2017.

1.2. Scientists discover tissue biomarkers linked to spine osteoarthritis

August 04, 2016

- Recent research shows elevated levels of tissue biomarkers, micro RNA-181a-5p and micro RNA-4454, that may cause inflammation, cartilage destruction, and cartilage depletion, contributing to joint degeneration associated with spine osteoarthritis.
- This is the first such study published in the Journal of Clinical Investigation by a research team from the Krembil Research Institute.

1.3. Study provides detailed picture of genetics underlying type 2 diabetes

August 12, 2016

- The world's largest study of type-2 diabetes (T2D) provides us with the most detailed picture of the genetics underlying the condition to-date.
- The findings published in the journal, Nature, by an international team of >300 scientists suggest that most of the genetic risk of T2D can be accredited to common, shared genetic variants each contributing a small amount to an individual's risk of the disease rather than many rare variants unique to individuals. This makes easier to understand the complex genetics of T2D that have puzzled researchers for decades.

1.4. FDA offers first major update to 'Orange Book' website

August 15, 2016

- The US FDA introduced an updated version of its "Orange Book" website, the internet version of its publication on drugs approved on the basis of safety and effectiveness.
- The site allow users to search approved drug products by active ingredient, proprietary name, applicant, application number, dosage form, route of administration, or patent number.

1.5. EMA releases list of medical events for pharmacovigilance

August 19, 2016

- A list of 62 standardized terms describing medical events that could occur after using health care products is released by the European Medicines Agency (EMA) to aid in the agency's pharmacovigilance activities and prioritize the review of suspected adverse events that require additional attention.
- The list includes MedDRA Preferred Terms that identify serious medical concepts often causally associated with drugs across multiple pharmacological/therapeutic classes. It will not address product specific issues, and conditions with high prevalence in the general population as they are excluded.

PHARMA INDIA

2.1. Indian pharma majors dominate list of 'Top Most Reputed Pharmaceuticals Brand'

August 17, 2016

- India's most reputed pharmaceutical brands study, prepared by BlueBytes in association with TRA (Trust Research Advisory), is dominated by leading Indian pharma companies. Lupin remained on top in reputation in the pharma segment.
- Sun Pharma is the second most reputed brand while Cipla is at third position. Dr Reddy`s Laboratories stands at fourth.
- Among global brands, GSK leads the way followed by Pfizer. Abbott is ranked as India`s third most reputed among international brands.

2.2 Low levels of vitamin B12 a big concern in India: SRL study August 17, 2016

- SRL Diagnostics has delivered a 3 year long study on vitamin B12 deficiency at PAN India level.
- Approximately 31% of the total samples were affected with vitamin B 12 deficiency.
- Vitamin B12 deficiency was found to be slightly more common in Indian men (35%) than women (28%) and also found more prevalent in older population aged >60 years.

2.3. Govt. puts up draft proposal of National Medical Commission bill for review to replace MCI

August 17, 2016

- To replace Medical Council of India (MCI) with National Medical Commission (NMC), a new apex regulator for the medical sector, Government of India has put the draft proposal of National Medical Commission Bill for stakeholders' review till August 31, 2016.
- The suggestions will go to the Council of Ministers for further consultation and finally to the Cabinet for its further enactment.
- Accordingly, NMC will become the main regulatory body and will take over all the roles and responsibilities of MCI.

2.4. India bouncing back in clinical trials as new norms spur growth August 20, 2016

- “India has begun to rebound in clinical trials with the new regulations issued at frequent intervals which have forced global pharmaceutical companies and clinical research organisations (CROs) to re-consider conduct of human studies in the country” quoted by Mr. Naz Haji, SVP and Head of India, Indonesia, Malaysia and Singapore operations, Quintiles.
- As specified by Mr. Haji, “this regulation change specific to clinical trials is progressive for both Indian companies and its patient population. However, the government along with the industry will need to bring back efforts to ensure that the regulatory enforcement system in the country is able to step up the pace of approvals and provide the required clearances in a time bound manner.”

REGULATORY ROUNDUP

3.1. India relaxes rules on clinical investigators and trial sites August 03, 2016

- India's Central Drugs Standard Control Organization (CDSCO) has decided to relax two clinical trial requisites that could make it more facile to run clinical trials.
- CDSCO allows trial investigators to be a part of more than three clinical trials at a time. Furthermore clinical trials now can be conducted in hospitals with less than 50 beds, which was a mandatory requirement earlier.

3.2. India allows parallel submission of trial filings for insulins, mAbs August 09, 2016

- The Drug Controller General of India (DCGI) has facilitated the drug approval process by allowing simultaneous filing of applications to his office and the Review Committee on Genetic Manipulation (RCGM).
- The advancement from sequential to simultaneous filing has potentially reduced the time to secure clearance to run clinical trials for developers of insulins, monoclonal antibodies and certain other products.

3.3. Australia's TGA issues warning on denosumab and QT prolongation August 15, 2016

- Australia's Therapeutic Goods Administration (TGA) has identified an emerging drug safety issue during the assessment of adverse event reports related to Prolia and Xgeva.
- QT prolongation and severe symptomatic hypocalcemia have been identified with these agents.

3.4. FDA warns of serious risks for syringe pumps at low infusion rates August 25, 2016

- The US FDA issued a warning to healthcare professionals that when using programmable syringe pumps to infuse therapies at low rates (e.g., less than 5 mL per hour, and especially at flow rates of less than 0.5 mL per hour), a lack of flow continuity can result in serious clinical consequences, including delay of therapy, over-infusion or under-infusion. Serious adverse events such as abnormal or unstable blood pressure, anxiety from loss of sedation and increased pain indicators in critically-ill infants are reported.
- FDA has provided manufacturers of the devices with incipient language to integrate to their injunctive authorizations for utilize that includes a list of admonishments and considerations to mitigate the risks.

DRUG APPROVALS AND LAUNCHES

4.1. FDA approves Silvergate's pediatric lisinopril- Qbrelis August 01, 2016

- The US FDA has granted approval on the first lisinopril oral solution - Qbrelis™ from Silvergate pharmaceuticals.
- Qbrelis™ is designed to treat high blood pressure (hypertension) in adult and pediatric patients aged 6 years and older, as an adjunct therapy for heart failure and acute myocardial infarction in adults.

4.2. Ipsen Biopharmaceuticals, Inc. announces FDA approval of Dysport® August 01, 2016

- The US FDA has approved Ipsen Biopharmaceutical's Dysport® (abobotulinumtoxinA) injection for the managemnet of lower limb spasticity in pediatric patients (2 years and more).
- Dysport® is the first and only FDA-approved botulinum toxin for the treatment of pediatric lower limb spasticity.
- FDA has given this approval based on the results from a randomized, multicenter, double-blind, placebo-controlled, international Phase III pivotal study involving 235 patients in the pediatric age group.

4.3. FDA approves Troxyca® ER extended-release capsules August 19, 2016

- The US FDA has given the approval to Troxyca ER® (oxycodone hydrochloride and naltrexone hydrochloride) extended-release capsules of Pfizer for the management of severe pain that requires, long-term opioid treatment and for which alternative treatment options are not adequate.
- Troxyca ER® characteristics as to being crushed and given by the oral and intranasal routes, may help reduce abuse.

4.4. India develops world's first leprosy vaccine August 22, 2016

- The world's first leprosy vaccine has been developed by India, which is soon to be orchestrated for trials within Bihar and Gujarat states (5 districts).
- Around 60% of world's leprosy cases are registered in India with almost 1.25 lakh leprosy cases registered every year.
- The mycobacterium indicus pranii (MIP) vaccine, developed by the National Institute of Immunology (NII), has been approved by the Drug Controller General of India and US FDA.

DRUG DEVELOPMENT AND CLINICAL TRIALS

5.1. More positive Phase III results for Pfizer's oral Xeljanz in ulcerative colitis August 01, 2016

- Positive top-line results from a third Phase III study of Xeljanz (tofacitinib citrate) in patients with ulcerative colitis (UC) have been announced by Pfizer.
- OCTAVE Sustain trial involving 593 adult patients, who previously completed and achieved clinical response in either the OCTAVE Induction 1 or OCTAVE Induction 2 studies, demonstrated that significantly greater proportion of patients achieved remission in both the tofacitinib 5 and 10mg BID groups compared to placebo as a maintenance treatment in moderately to severely active UC.

5.2. Eisai's Halaven shows survival benefit in metastatic soft tissue sarcoma August 05, 2016

- According to Eisai, Halaven (Eribulin mesilate) is the first and only single agent to show a significant improvement in overall survival for people with advanced liposarcomas. Results of a randomised, open-label, multicentre Phase III study comparing the efficacy and safety of eribulin to dacarbazine published in Lancet demonstrated a trend for extension in overall survival with eribulin.

5.3. Novartis' breast cancer drug ribociclib: Now first-line treatment for HR+/HER2-

August 05, 2016

- The USFDA has granted breakthrough therapy designation to Novartis' LEE011 (ribociclib - a selective cyclin dependent kinase [CDK4/6] inhibitor), in combination with letrozole, for the treatment of hormone receptor positive, human epidermal growth factor receptor 2-negative (HR+/HER2-) advanced or metastatic breast cancer.
- Phase III clinical study of LEE011 combined with letrozole compared to letrozole alone in postmenopausal women with HR+/HER2- advanced breast cancer who did not receive any previous therapy for their advanced disease demonstrated clinically significant improvement in progression-free survival (PFS) and supported the breakthrough designation of molecule.

5.4. Novartis' fevipiprant - a 'game changer' for asthma treatment

August 08, 2016

- Researchers from the University of Leicester have developed novel asthma pills named Fevipiprant (QAW039), which significantly reduces severe asthma conditions, attacks and symptoms.
- According to the researchers, fevipiprant is the first successful drug in almost two decades to show promising results in reducing the severe conditions of asthma. The clinical trial took place in 61 people to evaluate efficacy of the drug vs. placebo.

5.5. Abaloparatide reduces fracture risk in postmenopausal women with osteoporosis

August 17 , 2016

- Abaloparatide-SC, an injectable drug being studied for the treatment of postmenopausal osteoporosis, significantly reduced the rate of new spinal fractures, as well as provided statistically significant reductions in the fracture rate at other parts of the body, according to data from phase III ACTIVE fracture prevention trial (ACTIVE trial).
- The researchers found greater bone mineral density, fewer vertebral fracture and fewer other types of fractures with abaloparatide than placebo among postmenopausal women with osteoporosis.

MERGER/ ACQUISITIONS/ COLLABORATION

6.1. Pfizer acquires Bamboo Therapeutics, leads the way in gene therapy

August 01, 2016

- Bamboo Therapeutics has been fully acquired by Pfizer, considerably expanding the company's holdings in gene therapies for rare disease portfolio including neuromuscular conditions and central nervous system disorders.
- Significant gains of Pfizer, with this acquistion include several potential therapeutic agents, manufacturing facility for Phase I/II gene therapy and an advanced recombinant Adeno-Associated Virus (rAAV) vector design and production technology.

6.2. Quintiles and DaVita Clinical Research announce strategic alliance August 02, 2016

- Quintiles, a provider of product development and integrated healthcare services, and DaVita Clinical Research, a wholly-owned subsidiary of DaVita HealthCare Partners Inc., a leader in kidney care, have announced a global strategic alliance.
- Therapeutic expertise in clinical trials and industry-leading operational delivery distribution of Quintiles will amalgamate with the world-class clinical care and expansive footprint of research sites of DaVita.

6.3. Pfizer acquires Medivation in $14B deal August 22, 2016

- Pfizer announced a definitive merger agreement to acquire the cancer drug company Medivation for about $14 billion.
- This ends months of bidding for San Francisco's Medivation, one of the most sought after independent biotechs as it sells one of the leading prostate-cancer drug enzalutamide.
- Pfizer has agreed to pay $81.50 per share. Medivation shares moved up nearly 20% to $80.41 in trading in New York, as Pfizer shares fell 5 cents to $34.86.

6.4 AstraZeneca to sell molecule antibiotics business to Pfizer August 24, 2016

- AstraZeneca is selling the commercialisation and development rights of its late-stage small molecule antibiotics business in most markets outside the US to Pfizer for $550m upfront and a further $175m in January 2019.
- In addition to royalties, AstraZeneca will additionally get up to $250m in milestone payments and up to $600m in sales-related payments.
- This deal is expected to close in the fourth quarter of 2016.

6.5. New Phase I-IV data management system to provide access to clinical trial data in real time August 24, 2016

- Biomedical Systems, a Missouri-based clinical trial solutions provider, and Foundry Health, a digital health company, announced the collaboration regarding the new cloud based data management system that will allow access to clinical trial data in real time.
- Also, Biomedical System will target on applications from Phases II to IV, while Foundry Health on Phase I - as the company has developed ClinSpark™, which it said is the world's first CDISC ODM (Clinical Data Interchange Standards Consortium Operation Data Module) certified Phase I e-Source system.

PATENT (NEW APPROVAL/ LITIGATION/ SETTLEMENTS)

7.1. AbbVie files patent suit to stop Amgen's Humira biosimilar August 05, 2016

- AbbVie has filed a patent-infringement lawsuit against Amgen with allegations of violating 10 different patents of Humira and could well bring another lawsuit later that cites 51 more patents.
- The world's top grossing drug, Humira, generated 60% ($14 billion) of AbbVie's revenue of more than $22.8 billion in 2015. In its complaint, AbbVie asked the court to keep the biosimilar version from becoming available, if FDA issues an approval to Amgen.

7.2. Patent litigation resolved over Sandoz version of AstraZeneca's Faslodex August 14, 2016

- UCB Pharma, a Belgian pharmaceutical company, announced that the U.S. District Court for the District of Delaware confirmed the validity of its U.S. reissued patent RE38551 related to anti-epileptic drug Vimpat® (lacosamide).
- The patent challenge was brought by generic drug makers who had questioned the validity of the UCB's patent which is scheduled to expire in March 2022.
- The decision is currently under seal and will be released following an order from the court.

7.3. Mylan gets favourable US ruling against Teva's Copaxone 40 mg/mL patents August 26, 2016

- Mylan announced that the U.S. Patent and Trademark Office (PTO) has ruled in favor of Mylan in its inter partes review (IPR) proceeding and found all claims of two cognate Copaxone® 40 mg/mL patents to be unpatentable.
- The two U.S. patents are owned by Yeda Research & Development Co., Ltd. and licensed to Teva Pharmaceuticals Industries Ltd.
- Patent Trial and Appeal Board (PTAB) found Mylan's application against a fourth Copaxone 40 mg/mL patent, ineligible for post-grant review for procedural reasons. However, favourable ruling in the IPR against the '302 patent in current scenario is believed to strongly undermine the 776 patent and hence, Mylan will proceed with pursuing all possibilities to challenge the 776 patent.

TECHNOLOGY/ DISCOVERY

8.1 Microneedle system to monitor drugs August 01, 2016

- A microneedle drug monitoring system has been created by the researchers at the University of British Columbia and the Paul Scherrer Institute (PSI) that could one day replace costly, invasive blood draws that may help improve patient comfort.
- The new system consists of a small, thin patch that is pressed opposite to a patient's arm during medical treatment. It then measures drugs in their bloodstream painlessly without drawing any blood. The tiny needle-like projection, less than half a millimeter long, resembles a hollow cone and doesn't pierce the skin like a standard hypodermic needle. Microneedle technology is useful for painless vaccines and drug delivery.

8.2. FDA uses Malvern's bioequivalence evaluation technology August 18, 2016

- Malvern's Morphology G3-ID system has been used by the FDA to generate key data for the approval of the first generic nasal spray containing mometasone furoate.
- Morphology Directed Raman Spectroscopy (MDRS), a combination of static image analysis and Raman spectroscopy that provides the complete understanding of the characteristics of drug substance, excipients or any contaminant particles contained in the formulation, has facilitated FDA to validate the bioequivalence of the two products without the need for costly clinical endpoint bioequivalence studies.

8.3. Electron microscopy reveals how vitamin A enters the cell August 25, 2016

- The latest discovery of camera technology is quite significant to getting the images of the protein named STRA6.
- A recent study conducted by a team of researchers from Columbia University Medical Center has captured images of one of the smallest proteins- STRA6 using electron microscopy. This protein resides in cell membrane of the cells and plays a key role in the transport of vitamin A into the cell.
- This technology allowed researchers to find the smallest structural details of the inner parts of our cells through which they found that STRA6 only interacts with vitamin A via an intermediary protein that transports vitamin A in the bloodstream.