Clinical Research Newsletter Volume - 8, August 2015

LAMBDA

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GLOBAL NEWS

1.1. Biosimilars market could hit $55 billion by 2020 July 1, 2015

- The global biosimilars market value is expected to reach $20 billion by the end of 2015 and could hit $55 billion by 2020, with growth primarily driven by a promising pipeline in active development and government efforts to reduce healthcare spending, according to business intelligence provider GBI Research. Biologics currently account for between 1720% of the pharmaceutical arena, with a value of nearly $200 billion, and these products may replace 70% of chemical drugs in the next two decades.

1.2. Parkinson's disease market will be boosted by new drug approvals July 2, 2015

- The Parkinson's disease treatment market value across the eight major countries of the US, France, Germany, Italy, Spain, the UK, Japan, and Brazil will reach $4.7 billion by 2022, driven primarily by an aging population and increasing disease prevalence, according to research and consulting firm Global Data. The company's latest report states that most late-stage pipeline agents are set to meet the needs of advanced Parkinson's disease patients, with three drugs expected to launch by 2022, namely CVT-301, opicapone and tozadenant.

1.3. Hospira's Remicade biosimilar wins large French contract with deep discount July 6, 2015

- Hospira continues to forge a new market reality around biosimilars, capturing wide swathes of market share with deep discounts for its biosimilar of Merck's arthritis blockbuster Remicade. Hospira has reportedly captured a public contract in France by offering a price that amounts to a 45% savings. Pricing was always seen as key for uptake of biosimilars, which have been available in Europe for some years but which have yet to make an entry into the lucrative U.S. market. Two weeks ago, the National Institute for Health and Care Excellence (NICE), England's price watchdog, included Remicade biosimilars into new guidance for treating rheumatoid arthritis, which stipulates the least expensive drug should be used.

1.4. FDA toughens heart attack, stroke warning for non-aspirin NSAIDS July 10, 2015

The FDA issued a safety communication strengthening an existing label warning that non-aspirin non-steroidal anti-inflammatory drugs (NSAIDs) increase the chance of a heart attack or stroke. According to the FDA, the new data have led it to conclude that the drug class definitely causes an increased risk of heart attack and stroke, whereas the agency has long required a boxed warning saying it may be associated with a "potential increased risk of serious adverse [cardiovascular] events." Among the changes, the FDA said prescription labels will be revised to reflect that the risk of heart attack or stroke can occur as early as the first weeks of using an NSAID, and may increase with longer use. Further, the risk appears greater at higher doses, the agency said.

DOMESTIC NEWS

2.1. India drafting drug quality norms to match US FDA standards July 7, 2015

- After facing harsh criticism over drug manufacturing quality in the recent past, government is now set to draft a new set of guidelines to regulate drug quality in India. Health ministry and Central Drug Standards Control Organisation (CDSCO), jointly, plan to study the guidelines of global health regulators. While the new set of regulation guidelines will be referred from top global health regulators such as, the government plans to study regulations of lesser developed countries and BRICS countries as well.

2.2. IPC recommends caution on 3 life saving drugs in market to CDSCO based on ADRs

July 23, 2015

- Indian Pharmacopeia Commission's (IPCs) signal review panel recently submitted strategic recommendation to the CDSCO on the 3 important life saving drugs running in the market. Based on the evaluation report received from different AMCs under the Pharmacovigilance Programme of India (PvPI), it was found that use of carbamazepine is associated to cause Stevens Johnson Syndrome (SJS) in some patients. Apart from carbamazepine, IPC has also submitted recommendation to the Centre on two anti cancer drugs sunitinib and pazopanib as well. Considering the safety of the patients, the review panel recommended the CDSCO to direct all the manufacturers to insert a clear warning on its label on the possible side effects of the drug, to caution the patients.

REGULATORY NEWS

3.1. Electronic Application Forms Mandatory for EU Centralized Procedure July 01, 2015

- The European Medicines Agency (EMA) will require companies to use new electronic application forms (eAF) for all medicines applying to the centralized procedure. In March 2012, EMA piloted the use of electronic application forms as part of its efforts to modernize the marketing authorization process. Then in February 2015, following the adoption of the Heads of Medicines Agencies' eSubmission Roadmap the previous year, EMA announced it would no longer accept paper application forms for products applying to the centralized procedure beginning 1 July 2015. Following the announcement, EMA held an initial round of user testing that concluded on 5 March 2015.

3.2. Plasma fibrinogen receives FDA approval for use in COPD trials July 09, 2015

- The FDA approved the use of plasma fibrinogen as a clinical biomarker for use in interventional trials in patients with chronic obstructive pulmonary disease (COPD), the COPD Foundation announced Thursday. "This is the first COPD biomarker to receive qualification" by the agency, the group said. Specifically, the FDA issued draft guidance allowing drug developers to use plasma fibrinogen in investigational studies of patients with COPD who are at high risk for exacerbations or all-cause mortality. The agency noted that the move "does not change any regulatory status, decisions or labelling of any in vitro diagnostic test used in the medical care of patients."

3.3. Data management, SOP deficiencies cited often after 2014 GCP inspections, EMA report finds

July 16, 2015

- The latest EMA (European Medicines Agency) report on GCP (good clinical practice) inspections reveals that deficiencies around SOPs (standard operating procedures), sponsor monitoring, data management, and essential documents linked to trials were most often cited in 2014.The findings come as inspectors of the EU member states performed 57 GCP inspections in 2014, which was down from the 83 conducted in 2013. The inspections were conducted with 19 coming in European countries, 12 in US, 11 in middle east/Asia/Pacific region and 15 elsewhere.

3.4. House Passes 21st Century Cures Act: What Does it Mean for Clinical Research?

July 24, 2015

- On July 10, 2015, the U.S. House of Representative passed H.R. 6, the 21st Century Cures Act, with strong bipartisan support in a vote of 344-77.The bill includes several provisions related to federal oversight of clinical research, with implications for a wide range of stakeholders across the life sciences and health care industries, including drug and device manufacturers, hospitals, academic medical centers, universities/medical schools, institutional review boards, and contract research organizations.

3.5. Indian government task force calls to simplify clinical trial approval process

July 28, 2015

- As the number of clinical trials in India continue to taper off compared to years past, a government task force is now calling for a new expedited trial approval process. As the Indian Clinical Research Society put recently: “Inspite of being home to 17% of population of the world and having a fifth of the world's disease burden, our contribution to global drug trial is less than 1.5%”.The government seems to be doing what it can to change that, and specifically the task force calls to “create simplified and streamlined process along with well-defined timelines for approvals of clinical trials. Currently the industry is faced with a three tier structure for permitting clinical trial of a new drug with the chain of Expert Committee, Technical committee & Apex committee; having overlapping mandates.”The task force also says that a more computerized online process to apply for and approve trials could streamline the entire clinical trial, licensing and quality control processes, and increase transparency. “In addition, the Ministry should also create the single window medicine monitoring IT system to link the headquarters, state offices and government hospitals to seamlessly communicate drug related information,” the government group said. “We hope that as the regulatory environment improves, a new dimension would be unfold between the regulators and the patients, pushing clinical research not only by researchers and scientists in the country, but also as a preferred destination from overseas sponsors,” Samir Sethi, President, Indian Rett Syndrome Foundation, said. Other recommendations from the task force are to support issues around regulatory affairs, funding, infrastructure, R&D, price control and capacity building.

DRUG APPROVALS AND LAUNCHES

4.1. Vanda Pharmaceuticals' Hetlioz approved in Europe for sleep disorder July 08, 2015

- European Commission (EC) has approved Hetlioz for the treatment of non-24-hour sleep-wake disorder in totally blind adults. EC has also confirmed orphan drug designation for Hetlioz for this indication. According to company sources, non-24-hour sleep-wake disorder affects the majority of totally blind individuals. Approximately 130,000 people in the EU suffer from the disorder. Hetlioz was approved in the U.S. in Jan 2014 (launched in Apr 2014). It is the first and only FDA-approved treatment for non-24-hour sleep-wake disorder.

4.2. FDA OKs Novartis' mega blockbuster heart failure drug Entresto July 09, 2015

- Novartis announced Tuesday that the FDA approved Entresto (sacubitril/valsartan), previously known as LCZ696, to reduce risk of cardiovascular death and heart failure hospitalizations among heart failure patients with reduced ejection fraction. The first-in-class angiotensin receptor neprilysin inhibitor had been granted priority review by the agency earlier this year. Entresto will be available on prescription for patients whose condition is classified NYHA class II-IV, indicated to reduce the risk of cardiovascular death and heart failure hospitalisation.

4.3. FDA approves Lundbeck and Otsuka's Rexulti (brexpiprazole) for MDD and schizophrenia July 10, 2015

- The U.S. Food and Drug Administration approved Danish drugmaker H. Lundbeck A/S and Japan's Otsuka Pharmaceutical Co Ltd's Rexulti, an anti-psychotic drug used to treat schizophrenia. The drug, brexpiprazole, was also approved as an adjunctive therapy for major depressive disorder (MDD), a serious psychiatric condition that can lead to persistent feelings of sadness, frustration or anger, the health regulator said on Friday. The agency based its decision on seven clinical trials, three of which examined the drug's effect on schizophrenia and four testing it as an adjunctive therapy for MDD.

4.4. FDA approved gefitinib (IRESSA) for patients with metastatic NSCLC July 13, 2015

- The U. S. Food and Drug Administration approved gefitinib (IRESSA) for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test. This approval of gefitinib is being approved concurrently with a labeling expansion of the thera screen EGFR RGQ PCR Kit, a companion diagnostic test for patient selection. The approval of gefitinib was based on the results of a multicenter, single-arm, open-label clinical study of a total of 106 treatment naïve-patients with metastatic EGFR mutation positive NSCLC who received gefitinib at a dose of 250 mg daily until disease progression or intolerable toxicity.

4.5. World's first malaria vaccine wins regulatory go-ahead. July 26, 2015

- The world's first malaria vaccine got a green light from European drugs regulators who recommended it as safe and effective to use in babies in Africa at risk of the mosquito-borne disease.The shot, called Mosquirix and developed by British drugmaker GlaxoSmithKline and the PATH Malaria Vaccine Initiative, would be the first licensed human vaccine against a parasitic disease and could help to prevent millions of cases of the killer disease in countries that use it.

DRUGS IN DEVELOPMENT AND CLINICAL TRIALS

5.1. Roche reports positive results from two phase III studies of ocrelizumab in multiple sclerosis

July 01, 2015

- Roche announced positive results from two pivotal studies evaluating the investigational medicine ocrelizumab compared with interferon beta-1a (Rebif), a standard-of-care therapy, in people with relapsing multiple sclerosis (MS), the most common form of the disease. The studies called OPERA I and OPERA II met their primary and major secondary endpoints. Treatment with ocrelizumab significantly reduced the annualised relapse rate (ARR) over a two-year period compared with interferon beta-1a, the primary endpoint in both studies. Ocrelizumab also significantly reduced the progression of clinical disability compared with interferon beta-1a, as measured by the Expanded Disability Status Scale (EDSS). Additionally, treatment with ocrelizumab led to a significant reduction in the number of lesions in the brain (areas of disease activity) compared with interferon beta-1a, as measured by MRI.

5.2. Novo Nordisk's experimental diabetes drug semaglutide meets main goal in late-stage study

June10, 2015

- Novo Nordisk announced results from the Phase IIIa SUSTAIN 1 trial Friday demonstrating that its experimental GLP-1 analogue semaglutide led to "superior" improvements in HbA1c and weight loss, compared with placebo.In the study, 388 drug-naïve patients with type 2 diabetes were randomised to treatment with one of two doses of semaglutide administered once weekly as monotherapy, or placebo for 30 weeks. Results showed that the low and high doses of semaglutide were associated with HbA1c reductions of 1.5 percent and 1.6 percent, respectively, compared to no change in the placebo arm.

5.3. J&J's guselkumab shows superiority to placebo and Humira in Phase IIb trial

July 10, 2015

- The anti-interleukin-23 monoclonal antibody guselkumab performed significantly better than the anti-tumor necrosis factor therapy adalimumab in the treatment of plaque psoriasis. The results of the phase 2 randomized, placebo-controlled trial were published in the July 9 issue of the New England Journal of Medicine. At week 16 of the multisite trial, patients who received 50 mg or more of guselkumab had the best response, with greater doses generally leading to a greater numbers of trial participants achieving a Physician's Global Assessment (PGA) score of 0, meaning cleared psoriasis, or 1, meaning minimal psoriasis. The optimal performance was among patients receiving 100 mg every 8 weeks, with 86% of participants scoring a 0 or 1. Among patients in the adalimumab group, 58% scored a 0 or 1 at 16 weeks; 7% of those in the placebo group scored 0 or 1 (P= .002 for all comparisons).

5.4. Anika announces positive results from study evaluating safety of repeat injection of Cingal to treat osteoarthritis of the knee June 08, 2015

- Anika Therapeutics, Inc., a leader in products for tissue protection, healing, and repair based on hyaluronic acid (HA) technology, reported positive results from the Cingal 13-02 study evaluating the safety of a repeat injection of Cingal for symptomatic relief of osteoarthritis (OA) of the knee. Cingal combines the company's proprietary cross-linked sodium hyaluronate (currently marketed as the single-injection viscosupplement Monovisc with an FDA-approved steroid, triamcinolone hexacetonide. Earlier this year, Anika announced positive results from Cingal 13-01, a randomized, double-blind, placebo-controlled phase 3 study, which demonstrated the efficacy and safety of a single injection of Cingal for treatment of pain caused by OA of the knee.

5.5. Positive results for Otsuka's Deltyba for extensively drug-resistant tuberculosis July 20, 2015

- Otsuka Pharmaceutical Co., Ltd. announced that data from a post-hoc subset analysis of its Phase IIb clinical trial suggesting potential efficacy of delamanid for the treatment of extensively drug-resistant tuberculosis (XDR-TB) was reported in this week's New England Journal of Medicine. The analysis found that patients receiving delamanid, plus a World Health Organization (WHO)-recommended optimized background regimen (OBR), had a higher proportion of 2-month sputum culture conversion (SCC), a measurement by which patients are no longer infectious, compared to patients receiving placebo plus OBR alone (7/16, 43.8% vs. 1/10, 10%, p=0.0989)i. In this same open-label analysis, mortality trended lower when patients received six months or more of delamanid compared to patients treated for two months or less (0/17, 0% vs. 2/9, 22.2%, p=0.1108). XDR-TB is one of the most deadly and difficult forms of TB to treat.

5.6. Much awaited data on Lilly's solanezumab raise hopes for Alzheimer's patients July 22, 2015

- After decades of failed Alzheimer's drugs nearly 125, in fact new data released today raise hopes that the tide could be turning. In an extended analysis of two large clinical trials, Lilly concluded that mild Alzheimer's patients who begin early treatment with its drug, solanezumab, lose cognition and function at a slower rate than those who begin taking the drug later. The inability of “delayed-start” solanezumab patients to catch up to “early” solanezumab patients suggests the drug has a positive, modifying effect on Alzheimer's, according to Lilly.

MERGER/ACQUISITIONS/COLLABORATION

6.1. Epirus and Polpharma collaborate on advancing biosimilars portfolio targeting $6 billion addressable market July 14, 2015

- EPIRUS Biopharmaceuticals, Inc. and Polpharma Group announced the signing of a multi-product, multi-region profit-sharing collaboration for select EPIRUS biosimilars, including BOW015 (infliximab, reference biologic Remicade®), BOW050 (adalimumab, reference biologic Humira®) and BOW070 (tocilizumab, reference biologic Actemra®), representing $6 billion in innovator sales in the specified territories. Polpharma Group is a leading generics company based in Poland with annual sales of approximately $1 billion and a strong commercial infrastructure, including a sales force of over 1,700 employees globally.

6.2. Lupin to expand US generic business with acquisition of GAVIS Pharma July 23, 2015

- Pharma Major Lupin Limited (Lupin) has entered into a definitive agreement to acquire privately held GAVIS Pharmaceuticals LLC and Novel Laboratories Inc. (GAVIS), subject to certain closing conditions, in a transaction valued at USD 880 million, cash free and debt free. The transaction has been unanimously approved by the Boards of Directors of Lupin and GAVIS. The acquisition enhances Lupin's scale in the US generic market and also broadens Lupin's pipeline in dermatology, controlled substance products and other high-value and niche generics. GAVIS brings to Lupin a highly skilled US based R & D organization which would complement Lupin's Coral Springs, Florida, inhalation R&D center. GAVIS's New Jersey based manufacturing facility will become Lupin's first manufacturing site in the US.

6.3. Teva to Acquire Allergan Generics for $40.5 Billion July 26, 2015

- Teva Pharmaceutical Industries Ltd. announced that it has signed a definitive agreement with Allergan plc to acquire Allergan Generics in a transaction valued at $40.5 billion. Upon closing, Allergan will receive $33.75 billion in cash and shares of Teva valued today at $6.75 billion, representing an estimated under 10% ownership stake in Teva, with the number of Teva shares determined based on Teva's volume weighted average trading prices during the 15 days prior to the announcement and five days following the announcement. This strategic acquisition brings together two leading generics businesses with complementary strengths, brands and cultures, providing patients with more affordable access to quality medicines, and creating significant financial benefits for Teva stockholders.

PATENT (NEW APPROVAL/ LITIGATION/SETTLEMENTS)

7.1. Delhi HC stays order restraining Lupin from using disputed trademark July 14, 2015

- The Delhi high court stayed an earlier order, passed on 26 February, restraining Lupin Ltd from using the trademark LUCYNTA for its medicines, said to be deceptively similar to the trademark NUCYNTA used by Johnson and Johnson. Johnson alleged that Lupin's mark was illegal and malafide. The court ruled in favour of Johnson that such reversal could be brought about with the burden of proof on the one who alleges it, in this case Johnson and Johnson.

7.2. Indian High Court upholds B-MS' patent for cancer drug Sprycel (Dasatinib) July 14, 2015

- Bristol-Myers Squibb has won a court verdict to uphold its patent on Sprycel (dasatinib), fending off a challenge, for now, from India's BDR Pharmaceuticals, which sought a compulsory license to make the drug and sell it at a lower cost domestically. BDR cited a provision in the Indian Patent Act that disallows so-called ever greening of drugs as the basis for its compulsory license application, but Justice Manmohan of the Delhi High Court rejected the claim.

7.3. Court allows Sandoz to launch first US biosimilar in September July 22, 2015

- Novartis' Sandoz unit will begin selling a biosimilar for Amgen's cancer treatment Neupogen on September 2, thanks to an appeals court ruling released Tuesday. Sandoz biosimilar was approved by USFDA in March 2015. The matter was pending in the court after law suit filed by Amgen.

TECHNOLOGY/NDDS NEWS

8.1. Novartis introduces first app for visually impaired people for use with Apple Watch & other smart watches July 01, 2015

- Novartis Pharmaceuticals, a global healthcare company, announced the launch of new features for its ViaOpta applications, and the extension for use with smart watches. The discreet, hands-free nature of using ViaOpta app with wearable devices, such as Apple Watch and Android Wear, provides users with an experience that seamlessly fits into their existing routines allowing those with visual impairments to navigate daily life with even greater ease."With the help of ViaOpta apps, people with impaired vision can do things such as walk to a nearby café, go to the pharmacy, and pick up their grandchildren at the kindergarten - helping to increase confidence and independence and maintaining discretion," explains Ian Banks, chair, The European Forum Against Blindness (EFAB).

8.2. CytRx introduces novel LADR technology platform July 02, 2015

- CytRx Corporation, a biopharmaceutical research and development company specializing in oncology, has launched its proprietary LADR (Linker Activated Drug Release) technology platform, a discovery engine designed to leverage the company's expertise in albumin biology and linker technology for the development of a new class of anti-cancer therapies. CytRx expects the LADR platform to rapidly expand its pipeline of oncology drug candidates, providing an avenue for the development of propriety drug candidates that complement its global phase 3 aldoxorubicin programme. Among the cancers being pursued are liver, pancreatic, and non-small cell lung cancer.

8.3. Lilly introduces Android version of Glucagon mobile app to support people with diabetes July 16, 2015

- Lilly Diabetes, a global leader in diabetes care, has launched Lilly Glucagon Mobile App, an Android version of its mobile application designed for caregivers and healthcare providers who support people with diabetes. Through an injection tutorial and emergency instructions, the App can help people practice the injection steps ahead of time, which may help them, feel better prepared to assist. Other features of the App include a kit location log, so kits can be easily located during an emergency, and an expiration date log that sends a reminder when a kit is getting close to its expiration date, so a new kit can be obtained before this date.