Lambda Research Newsletter

January 2018

LAMBDA

Research Accelerated

Contact Us

Dr. Tausif Monif
President - Global operations
tausifmonif@lambda-cro.com

Dr. Mrinal Kammili
Ex. Director – Global Head, BD
mrinal@lambda-cro.com

LAMBDA

Research Accelerated

Volume 1 / January 2018

Clinical Research NEWSletter

www.lambda-cro.com

Contents

LAMBDA

Research Accelerated

Volume 1 / January 2018

Clinical Research NEWSletter

www.lambda-cro.com

Contents

Disclaimer: "The information compiled and published in this newsletter has been sourced, collected and derived from various resources which are in the public domain available on the web and relevant sites. Lambda makes no claims, promises or guarantees about the accuracy, completeness, or adequacy of the contents of the newsletters and expressly disclaims liability for errors and omissions in the contents of this newsletter. The intent and object of this Newsletter is to only disseminate scientific information for knowledge up-gradation. The transmission or reproduction of any items covered in this newsletter beyond that allowed by fair use as defined in the copyright laws may require the written permission of the copyright owners, if any. Neither Lambda, nor its employees and contractors make any warranty, expressed or implied or statutory, including but not limited to the warranties of non-infringement of third party rights, title, and the warranties of merchantability and fitness for a particular purpose with respect to content available from the newsletters. This is not a service by Lambda Therapeutic Research and it does not hold any responsibility for the accuracy of the news/information provided herein."

LAMBDA
Research Accelerated

Clinical Research NEWSletter
www.lambda-cro.com

Volume 1 / January 2018

GLOBAL NEWS

1. Brexit may impose burden on pharma companies

According to the recent statements, from global drug makers Johnson & Johnson to AstraZeneca Plc, potential regulatory hurdles and trades may burden the companies for additional cost after the separation of Britain from the European Union (EU).

The UK government provided a written testimonial to pharmaceutical companies for the continued ease of access to the EU market. The testimonial ensures that the pharma companies will not have to face restrictive tariffs, delays at ports and divergent rules after Brexit. Another concern raised was about the departure of skilled workers.

Johnson & Johnson stated that if mutual reorganization between the UK and EU is not done, then the company could face as many as 50,000 additional tests for its products with the annual cost of approximately 1 million pounds ($1.35 million). Similarly, Brexit could pose significant costs for German companies.

After Brexit, the companies without EU membership, i.e. UK drug makers, have to pay duties as high as 6.5% on exports of products and ingredients. This will cost the Cambridge England-based companies as much as $31 million in annual duties.

Source: bloomberg.com

LAMBDA
Research Accelerated

Volume 1 / January 2018

Clinical Research NEWS letter
www.lambda-cro.com

GLOBAL NEWS

2. Global biosimilar monoclonal antibodies market expected to rise

MarketResearch.biz published a research report, which explains complete view on the global market of biosimilar monoclonal antibiotics. The report contains a systemic segment which covers each and every aspect of the targeted markets. According to the report, the first five years (2017-2021), the cumulative revenue is projected to be US$ 20,543.2 Million. This revenue is expected to rise in the next five years.

The report was entitled as "Global Biosimilar Monoclonal Antibodies Market by Drug Class (Rituximab, Infliximab, Abciximab, Trastuzumab, Adalimumab, and Bevacizumab), Application, and Region - Global Forecast to 2026". Monoclonal antibodies (mAbs) are produced from the identical immune cells and are similar to each other, so are termed as biosimilar monoclonal antibodies.

The report shows that mAbs have a dynamic market as there are many products in the pipeline, and biosimilars are priced lower as compared to that of biological drugs. The development of mAb for various therapeutic areas like oncology, autoimmune, inflammation, immunology, CNS disorders, infectious disease, and metabolic disorders will promote the growth of the biosimilar market.

Patent expiry of some major biologicals such as Neupogen, Lantus, Humira and Remicade will also influence the market of biosimilars, and expected to widen the market for biosimilars.

Source: biosimilardevelopment.com

LAMBDA
Research Accelerated

Volume 1 / January 2018

Clinical Research NEWSletter
www.lambda-cro.com

GLOBAL NEWS

3. Brexit leads to relocation of EMA headquarters to Amsterdam

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

The European Council (EC) has resulted in the relocation of European Medicines Agency's (EMA) headquarters from London to Amsterdam. This transition will not only relocate EMA headquarters, but will also relocate nearly 900 staffers to Amsterdam. This complete transition is expected to complete by 30 March 2019.

This decision was made after UK decided to leave EU. In total 19 cities was enlisted initially for the relocation of EMA headquarters and the EU members voted.

For the first round of voting Milan (with 25 votes), Copenhagen and Amsterdam (with 20 votes each) advanced out the other cities. Milan (with 12 votes) and Amsterdam (with 9 votes) then proceeded into the third round of voting. In the final round of voting, Milan and Amsterdam both tied with 13 votes each, sending the final vote to a drawing of lots, which Amsterdam won.

In a survey of employees, Amsterdam, Barcelona and Vienna were on the top choices whereas Warsaw, Poland, Bucharest, Romania, and Sofia, Bulgaria were rated the lowest.

Source: raps.org

LAMBDA
Research Accelerated

Volume 1 / January 2018

Clinical Research NEWS letter
www.lambda-cro.com

GLOBAL NEWS

4. Global market for Insulin biosimilar: 2017-2023

The latest statical publication of Global Insulin Biosimilars market shows that the market of the Insulin biosimilars is growing with a very fast rate mainly for the type 1 diabetes. The ongoing approvals by the government authorities are nurturing the market growth of the products.

Growing population exposures, technological developments and favorable medical repayment scenario in developed countries are some of the factors, which are favorable for the positive growth of the market. But some of the factors like patent protection of Insulin and other products are limiting the market.

Patents expiry of the number of products in next few years will also help in the expansion of the market. The prices of the biosimilar drugs are expected to decrease as compared to that of the branded drugs, which will help to widen the market.

Wockhardt Limited, NOVO Nordisk A/S, Ypsomed AG, Pfizer Inc., Biocon Limited, Eli Lilly & Co, Mylan N.V., Boehringer Ingelheim GmbH, Sanofi S.A., and Merck & Co., are the top leaders in the market of diabetic products. The products of these companies are approved for both Type I Diabetes and Type II Diabetes. The biosimilars covered by these companies are:

- Rapid-Acting Biosimilars
- Long-Acting Biosimilars
- Premixed Biosimilars

Source: biosimilardevelopment.com

LAMBDA
Research Accelerated

Clinical Research NEWSletter
www.lambda-cro.com

Volume 1 / January 2018

PHARMA INDIA

1. Indian Pharma shows a positive growth with an increase of 8.1%

By the end of November 2017, the growth of Indian Pharma market improved by 8.1% (10,291 crore) which was 4.6% for April-November 2017, after Goods and Services Tax (GST) implementation. The Global Distribution Systems (GDs) volume also increased by 6.5% but decline in the prices was noted by 1.5%, which impacted the growth.

MNCs also grew by 4.4% by the end of the November 2016. As compared to MNCs, Indian companies moved faster at 9% resulting in an overall growth of 8.1 per cent for the month of November 2017.

Overall, 29 regions have shown a positive growth with Jharkhand showing a maximum growth of 21.3%, followed by UP East 17.6% and North Karnataka with 16.1%.

Table mentioning top pharma companies with maximum growth and top drug category

Drug category	Growth noted
Anti-infectives	7.9%
Dermatology	11.9%
Gastro intestinal	6.8%
Anti-diabetic	-6.0%
Cardio segment	4.4%
CNS	7.6%
FDC Related	16.5%
Non FDC related	12.8%

Top companies	Growth
Mankind	27.6%
Alkem	13.9%
Lupin	12.5%
Top MNCs	**Growth**
Allergan	22.1%
Eli Lilly	12.7%
Novartis	11.5%

CNS: central nervous system; FDC: Fixed dose combination; MNCs: Multinational companies

Source: pharmabiz.com

LAMBDA
Research Accelerated

Clinical Research NEWS letter
www.lambda-cro.com

Volume 1 / January 2018

PHARMA INDIA

2. Gujarat FDCA join hands with US FDA to train Indian drug regulators

The Gujarat Food and Drug Control Administration (FDCA) and the US Food and Drug Administration (FDA) have signed a Memorandum of understanding (MoU) for the training of drug control officials of Gujarat on par with US FDA inspectors. This MoU has been signed to provide safe and efficacious medicines in the global market.

This MoU was signed after the US FDA officials visited the Gujarat FDCA, as a part of the global harmonization programme for capacity building, training, networking, knowledge sharing and compliance. This is more important because Gujarat exports around 28% of drug exports to developed markets and the US.

Some senior members of the US FDA were part of the US FDA team which visited the Gujarat FDCA office. Gujarat FDCA held a presentation for the US FDA team which was appreciated by them.

The recent MoU is in line with the series of MoUs between the regulatory agencies since 2008, which helped Gujarat drug officials to better understand the regulatory requirements for US FDA submissions.

Source: pharmabiz.com

LAMBDA
Research Accelerated

Clinical Research NEWS letter
www.lambda-cro.com

Volume 1 / January 2018

PHARMA INDIA

3. Indian pharma market exports expected to touch $20 billion by 2020

With an annual growth rate of about 30%, Indian Pharma market is expected to touch $20 billion by 2020. At present, Indian pharma market exports amount to about $16.5 billion. Whereas the total Indian Pharma market is expected to register a growth of about 16% in 2018 and likely to touch $55 billion by 2020, with present level of $28 billion.

At present, in the global generic Active Pharmaceutical Ingredient (API) manufacturers, India is ranked at number 3 in terms of market share and generic drugs form the largest segment. India is the largest provider of generic drugs globally by volume. Other than API, India is on number 2 for the Abbreviated New Drug Applications (ANDAs) and is the world lead for Drug Master Files (DMFs) applications with the US.

Around 24,000 pharmaceutical companies are there in India, out of which 250 are in the organized category and these organized category companies' control nearly 70% of the market. Other than organized category, India has around 8000 small scale units of pharmaceutical industries.

A number of highly profitable drugs are going to be off-patent in the coming years, which will also help Indian pharmaceutical companies to earn more profits.

Source: business-standard.com

LAMBDA
Research Accelerated

Clinical Research NEWS letter
www.lambda-cro.com

Volume 1 / January 2018

PHARMA INDIA

4. Indian R & D based pharma companies secure 36% of total ANDAs approvals in 2017

In the year of 2017, the US Food and drug administration (FDA) approved 846 Abbreviated New Drug Applications (ANDAs) and out of those, Indian R & D based pharma companies received 304 ANDAs approvals. The number of approvals in the previous year was 201. With the enhanced R & D investments from the last couple of years, now Indian companies managed to secure almost 36% of the total approvals.

Other than ANDS, the USFDA approved 171 tentative approvals, and out of those approvals, 61 were grabbed by Indian companies. This higher rate of approval will lead to higher revenues in the future. During the last 10 years (2008-2017), US FDA approved a total of 5,020 ANDAs and 1184 tentative approvals. The Indian pharma managed to secure 1,695 ANDAs and 455 tentative approvals i.e. almost 34% of the total approvals.

In the Indian Pharma, Cadila Healthcare and its US based subsidiary Zydus Pharmaceutical USA Inc., remained on the top with 71 approvals. Cadila was followed by Aurobindo Pharma (51), Sun Pharma & Taro Pharma (21) Glenmark Pharmaceutical (18), Gland Pharma (16), Alkem Laboratories (15), Macleods Pharma (15), Lupin (13), Cipla and Dr Reddy's Laboratories with 10 each, and Strides Shashun and Alembic Pharma with 9 ANDA approvals.

Besides above pharm companies, others like Jubilant Lifesciences, Ajanta Pharma, Micro Labs, Unichem Laboratories, Torrent Pharma, Natco Pharma, Orchid Pharma, Panacea Biotic, Granules India, Hetero Labs, Intas Pharma, Marksans Pharma and Vintage Pharma also received drug approvals from US FDA in 2017.

Source: pharmabiz.com

LAMBDA
Research Accelerated

Clinical Research NEWSletter
www.lambda-cro.com

Volume 1 / January 2018

REGULATORY ROUND-UP

1. FDA introduces two new draft guidances for developing targeted therapies

The US Food and Drug Administration (FDA has released two new draft guidance documents to support the development of genetic mutation treatment options, which causes diseases. The draft guidances also mention as to how to determine if any of the in vitro diagnostic devices (IVD) used in the study should undergo its own FDA review, different from the drug study.

A number of new drugs are under development for targeting the underlying cause of genetic mutations. When drugs successfully target the molecules responsible for the mutations, the effects can be reversed to cure the diseases. The agency is trying to develop a pathway which will allow the new drugs to pursue approvals in each novel setting on the basis of targeted molecular marker.

In the year of 2017, for the 1st time, the FDA approved a tissue-agnostic treatment as Merck's Keytruda (pembrolizumab). This approval was based on a common biomarker rather than the location in the body where the tumor originated. These two guidelines will help other companies to take approval by the same route as that followed by Merck.

The guidance document will help the companies to develop certain targeted therapies on the basis of targeting a molecular subtype that is common across different phenotypes. These guidances mainly focus on the type and quantity of evidence to demonstrate efficacy across these molecular subsets within a disease.

Source: raps.org

LAMBDA
Research Accelerated

Volume 1 / January 2018

Clinical Research NEWSletter
www.lambda-cro.com

REGULATORY ROUND-UP

2. European commission creates a new roadmap for the evaluation of pediatric rare disease legislation

The European Commission (EC) has developed a new road map for the evaluation of legislations covering pediatrics' rare diseases. Officials have developed a two year evaluation plan to understand the failure of regulations and orphan medicines to translate into hoped-for medical advances.

From the report provided on Paediatric Regulation, the officials want to assess that whether the laws have met their objectives or not. This will help the officials to look into the strengths and weaknesses of the legislation in combination and separately. This evaluation is mainly designed for the development of treatment options for unmet need.

This evaluation by EC will provide sound evidence for the functioning of the two legal instruments from a public health and a socioeconomic perspective. The officials are also planning for the inclusion of factors related to global development, mainly in the US, into their analysis.

The 12 week public consultation will be started by the 3rd quarter of 2018 with a stake holder meeting organized by the Commission scheduled to follow in the first quarter of 2019. The officials will publish a summary of the findings after its completion.

Source: raps.org

LAMBDA
Research Accelerated

Volume 1 / January 2018

Clinical Research NEWS letter
www.lambda-cro.com

REGULATORY ROUND-UP

3. FDA introduces new draft guidances for homeopathic products

The US Food and Drug Administration (FDA) has introduced new draft guidances to take in the new risk-based enforcement approach for the drug products labeled as homeopathic in the market. These guidances will come into action for prioritizing enforcement actions against these homeopathic drugs.

At present, without any new Congressional action, the agency will not be able to remove products from the market. In addition to draft guidances, the agency also released new warning letters for the Canada based Deserving Health International. This company offers a product for ophthalmic use that was manufactured with non-sterile water which may be contaminated.

According to the FDA, their intention is not to remove all the homeopathic medical products from the market but the option to take action against the products that contain or purport to contain ingredients associated with potentially significant safety concerns.

Source: raps.org

LAMBDA
Research Accelerated

Volume 1 / January 2018

Clinical Research NEWSletter
www.lambda-cro.com

REGULATORY ROUND-UP

4. FDA introduces new guidelines for BA/BE Studies

The US Food and Drug Administration (FDA) introduced new guidelines for the sponsors wishing for the waiver of an *in vivo* bioavailability (BA) and/or bioequivalence (BE) study. These guidelines are specifically for the immediate release (IR) solid oral dosage forms based on the Biopharmaceutics Classification System (BCS).

These guidelines are modifications of the 2015 draft guidelines. These guidelines explain the necessary requirements to the sponsors for the investigational new drugs (INDs) and applicants of new drug applications (NDAs), abbreviated new drug applications (ANDAs) and supplements who wish to request a waiver. These guidelines are intended to apply to the wavier required during IND period and NDA stages.

The BCS is a scientific frame work by the FDA to classify drug substances based on their solubility and intestinal permeability. BCS takes into account three major factors which govern the rate and extent of drug absorption of IR solid oral dosage forms. The 3 main factors are dissolution, solubility and intestinal permeability.

According to the BCS, drug substances are classified as follows:

- Class 1: High Solubility – High Permeability
- Class 2: Low Solubility – High Permeability
- Class 3: High Solubility – Low Permeability
- Class 4: Low Solubility – Low Permeability

Source: raps.org

LAMBDA
Research Accelerated

Clinical Research NEWSletter
www.lambda-cro.com

Volume 1 / January 2018

MERGERS /ACQUISITIONS /COLLABORATIONS

1. Pfizer acquires licensing rights for Cresemba of Basilea Pharmaceutica in China

Pfizer has signed an in-licensing agreement with Basilea Pharmaceutica for the exclusive development and commercialization rights of Cresemba (isavuconazole) in China and the Asia Pacific region. Isavuconazole is developed for the treatment of adults with invasive aspergillosis and mucormycosis. Isavuconazole is an oral azole anti-fungal and an active ingredient of isavuconazonium sulfate prodrug, administered intravenously.

This is the second in-licensing agreement between Pfizer and Basilea Pharmaceutica for this product. The last in-licensing agreement was signed in July 2017 for the rights of Cresemba in Europe, except Nordic countries.

Currently, Pfizer is marketing the drug in Austria, France, Germany, Italy, UK and Spain, and plans to launch in other countries over time. Now, this in-licensing deal will allow Pfizer to launch the drug in China and 16 Asia Pacific countries, except Japan.

Cresemba was approved by the US Food and Drug Administration (FDA) in March 2015 for invasive aspergillosis and mucormycosis treatment in adult patients.

Source: pharmaceutical-technology.com

LAMBDA
Research Accelerated

Volume 1 / January 2018

Clinical Research NEWS letter
www.lambda-cro.com

MERGERS /ACQUISITIONS /COLLABORATIONS

2. Astellas Pharma acquires Mitobridge for the development of a new drug to target mitochondrial functions

Astellas Pharma has acquired the US based biotechnology company Mitobridge. This acquisition will accelerate the discovery and development of new treatment options to target mitochondrial functions. This acquisition has been carried out with an amendment in the partnership agreement signed in October 2013.

The partnership agreement was established for the research and development (R&D) collaboration between the two companies. Under this acquisition, an amount of $225m was paid as an upfront payment to Mitobridge by Astellas Pharma. Depending on the progress of the various programs, in addition to the upfront amount, Mitobridge will be eligible for additional payments totaling up to $225m.

Mitobridge is a shareholder of this program, so Astella Pharma will actually pay an amount of $165.5m. This amount will make Mitobridge a wholly owned subsidiary of Astellas. The amount will be paid on a fully diluted basis.

MA-0211 is the most advanced investigational therapy from this partnership. MA-0211 is a potential treatment of duchenne muscular dystrophy (DMD) and currently in Phase 1 development.

Source: pharmaceutical-technology.com

LAMBDA
Research Accelerated

Volume 1 / January 2018

Clinical Research NEWSletter
www.lambda-cro.com

MERGERS /ACQUISITIONS /COLLABORATIONS

3. Bayer extends collaboration with Broad Institute of MIT and Harvard for the development of new cancer treatment options

Bayer has extended its 4 year old collaboration with the Broad Institute of MIT and Harvard, to develop new options for the treatment of cancer. In this collaboration, the firms will identify additional three new investigational drugs (INDs) for new oncology targets.

In addition to the development, the firms will also generate related intellectual property to share the biological knowledge openly with the scientific community.

The collaboration established with the Broad Institute's cancer research and chemical biology expertise in 2013 leverages Bayer's experience on molecules and biologics drug discovery. This collaboration was extended in 2015, and now the latest extension is upto 2023.

In the 2015 extension, new genomics and drug discovery in cardiovascular disease was added; whereas the latest extension will include the contribution of the institute's expertise in biomarker development, patient selection and design of clinical trials.

Source: pharmaceutical-technology.com

MERGERS /ACQUISITIONS /COLLABORATIONS

4. Array BioPharma enters into a strategic collaboration with Pfizer

Array BioPharma has entered into a strategic collaboration with Pfizer, for conducting clinical trials to demonstrate safety and efficacy of several novel anti-cancer combinations. This collaboration includes clinical trials for Array's MEK inhibitor, binimetinib along with Pfizer's investigational poly ADP ribose polymerase (PARP) inhibitor talazoparib and avelumab - a human anti- programmed death-ligand 1 (PD-L1)-Immunoglobulin G 1 (anti-PD-L1 IgG1) monoclonal antibody.

The aim of this collaboration is to explore the potential benefits, which can be obtained by combining molecularly targeted therapeutics with innate immunotherapy i.e. body's innate ability for fighting cancer. These novel combinations of targeted therapy and immunotherapy have the potential for treatmenting several different types of cancers. The collaboration is initially focused on lung and pancreatic cancers.

Data obtained from preclinical studies indicate that, the combination of binimetinib with an immune checkpoint inhibitor and talazoparib could be rational. Now, Pfizer is looking forward to initiate clinical trials for dual and triple FDCs with Array BioPharma to explore anti-tumor activities of various novel combinations.

Under this collaboration, Array and Pfizer will initiate Phase 1b clinical trial to explore the safety and efficacy of different combinations. It is expected to be a multi-arm clinical trial to establish recommended doses of different regimens of the combiantions of these drugs.

Source: pharmpro.com

LAMBDA
Research Accelerated

Volume 1 / January 2018

Clinical Research NEWSletter
www.lambda-cro.com

DRUGS: APPROVALS AND LAUNCHES

1. GSK receives EC approval for Benlysta to treat SLE patients

GSK has received the European Commission (EC) approval for Benlysta (belimumab) for the treatment of patients with active autoantibody-positive systemic lupus erythematosus (SLE). GSK has introduced Benlysta as an add-on therapy in Europe for the treatment of adult patients with active autoantibody-positive SLE and a high degree of disease activity despite standard therapy.

Benlysta is approved in the form of intravenous (IV) and subcutaneous (SC) formulations. The injection is available as a single-dose prefilled syringe and a single-dose prefilled pen (autoinjector) administered as a once-weekly injection of 200 mg. This GSK therapy is currently the only medicine particularly developed and approved for SLE.

The approval was based on the results of a Phase 3, BLISS-SC trial. This was a 52- week randomized, double-blind, placebo-controlled study carried out at 177 sites in 30 countries in North, Central, and South America, Eastern and Western Europe, Australia, and Asia between November 2011 and February 2015. The study was conducted on more than 800 patients with active SLE. The results of the study are published in the '***Journal of Arthritis & Rheumatology***'.

Benlysta is a human monoclonal antibody, which acts as a specific B-lymphocyte stimulator (BLyS) inhibitor. SLE is a chronic, incurable, autoimmune disease. The disease is accompanied with a range of symptoms that can fluctuate over time and affect almost any system in the body. SLE results in painful or swollen joints, extreme fatigue, unexplained fever, skin rashes and organ damage.

Source: pharmaceutical-technology.com

LAMBDA
Research Accelerated

Clinical Research NEWSletter
www.lambda-cro.com

Volume 1 / January 2018

DRUGS: APPROVALS AND LAUNCHES

2. USFDA approves buprenorphine once monthly injection for the treatment of moderate-to-severe OUD

The US Food and Drug Administration (FDA) has approved the first once-monthly injectable buprenorphine (Sublocade) for the treatment of moderate-to-severe opioid use disorder (OUD) in adult patients. This treatment option can only be used in the patients who have initiated treatment with a transmucosal buprenorphine-containing product and were found to be stable for a minimum of seven days.

OUD is associated with the chronic neurobiological disease characterized by a problematic pattern of opioid use. OUD?? can lead to a significant impairment or distress and includes signs and symptoms that reflect compulsive, prolonged self-administration of opioid substances for no legitimate medical purpose. In some another medical conditions where opioid treatment is required, a very high dose of opioid is needed for the therapeutic effect.

Sublocade is a combination of drug and device which contains buprenorphine and the Atrigel Delivery System in a pre-filled syringe. The drug is injected by the health care professional (HCP) subcutaneously as a solution. Sublocade provides sustained therapeutic plasma levels by forming a solid deposit of buprenorphine and then the drug is released by degradation of the deposit over a one-month period.

The approval was based on the two clinical studies conducted on 848 patients with moderate-to-severe OUD, who began treatment with buprenorphine/naloxone sublingual film. Results of these trials indicate that Sublocade-treated patients had more weeks without positive urine tests or self-report of opioid use throughout the treatment period as compared to the placebo group.

Source: pharmabiz.com

LAMBDA
Research Accelerated

Volume 1 / January 2018

Clinical Research NEWS letter
www.lambda-cro.com

DRUGS: APPROVALS AND LAUNCHES

3. Cipla receives USFDA approval for Budesonide Inhalation Suspension

The United States Food and Drug Administration (USFDA) has approved Cipla's anti-asthma product Budesonide Inhalation Suspension.

Budesonide Inhalation Suspension was filed for approval under abbreviated new drug application (ANDA) in different concentrations of 0.25mg/2mL, 0.5mg/2mL, and 1mg/2mL.

Budesonide Inhalation Suspension is a generic version of AstraZeneca's Pulmicort Respules. Pulmicort Respules are recommended for the maintenance treatment of asthma and as a prophylactic therapy in children.

The sale of Pulmicort Respules and generic equivalents in US was USD 825 million for the 12 months to September 2017.

Source: health.economictimes.indiatimes.com

LAMBDA
Research Accelerated

Volume 1 / January 2018

Clinical Research NEWSletter
www.lambda-cro.com

DRUGS: APPROVALS AND LAUNCHES

4. USFDA approves Pfizer's sunitinib as first and only adjuvant treatment for high risk recurrent renal cell carcinoma

Pfizer received the U.S. Food and Drug Administration (FDA) approval for the use of SUTENT® (sunitinib malate) for a new indication. Sunitinib is now approved for the adjuvant treatment of adult patients at high risk of recurrent renal cell carcinoma (RCC) following nephrectomy. Drug was initially approved as a standard-of-care for the treatment of advanced RCC.

Sunitinib is a multiple receptor tyrosine kinase inhibitor, which acts on the tumorous growth of the cells. The drug approval was based on the results from the S-TRAC trial. The S-TRAC trial was a multicenter, international, randomized, double-blind, placebo-controlled Phase 3 trial of SUTENT versus placebo in 615 patients with clear cell histology and a high risk of recurrent RCC following nephrectomy.

The results of S-TRAC trial showed that sunitinib had significant reduction in the risk of a disease-free survival (DFS) event for patients at high risk of RCC recurrence who received SUTENT compared to placebo in the adjuvant setting. The results of the study were published in the *New England Journal of Medicine* in October 2016.

In the S-TRAC trial, the Hazard Ratio (HR) was found to be 0.76 with a 2-sided p-value of 0.03 in favor of SUTENT, representing a statistically significant relative reduction of 24% in the risk of a DFS event. The median DFS was 6.8 years in the SUTENT arm as compared with 5.6 years in the placebo arm. At five years, the DFS rate for patients receiving SUTENT was 59.3% and 51.3% for placebo. This represents an absolute benefit of 8%. No new safety issues were found in the S-TRAC trial.

Source: worldpharmanews.com

LAMBDA
Research Accelerated

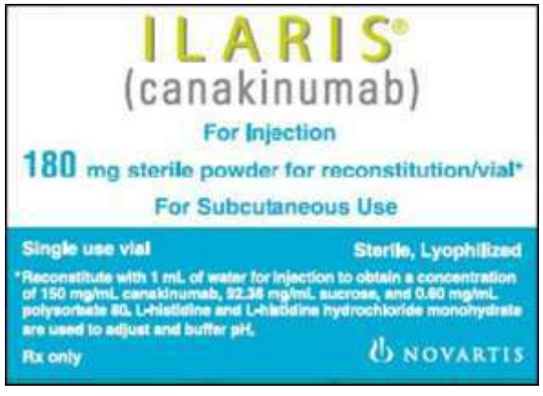
Clinical Research NEWSletter
www.lambda-cro.com

Volume 1 / January 2018

DRUGS: DEVELOPMENT & CLINICAL TRIALS

1. Canakinumab shows 25% reduction in cardiovascular risk in Phase 3 subgroup analysis

Novartis Pharmaceutical's canakinumab showed positive results in the Phase 3= CANTOS study for the reduction of cardio vascular events by 25%. The results of the study was presented in the American Heart Association (AHA) Scientific Sessions 2017 and published in The Lancet.



This was a pre-planned secondary analysis of CANTOS study. In the exploratory endpoints, the study showed that the people with prior heart attacks who achieved high-sensitivity C-reactive protein (hsCRP) levels below 2mg/L after three months following the 1st dose of canakinumab, had reduced major adverse cardiovascular events (MACE) versus placebo by 25% ($p<0.0001$).

Canakinumab showed a significant reduction in cardiovascular deaths by 31% ($p=0.0004$) and all cause deaths ($p<0.0001$). There was no significant reduction in the events with hsCRP levels ≥2mg/L. The patients needed to treat (NNT) were also evaluated in the analysis.

The CANTOS trial was a one of the largest and longest trial by the Novartis. In this study, >10,000 patients were enrolled for a period of 6 years. Previous data from the trial showed that quarterly treatment with 150mg canakinumab shows statistically significant 15% reduction in MACE.

Source: pharmpro.com

LAMBDA
Research Accelerated

Volume 1 / January 2018

Clinical Research NEWSletter
www.lambda-cro.com

DRUGS: DEVELOPMENT & CLINICAL TRIALS

2. Drops of new drug can treat retinal diseases instead of injections

Sylentis biotechnology has developed a compound SYL136001v10 for the treatment of retinal diseases such as macular degeneration and diabetic retinopathy. The drug is developed for the ophthalmic insertion in the form of eye drops instead of intraocular injections.

SYL136001v10 is 10 times smaller interfering RNA as compare to other treatment options and due to its small size, it is capable of penetrating retinal cells. In the retinal cells, it prevents the synthesis of NOTCH Regulated Ankyrin Repeat Protein (NRARP) and blocks the formation of new blood vessels. This new drug is developed by biotechnology and is able to penetrate the retina to treat age-related macular degeneration and diabetic retinopathy.

SYL136001v10 is still in its preclinical phase and its effectiveness was proven on animal models. Human trials are expected to begin by the end of 2018. The results were presented at the XIII Annual Meeting of the Oligonucleotides Therapeutics Society, held in Bordeaux (France).

The efficacy study shows that reduction of NRARP in the retina by means of siRNA reduced new blood vessel formation.

Source: eurekalert.org

LAMBDA
Research Accelerated

Volume 1 / January 2018

Clinical Research NEWSletter
www.lambda-cro.com

DRUGS: DEVELOPMENT & CLINICAL TRIALS

3. Ionis Pharmaceuticals develops a new drug for Huntington's disease

For the first time ever, the researchers at Ionis Pharmaceuticals have developed a new drug IONIS-HTT(Rx) for the treatment of Huntington's disease. This new drug will fix the protein defect responsible for Huntington's disease by injecting the drug in spine.

Huntington's disease is a progressive neurodegenerative disorder affecting mental ability as well as physical control. The disease mainly affects between the ages of 30 and 50 years. Currently, there is no treatment option available with drugs only available for symptomatic treatment.

After the success of the early stage study, Roche has in-licenseed the product at a cost of $45 million. Now, Roche will be responsible for all development plans and commercialization of IONIS-HTT(Rx). Researchers are now planning to run a large clinical trial very soon to show that the drug slows down the progression of the disease.

IONIS-HTT(Rx) uses an approach of antisense to stop a gene producing a particular protein responsible for the disease.

Source: health.economictimes.indiatimes.com

LAMBDA
Research Accelerated

Volume 1 / January 2018

Clinical Research NEWSletter
www.lambda-cro.com

DRUGS: DEVELOPMENT & CLINICAL TRIALS

4. Addition of Roche's Polatuzumab vedotin to standard therapy shows better results in lymphoma patients

The data presented at a medical meeting, shows that the addition of polatuzumab vedotin to the standard lymphoma treatment leads to a far higher rate of remission and significant longer life of patients than the standard treatment alone. Polatuzumab vedotin is the new investigational drug by Roche Pharmaceutical for the treatment of large B-cell lymphoma.

The data presented in the meeting was from mid-stage trial. In the trial, 80% patients with diffuse large B-cell lymphoma (DLBCL) were enrolled, which showed disease progression even after treatment with several treatment regimens. Addition of polatuzumab vedotin in the standard therapy increased the response rate by 40% as compared to 15% with standard therapy alone in DLBCL patients with the complete response and no detectable symptoms of cancer.

Rituxan (Roche) and Treanda (Teva) were used as standard therapies. In a study presented in the ***American Society of Hematology meeting*** in Atlanta, polatuzumab showed 65% reduction in the risk of death. The overall median time survival was 11.8 months for polatuzumab compared with only 4.7 months for the standard therapy.

Polatuzumab is an antibody drug conjugate mainly designed to link therapeutic antibodies to cancer cell killing agents with minimum effect on normal cells. Polatuzumab acts on a specific protein mainly expressed in majority of B-cell lymphoma patients.

Source: health.economictimes.indiatimes.com

LAMBDA
Research Accelerated

Volume 1 / January 2018

Clinical Research NEWSletter
www.lambda-cro.com

PATENTS: NEW APPROVALS /LITIGATIONS /SETTLEMENTS

1. Mesoblast limited grants global patent license for Cx601 to TiGenix for the treatment of fistulae

TiGenix receives exclusive access to certain patents of Mesoblast Limited, to support global commercialization of the adipose-derived mesenchymal stem cell product Cx601 for the local treatment of fistulae. This agreement will also provide rights to TiGenix to provide license to sublicense to affiliates as third parties, including TiGenix's current development and commercialization partner ex-United States.

For this agreement, Mesoblast will receive upto €20 million (approximately USD$24 million) in payments. From the total amount, Mesoblast will receive €5 million upfront, €5 million within 12 months, and up to €10 million in product regulatory milestones. Mesoblast will also receive single digit royalty from the net sale of the product.

TiGenix is advancing their pivotal Phase 3 clinical trial and further Biologics License Application (BLA) to the US FDA for pursuing the development of new indications for Cx601 to expand its potential market. With this newly added IP protection, TiGenix hasa strong intellectual property position that supports the use of Cx601 for the treatment of all fistulae.

Source: biospace.com

LAMBDA
Research Accelerated

Volume 1 / January 2018

Clinical Research NEWSletter
www.lambda-cro.com

PATENTS: NEW APPROVALS /LITIGATIONS /SETTLEMENTS

2. Roche sues Pfizer for Herceptin patent infringement

Roche has sued Pfizer for infringement over biosimilar of Herceptin for 40 patent protections. Pfizer's biosimilar is a biosimilar of Roche Pharma's Herceptin (Trastuzumab) for the treatment of breast cancer. Roche claimed that Pfizer's US Food and Drug Administration (FDA) application for its proposed biosimilar amounts to patent infringement.

Roche has asked the court to block the potential launch of the biosimilar in the market. The lawsuit claims that for the development of Herceptin, Genetech unit has spent over 2 decades and billions of dollars and now Pfizer is showing its biosimilar safety and efficacy using data of Roche's Herceptin.

The biosimilar of Pfizer is not yet approved, only their application has been accepted by the USFDA. Herceptin had a market of $2.5 billion in the US last year and will get off-patent in 2019. Other than Pfizer, Mylan is also looking to challenge the Roche blockbuster with its own biosimilar. Mylan is in license with Roche for marketing the product around the world.

Source: fiercepharma.com

LAMBDA
Research Accelerated

Volume 1 / January 2018

Clinical Research NEWS letter
www.lambda-cro.com

PATENTS: NEW APPROVALS /LITIGATIONS /SETTLEMENTS

3. Lincoln Pharma receives patent for its anti-malarial drug Arteether in India

Lincoln Pharmaceutical has received the patent protection for its anti-malarial drug Arteether in India. The patent protection is provided by the Indian government for Arteether injection to treat malaria, according to a BSE filing.

According to the company, injection of Arteether is painless and provides faster relief to the malaria patient. The company is also planning to introduce the drug in the African market and is expected to have good market in Africa.

At present, the company exports anti-malarials to Africa with an approximate amount of Rs. 50 crores which is expected to increase by Rs. 35-40 crores after the introduction of Arteether injection in the African market.

Source: economictimes.indiatimes.com

LAMBDA
Research Accelerated

Volume 1 / January 2018

Clinical Research NEWSletter
www.lambda-cro.com

PATENTS: NEW APPROVALS /LITIGATIONS /SETTLEMENTS

4. Orthocell receives European patent for tenocytes

Orthocell has received the patent from the European Patent Office for culture medium, culturing method and use of tenocytes.

Tenocytes are tendon regeneration cells and form the Autologous Tenocyte Implantation (Ortho-ATI®) product. The patent is granted till 2027 and will provide intellectual property (IP) to protect Orthocell's tendon repair applications. The patent is now granted at EU, USA, China, Australia, Singapore, Hong Kong and New Zealand.

This patent will strengthen the company in the novel world leading tendon repair product into the global market.

Orthocell is well positioned to commercialize Ortho-ATI® with mature manufacturing facilities in place, with proven safety and efficacy. The complete published clinical data is available for the product with a clear pathway for the market.

Source: biospace.com

LAMBDA
Research Accelerated

Clinical Research NEWSletter
www.lambda-cro.com

Volume 1 / January 2018

TECHNOLOGY /NDDS

1. Novel method can improve delivery of nano-drugs for chemotherapy

Researchers of the Carnegie Mellon University have developed a new method for delivering chemotherapy nano-drugs at the site of action. This technology will release the drug at the target site and in-turn will increase the bioavailability of the drug and decrease the side effects.

Carnegie Mellon University researchers have developed a novel method of delivering the drug at target tumors site by using Intralipid®. Intralipid® is an FDA approved nutrient source, which temporarily blunts the reticuloendothelial system and can reduce the toxic effect of the drug in the spleen, liver and kidney. The reticuloendothelial system is a network of cells and tissues found throughout the body. The complete study of its development was published in the ***Scientific Reports***.

The study was conducted on rat model of cancer. In the study, Intralipid® was administered one hour before giving the chemotherapy nano-drug to the animal. It was found that a reduced amount of drug was found in liver, spleen and kidney and a high amount was found at the target site.

Nano-drugs are attached to some tiny biocompatible particles and shows great promise in the treatment of various diseases, including various types of cancers. But delivery of these particles is about 0.7% at the site of target tumor cells and the drug is absorbed by other cells which results in toxicity.

Source: news-medical.net

LAMBDA
Research Accelerated

Volume 1 / January 2018

Clinical Research NEWS letter
www.lambda-cro.com

TECHNOLOGY /NDDS

2. New skin patch may prevent antibiotic resistance crisis

Researchers of the Queen's University Belfast have developed a new kind of skin patch to deliver drug directly into the bloodstream. Thousands of individual microneedles will be embedded in this skin patch, which will deliver drug directly into the bloodstream.

These skin patches are discreet, microarray patches which contain an array of microneedles, which penetrate painlessly in the top layer of the skin and deliver the drug. Oral administration of antibiotics leads to the development of resistance due to interaction with bacteria inhabiting in the human gut.

Injection of antibiotics significantly reduces the resistance and can prevent exposure of the antibiotic to gut bacteria but self-administration is not possible for injections. On the surface of this antibiotic patch, tiny needles are fixed which will penetrate painlessly and gets converted into jelly like material. This Jelly material will deliver drug into the blood stream.

As if now these skin patches containing placebo have been already tested on 10 volunteers and the study published in the *International Journal of Pharmaceutics*.

Source: news-medical.net

LAMBDA
Research Accelerated

Volume 1 / January 2018

Clinical Research NEWSletter
www.lambda-cro.com

TECHNOLOGY /NDDS

3. Gas-sniffing pill to diagnose gastrointestinal ailments

Researchers of RMIT University, Australia, have developed an electronic gas-detecting pill. This pill is a swallowable capsule, which could help in the diagnosis of gastrointestinal ailments, including irritable bowel syndrome and transmit data to the mobile phone.

The capsule was initially developed in 2015. Now, the researchers released the data from the first human trials of the capsule, which collects data about the gases present and transmits to the mobile phone of the doctor. The trial was conducted on 26 people showing that the capsule was found to be safe for human use.

In addition to the detection of gases, the trial surprisingly also delivered a batch of new information about the working of gut's microbiome. The researchers discovered that the stomach releases oxidizing chemicals to get rid of foreign bodies, possibly as a protection mechanism. People with high fiber diet had a high amount of oxygen in their colon.

Now, the researchers are planning for the next round of clinical trial in 300 patients including irritable bowel syndrome and intestinal bacterial overgrowth. The capsule is expected to be launched in the market by 2020. The results from the first human trials were published in the journal ***Nature Electronics***.

Source: theguardian.com

LAMBDA
Research Accelerated

Clinical Research NEWSletter
www.lambda-cro.com

Volume 1 / January 2018

TECHNOLOGY /NDDS

4. Living pancreatic cells containing implant to control blood sugar without insulin injection

The researchers of Cornell University are working with Novo Nordisk and University of Michigan Medical School and have developed an implantable device for the treatment of type 1 diabetes. The implant contains cell derived cluster of pancreatic cells termed as islets. This implant is capable to generate insulin as generated by the healthy pancreas.

The research was published in the ***Proceedings of the National Academy of Sciences***. The published research describes the process of encapsulation of hundreds of thousands of islet cells within a hydrogel and binds the cells to a polymer thread by the researchers.

According to the researchers, the islets will not be a part of proper organ and will have a lifetime after which it will not be useful. Being a part of the polymer thread, the islets can be easily removed. The islet cells are coated with hydrogel to prevent immune system attack.

This technology is presently in preclinical stage and tested on the mice and dogs. In mice, the technology is tested for glucose control and for demonstration of its effect in diabetic mice. The implant achieved normal glucose level in just 2 days. In dogs, it was tested for the removal of thread from the body, and the study shows that it is easy to remove and does not adhere to the tissues. The thread is useful for many months, potentially up to 2 years.

Now the researchers are planning for the initial testing on humans with large studies for the implant.

Source: medgadget.com

LAMBDA
Research Accelerated

Clinical Research NEWSletter
www.lambda-cro.com

Volume 1 / January 2018

WHAT'S NEW AT LAMBDA

1. Central Clinical Lab successfully completes its 7th cycle of CAP audit

Lambda offers a state of the art Central Lab with advanced equipment for performing various assessments. The lab is accredited by the College of American Pathologists (CAP) and National Accreditation Board for Testing and Calibration Laboratories (NABL). Periodic audits are performed by these agencies to continue the accreditation.

In the month of December 2017, CAP audited the Central Clinical Lab and was completed successfully. This is the 7th successive cycle of CAP audit accreditation which demonstrates the quality and consistency in the functions of our Central Lab.

Apart from safety laboratory assessments for in house bioequivalence/bioavailability studies, the Central Clinical Lab also serves as a central laboratory for supporting multi-centric clinical trials. The various facilities provided by the clinical lab include: Immunogenicity, Biomarkers, Hematology/Biochemistry, Biosimilars, Assay Development, Oral care Microbiology, Various Time kill assay (In vitro and In vivo model), Bad breathe measurement, skin hydration measurement and Transepidermal water loss measurement.

Research Accelerated