

# Lambda Research Newsletter

December 2017



## Contact Us

Dr. Tausif Monif  
President - Global operations  
[tausifmonif@lambda-cro.com](mailto:tausifmonif@lambda-cro.com)

Dr. Mrinal Kammili  
Ex. Director - Global Head, BD  
[mrinal@lambda-cro.com](mailto:mrinal@lambda-cro.com)



LAMBDA

Research Accelerated



**LAMBDA**

Research Accelerated

Volume 12 / December 2017

Clinical Research

**NE**

**S** letter

[www.lambda-cro.com](http://www.lambda-cro.com)

## Contents

<b>GLOBAL NEWS</b>	1-4
1. Ranibizumab manufacturers threaten NHS for legal action over unlicensed cheaper drug entry	1
2. Major deregulation by USFDA in the medicinal world	2
3. Diabetes drug sales rise from 151 crore to 842 crore in 9 years	3
4. EMA introduces new guidance on Post-Brexit changes for transition period	4
<b>PHARMA INDIA</b>	5-8
1. Intas to acquire Mallinckrodt's US generics business	5
2. CTRI to register only prospective studies from April 2018	6
3. DCGI initiates measures for smooth processing of applications for manufacturing licenses	7
4. NPPA to revisit coronary stents ceiling prices	8
<b>REGULATORY ROUND-UP</b>	9-12
1. FDA draft guidelines for controlled correspondence under GDUFA II	9
2. European Commission to change orphan drug regulation	10
3. European Commission introduces new guidelines on GMP for advanced therapies	11
4. FDA updates Orange Book with patent submission dates	12
<b>MERGERS /ACQUISITIONS /COLLABORATIONS</b>	13-16
1. Amgen and Novartis to expand collaboration with Banner Alzheimer's Institute for new API trial	13
2. AbCheck and Molecular Templates collaborate to develop new cancer treatment option	14
3. Sanofi buys Principia's rights to BTK inhibitors	15
4. Spark Therapeutics and Pfizer amend license agreement for further trials of SPK-9001	16
<b>DRUGS: APPROVALS AND LAUNCHES</b>	17-20
1. Alexion Pharmaceuticals receives FDA approval for eculizumab as new treatment option for Generalized Myasthenia Gravis	17
2. European Commission approves GlaxoSmithKline's new triple lung drug	18
3. USFDA approves Yescarta <sup>®</sup> as new therapy for the treatment of B-cell lymphoma	19
4. Abbott receives European confirmation for Xience Sierra	20



**LAMBDA**

Research Accelerated

Volume 12 / December 2017

Clinical Research

**NE**

**S** letter

[www.lambda-cro.com](http://www.lambda-cro.com)

## Contents

<b>DRUGS: DEVELOPMENT &amp; CLINICAL TRIALS</b>	21-24
1. New drug by Jazz Pharmaceuticals found promising for obstructive sleep apnea	21
2. AstraZeneca to run a new pivotal trial with Incyte for lung cancer	22
3. Latest discovery to stop glaucoma in its tracks	23
4. Novartis brolicicizumab shows superiority over aflibercept in nAMD	24
<b>PATENTS: NEW APPROVALS /LITIGATIONS /SETTLEMENTS</b>	25-28
1. Teva files patent infringement lawsuit against Lilly for galcanezumab	25
2. Sanofi files a lawsuit against Mylan for patent infringement on Lantus	26
3. German Federal patent court grants compulsory license on raltegravir on HIV drug raltegravir	27
4. Canada provides additional guidance on diagnostic methods patent eligibility	28
<b>TECHNOLOGY/NDDS</b>	29-32
1. Synthetic beta cells to secrete insulin for high blood sugar level	29
2. Synovial tissue analyzer for rheumatoid arthritis therapies	30
3. New optical biosensor for detection of dry eye syndrome	31
4. First ever digital drug as antipsychotic pill	32
<b>WHAT'S NEW AT LAMBDA</b>	33-35
1. An Expansion of Excellence	33
2. Regulatory Inspections and Approvals	34

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

Volume 12 / December 2017

Clinical Research

NE

S letter

www.lambda-cro.com

## GLOBAL NEWS

### 1. Ranibizumab manufacturers threaten NHS for legal action over unlicensed cheaper drug entry



Two multinational companies Novartis and Bayer are threatening National Health Service (NHS) for legal action to prevent the entry of new cheaper option for the treatment of macular degeneration, one of the commonest cause of blindness in the older age. According to twelve NHS clinical commissioning groups (CCGs) unlicensed drug Avastin (bevacizumab) could be used as a cost effective alternative for Lucentis (ranibizumab) for the treatment of wet macular degeneration (wet AMD).

Lucentis (ranibizumab) is the licensed drug for the treatment of wet macular degeneration by Novartis and Bayer. Avastin, an anti-cancer drug, could be used for the treatment of wet age related macular degeneration as a cost-effective option. According to the doctors, when Avastin is split into smaller injections for the treatment of wet AMD, it gives as good results as Lucentis.



IVAN trial was funded by NHS and conducted in 2012; it showed that both the drugs were equally effective and safe for the treatment of the disease. This new option can save more than £84m for NHS in a year.

Now, the National Institute for Health and Care Excellence (NICE) has drafted new guidelines for Avastin use in the treatment of macular degeneration. These new guidelines endorse the safety and effectiveness of Avastin but the regulatory position is mentioned as not licensed for the condition. According to Novartis and Bayer, dose splitting of Avastin into tiny injections creates a new unlicensed medicine which can be used only for the unmet need, but at present, another licensed option is available for the condition. Furthermore, Genentech, the manufacturer of Avastin, has refused to apply for a license to treat macular degeneration.

Source: theguardian.com



LAMBDA

Research Accelerated

Volume 12 / December 2017

Clinical Research

NEWS

letter

www.lambda-cro.com

## GLOBAL NEWS

### 2. Major deregulation by USFDA in the medicinal world



Almost a year back, when Mr. Donald Trump started working as President of the USA, he mentioned to cut 75-80% of the US Food and Drug Administration (FDA) regulation at a level never seen before. After this statement by the president, the US FDA has withdrawn the most rulemakings of any Department of Health and Human Services (HHS) agency.

The USFDA retained only a handful of regulations related to medical products (the others are tobacco related), but it is unclear as to how this will affect patient safety or industry burdens. The withdrawals of rulemaking and regulation related to medicines occurred in April and June 2017. These changes focused on:

- Patient labeling to use prescription drug product effectively and safely
- Clinical trials for updating investigational new drug application to better protect the rights, safety, and welfare of subjects and help ensure the integrity of data from clinical trials
- Updating and harmonizing current good manufacturing practice (cGMP) regulations for finished pharmaceuticals
- Revision of regulations for cGMP about components used in manufacturing finished pharmaceuticals
- Regulation of the format and content of reports intended to demonstrate substantial equivalence.

Source: raps.org



**LAMBDA**

Research Accelerated

Volume 12 / December 2017

Clinical Research

**NE**

**S** letter

www.lambda-cro.com

## ▶ GLOBAL NEWS

### 3. Diabetes drug sales rises from 151 crore to 842 crore in 9 years

A recent study from Fortis C-DOC Hospital for Diabetes and Allied Specialties assessed the trends and sales of anti-diabetic drugs in India. They also assessed their prescription pattern by comparing new and old drugs.

Sales of Insulin:

- From Rs. 151.2 to 218.7 crores (44% growth) between 2008 and 2012 - due to reduced inertia of patients and physicians to use insulin
- From RS 218.7 to 467.8 crores (114% growth) between 2012 and 2014 - due to increased availability and aggressive marketing of newer insulin analogues
- From RS 467.8 to 842 crores (80% growth) between 2014 and 2016 - probably due to the availability of new basal insulin and newer premix insulin to the armamentarium

The growth rate of oral anti-diabetics (OADs) sales:

- From RS 278.5 to 570.9 crores (105% growth) between 2013 and 2015 - due to introduction of new drugs, combination drugs, and more affordable drugs by the Indian Pharma
- From RS 570.9 to RS 700 crores (23% growth) between 2015 and 2016 - due to aggressive marketing strategies

The sale of anti-diabetic drugs is rising continuously, but still in low socio-economic stratum; the supply of new oral drugs and insulin analogues is inadequate.

Source: [health.economicstimes.indiatimes.com](http://health.economicstimes.indiatimes.com)



LAMBDA

Research Accelerated

Volume 12 / December 2017

Clinical Research

NEWS

letter

www.lambda-cro.com

## GLOBAL NEWS

### 4. EMA introduces new guidance on Post-Brexit changes for transition period

For the continued marketing of the medicines in the European Economic Area (EEA) after separation of the UK and EU, the European Medicines Agency (EMA) provided some guidance as to the requirements that a company should follow when they apply for the changes of their marketing authorisation.



The guidance was introduced in the form of nine questions and answers anticipating that the UK will leave the EU as of 30 March 2019. This guidance was introduced as the EU pharmaceutical industry groups called on Brexit negotiators to establish a transition period and all relevant EU authorities can adapt to changes resulting from the UK's exit.

According to the guidance, marketing authorization holders (MAHs) which are established in the UK need to be replaced with a MAH established in one of the remaining countries of the EEA, which requires an application to transfer the marketing authorization.

In addition to the marketing authorisation, the company's qualified person for pharmacovigilance (QPPV) must reside and carry out his/her tasks in an EEA member state, and the pharmacovigilance master file (PSMF) also must be located within EEA, the guidance notes.

Source: raps.org



**LAMBDA**

Research Accelerated

Volume 12 / December 2017

Clinical Research

**NE**

**S** letter

[www.lambda-cro.com](http://www.lambda-cro.com)

## PHARMA INDIA

### 1. Intas to acquire Mallinckrodt's US generics business



Intas Pharmaceuticals is closer to the biggest cross-border buyout by an Indian pharma company. Intas Pharma is the emerging front runner to acquire Mallinckrodt's generics drug business in the US for \$1.5 billion. The company, Intas Pharmaceuticals, is backed by Temasek and ChrysCapital.

This acquisition can turn Intas Pharmaceutical into the largest privately held pharmaceutical company in India with an annual turnover of over \$1 billion. This will also provide Intas Pharmaceuticals access to the attractive therapeutic segment of controlled substances or opioids that have steep entry barriers and high margins.

Source: [economictimes.indiatimes.com](http://economictimes.indiatimes.com)



**LAMBDA**

Research Accelerated

Volume 12 / December 2017

Clinical Research

**NE**

**S** letter

www.lambda-cro.com

## PHARMA INDIA

### 2. CTRI to register only prospective studies from April 2018



The Clinical Trials Registry of India (CTRI) by the Indian Council of Medical Research (ICMR) will register only prospective studies from 1<sup>st</sup> April 2018 onwards. This release clearly indicates that the CTRI will register clinical trials/studies only before the enrolment of the 1<sup>st</sup> patient. Currently, CTRI is also accepting trials which are ongoing or completed.

The present working system will be discontinued from 1<sup>st</sup> April 2018. As some Journals ask about the prospective registration of trial; to ensure that it is a prospective trial, the sponsor needs to register the trial before the enrollment of the 1<sup>st</sup> Patient. According to the new rules, if the trial is not registered before the enrollment of 1<sup>st</sup> patient, the trial will be flagged as 'Trial Registered Retrospectively' and later on registration status cannot be changed.

CTRI was launched by the government of India in 2007 for the registration of clinical trials being conducted in India. This was initiated as a voluntary measure but later the registration was made mandatory by the Drugs Controller General of India (DCGI) from 2009. Editors of 11 major Biomedical Journals of India have declared that only registered trials will be considered for publication.

This site was introduced to ensure that the trials which are conducted in the regions should be prospectively registered. This is also aimed to provide all the information of the trials to the public and researchers at a single point, and to make trails more transparent.

Source: pharmabiz.com



**LAMBDA**

Research Accelerated

Volume 12 / December 2017

Clinical Research

**NE**

**S** letter

[www.lambda-cro.com](http://www.lambda-cro.com)

## PHARMA INDIA

### 3. DCGI initiates measures for smooth processing of applications for manufacturing license

The Drug Controller General of India (DCGI) has made some amendments in the Drugs and Cosmetics Rules, and further initiated some measures to ensure smooth processing of applications for manufacturing licenses. According to the new amendments, the central and state drug inspectors will jointly conduct an inspection of the manufacturing plant every 3 year to verify the compliance with the conditions and provisions under the Drugs and Cosmetics Act, 1940.

For the smooth effective and uniform implementation of this joint inspection, detailed guidelines would be prepared with consultations from the state drug controller and other stakeholders.

The Union Health Ministry amendment in the Drugs and Cosmetics Rules, 1945 vide Notification No. G.S.R.1337 (E) mention that approval of drugs/cosmetics testing laboratories shall remain valid if the licensee deposits license retention fee before the expiry of the period of every succeeding five years from the date of issue, unless, it is suspended or cancelled by the licensing authority.

The amendment mentions that before the grant of licence in Forms 25, 25A, 25B, 25F, 28, 28A, 28B, 28D, or 28DA for the sale and distribution of drugs by the manufacturers or in Forms 32, 32A, or 33 for manufactures of cosmetics, the State Licensing Authority shall have the manufacturing premises inspected jointly by the Central and State Drugs Inspectors.

Source: [pharmabiz.com](http://pharmabiz.com)



**LAMBDA**

Research Accelerated

Volume 12 / December 2017

Clinical Research

**NE**

**S** letter

www.lambda-cro.com

## PHARMA INDIA

### 4. NPPA to revisit coronary stents ceiling prices



After completion of around 1 year of price fixation for coronary stents, now the National Pharmaceutical Pricing Authority (NPPA) is again revisiting the notification released on 13 February 2017. As this price fixation drew sharp criticism from the manufacturers due to the very high price capping, the NPPA asked domestic stent manufacturers and importers to submit representation or suggestions for the new prices of the stents.



This decision needs to be revised by January or February 2018, and NPPA has already received some representations from the stent manufacturers or importers.

The Department of Pharmaceuticals (DoP) was appointed as a core committee for bringing coronary stent price under control in 2016. The committee reported that there was a very high incidence of coronary artery disease (CAD) in India, which was associated with a higher rate of mortality due to the very high cost of life-saving coronary stents. Hence, coronary stents are essential for public health. Later, NPPA carried out an exhaustive exercise with consultation of stakeholders for fixing the price of the stents.

Source: pharmabiz.com



LAMBDA

Research Accelerated

Volume 12 / December 2017

Clinical Research

NE

S  
letter

www.lambda-cro.com

## ▶ REGULATORY ROUND-UP

### 1. FDA draft guidelines for controlled correspondence under GDUFA II

The US Food and Drug Administration (FDA) released a new draft guideline for Generic Drug User Fee Amendments (GDUFA II) on agency's new commitments based on controlled correspondence.

The new finalized guidelines will replace GDUFA I guidelines from 2015. The new GDUFA II commitment letter defines complex controlled correspondence as correspondence related to:

- ✓ Clinical content evaluation
- ✓ Bioequivalence (BE) protocol review for reference listed drugs
- ✓ Evaluation of requested alternative BE approach for the same study type

Under this new performance goal, FDA will review and respond to 90% of standard controlled correspondence within 60 days of submission. The FDA will also review and respond to complex controlled correspondence within 120 days.

This guidance also provides additional detail and recommendations on FDA considerations for controlled correspondence and various other requirements.

Source: raps.org



LAMBDA

Research Accelerated

Volume 12 / December 2017

Clinical Research

NE

S  
letter

www.lambda-cro.com

## ▶ REGULATORY ROUND-UP

### 2. European Commission to change orphan drug regulation



The European Commission (EC) has proposed some changes to its orphan drug regulation due to the rise of cell based therapies. The regulatory agency wants to change few key definitions in the 17-year-old text which does not account for cell therapies and other advanced medicinal products.

According to the present text, similar active substances are defined as substances that are “identical to or having the same principal molecular structural features as another substance with the same mechanism of action”.

But it is very difficult to understand or “identify the principal molecular structural features” by scientists as defined in the current regulations. Hence, the definition is planned to be modified on the “basis of the biological and functional characteristics if the principal molecular structural features are unknown”.

Similar thinking has been applied for both cell based and gene based therapies. In cell based therapies, if the starting materials are different, or there is a difference in the final product or if there is difference in the technology used in the manufacturing which may affect the biological characters, it can be termed not similar as per the current definition. But products can have the same effect with different starting materials. Similar thought process has been applied for gene based therapies.

Source: raps.org



European Commission



**LAMBDA**

Research Accelerated

Volume 12 / December 2017

Clinical Research

**NE**

**S** letter

[www.lambda-cro.com](http://www.lambda-cro.com)

## ▶ REGULATORY ROUND-UP

### 3. European Commission introduces new guidelines on GMP for advanced therapies

The European Commission has introduced the latest guidelines on Good Manufacturing Practices (GMP) for some specific advanced therapy medicinal products (ATMPs). The ATMPs include medicines for human use, which are based on the genes or cells.

These new guidelines will provide new therapies for the treatment of diseases and injuries. These guidelines are mainly important for the treatment of severe, untreated or chronic diseases, for which conventional options are not available or insufficient.

The latest guidelines will adapt the European Union GMP requirements for the specific characters of ATMPs and address the novel and complex manufacturing processes. These guidelines promote the risk based approach for the manufacturing and testing agencies of such products.

These guidelines also ensure that these novel medical products are constantly produced and should have the required quality with respect to the quality standards. These guidelines are part of the joint action plan launched by the Directorate General for Health and Food Safety (DG SANTE) icon and the European Medicines Agency (EMA) in October 2017 to promote the development of ATMPs.

Source: [pharmabiz.com](http://pharmabiz.com)



**LAMBDA**

Research Accelerated

Volume 12 / December 2017

Clinical Research

**NE**

**S** letter

www.lambda-cro.com

## ▶ REGULATORY ROUND-UP

### 4. FDA updates Orange Book with patent submission dates

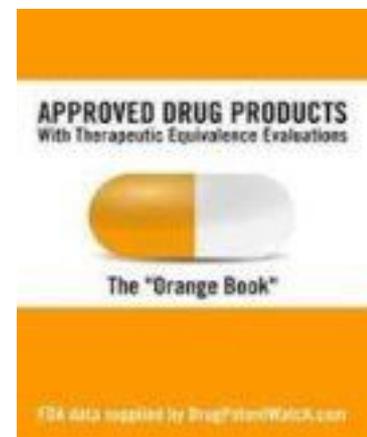


The US Food and Drug Administration (FDA) have updated the Orange Book with patent dates to increase the transparency and for promoting the generic drug competition. This updated status of patents will help the generic makers to determine the earliest date for the marketing of generics.

The process of patent data collection was started in 2013 and at present about 4,000 patents' submission dates are available. This latest update is due to the October 2016 rule of adding patent submission date for all new products in the Orange Book.

This update in the patent dates of submission of new drug application (NDA) can increase the generic competition in the market. The USFDA also notified that NDA holders can email error correction requests, including justifications for the requests, to [orangebook@fda.hhs.gov](mailto:orangebook@fda.hhs.gov).

Source: [raps.org](http://raps.org)





**LAMBDA**

Research Accelerated

Volume 12 / December 2017

Clinical Research

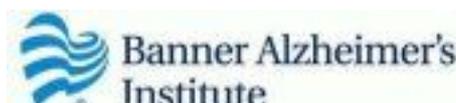
**NE**

**S** letter

www.lambda-cro.com

## ▶ MERGERS /ACQUISITIONS /COLLABORATIONS

### 1. Amgen and Novartis to expand collaboration with Banner Alzheimer's Institute for new API trial



Amgen and Novartis have expended their collaboration with the Banner Alzheimer's Institute (BAI) to initiate a new trial on the Alzheimer's Prevention Initiative (API) Generation Study.

This trial will follow the Generation Study 1 and will try to find whether the beta-site amyloid precursor protein cleaving enzyme 1 (BACE1) inhibitor CNP520 can delay or prevent the onset of Alzheimer's disease symptoms in a high-risk population.

BACE1 is an enzyme which plays an important role in the production of Amyloid  $\beta$ . Amyloid  $\beta$  is a protein which gets accumulated in the brain of the individuals before the detection of any symptoms of the disease.

Two phase 2/3 pivotal trials were involved in the Generation Program. These studies were initiated in the US in August 2017 including 180 sites in 20 countries, globally. This study will run for five years enrolling approximately 2,000 cognitively healthy participants.

Source: worldpharmanews.com



**LAMBDA**

Research Accelerated

Volume 12 / December 2017

Clinical Research

**NE**

**S** letter

[www.lambda-cro.com](http://www.lambda-cro.com)

## ▶ MERGERS /ACQUISITIONS /COLLABORATIONS

### 2. AbCheck and Molecular Templates collaborate to develop new cancer treatment option

AbCheck has entered into a new strategic collaboration with Molecular Templates for the development of new cancer treatment options.

Under this agreement, Molecular Templates and AbCheck will work on the AbSieve discovery platform of AbCheck for the delivery of antibodies against the biological targets selected by the Molecular Templates.

AbCheck is a pharmaceutical company mainly focusing on the discovery and optimization of high-quality human antibodies. Molecular Templates Inc. is a biopharmaceutical company involved in the development of next generation immunotoxins for the treatment of cancer.

In this collaboration, AbCheck initially will leverage its expertise in phage/yeast display through its AbSieve platform but further details of the collaboration were not disclosed.

Source: [drugdiscoveryonline.com](http://drugdiscoveryonline.com)



**LAMBDA**

Research Accelerated

Volume 12 / December 2017

Clinical Research

**NE**

**S** letter

www.lambda-cro.com

## ▶ MERGERS / ACQUISITIONS / COLLABORATIONS

### 3. Sanofi buys Principia's rights to BTK inhibitors



Sanofi has brought the rights for Principia BioPharma's experimental tyrosine kinase (BTK) inhibitor PRN2246 in a deal worth >\$800 million.

BTK inhibitor is an experimental oral therapy to access the brain and spinal cord by crossing the blood brain barrier. Inhibitors will act on the immune cells and brain cells signaling. The BTK inhibitor has shown effectiveness in the treatment of multiple sclerosis (MS) and in various other central nervous system (CNS) diseases.

Under this deal, Principia will provide Sanofi an exclusive worldwide license for the development and commercialization of PRN2246 and Sanofi will provide an upfront payment of \$40 million and in future \$765million for milestone payments. Sanofi will also provide royalties on the sale of product.

Principia also has the option to co-fund the Phase 3 trial, and in return will have increased royalty or a profit and loss sharing arrangement in the US.

Source: pharmatimes.com



**LAMBDA**

Research Accelerated

Volume 12 / December 2017

Clinical Research

**NE**

**S** letter

www.lambda-cro.com

## ▶ MERGERS /ACQUISITIONS /COLLABORATIONS

### 4. Spark Therapeutics and Pfizer amend license agreement for further trials of SPK-9001

Spark Therapeutics and Pfizer Inc. have amended their licensing agreement further for the investigation of new gene therapy SPK-9001 for the treatment of hemophilia B. This licensing agreement was initially done in December 2014 for Phase 1/2 studies of the SPK-FIX program by Spark Therapeutics and pivotal studies by Pfizer.

Under this amendment, Spark Therapeutics will enroll up to 5 additional participants in Phase 1/2 trials who will be administered SPK 9001 manufactured by an enhanced process to test its compatibility with the other normal ongoing trial patients.

One of the new participants received the modified SPK-9001, and was followed-up for 32 weeks. The level of factor IX was found within the range that is considered compatible for the rest of the participants (10).

Data of the 11<sup>th</sup> participant indicates the potential for clinical compatibility with the safety and efficacy when compared to that of 10 patients. Spark Therapeutics will transfer the enhanced SPK-9001 manufacturing process to Pfizer for further Phase 3 clinical trials of SPK-9001.

Source: worldpharmanews.com



Research Accelerated

Volume 12 / December 2017

Clinical Research

NE

S letter

www.lambda-cro.com

## DRUGS: APPROVALS AND LAUNCHES

### 1. Alexion Pharmaceuticals receives FDA approval for Eculizumab as new treatment option for Generalized Myasthenia Gravis



The U.S. Food and Drug Administration (FDA) has approved a new treatment option for generalized myasthenia gravis (gMG) by Alexion Pharmaceuticals Inc. Soliris (eculizumab) is effective in those patients who are anti-acetylcholine receptor (AChR) antibody-positive.

Soliris is a complement inhibitor which acts by inhibiting the terminal part of the complement cascade. It is already approved in the US, EU, Japan and some other countries for paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome (aHUS), and now for anti-acetylcholine receptor (AChR) antibody-positive gMG

Soliris is effective in patients with anti-AchR antibody-positive gMG, who are unresponsive to previous immunosuppressive treatment and still suffering with difficulties in seeing, talking, swallowing, walking, and breathing. These patients are at a high risk of disease exacerbations and crises and may require hospitalization or intensive care as it may be life threatening. The extended indication approval by the USFDA is based on a Phase 3, randomized, double-blind, placebo-controlled, multicenter REGAIN study (ECU-MG-301) and an ongoing open label extension study. Patients were treated with eculizumab or placebo for a total of 26 weeks.

Source: drugs.com



**LAMBDA**

Research Accelerated

Volume 12 / December 2017

Clinical Research

**NE**

**S** letter

[www.lambda-cro.com](http://www.lambda-cro.com)

## ▶ DRUGS: APPROVALS AND LAUNCHES

### 2. European Commission approves GlaxoSmithKline's new triple lung drug

GlaxoSmithKline (GSK) received the European Commission's (EC) approval for new three-in-one inhaler for chronic obstructive pulmonary disease (COPD).

Trelegy Ellipta is a combination of fluticasone furoate/umeclidinium/vilanterol and is the first once daily triple medicine for COPD. Trelegy Ellipta was approved in the US in September 2017.

This decision of the European Commission will provide marketing authorization to GlaxoSmithKline, to market the product in the countries included in the European Union. This product is expected to enter the market by the end of 2017.

This combination was introduced by GSK as the patients are already using 3 drugs for the control of their COPD disease. Now, this combination in one inhaler will increase the compliance of the patients who were taking these medicines separately.

Source: [foxbusiness.com](http://foxbusiness.com)



Research Accelerated

Volume 12 / December 2017

Clinical Research

NE

S letter

www.lambda-cro.com

## DRUGS: APPROVALS AND LAUNCHES

### 3. USFDA approves Yescarta<sup>®</sup> as new therapy for the treatment of B-cell lymphoma



Kite Pharma received the US Food and Drug Administration (FDA) approval for Yescarta<sup>®</sup> (axicabtagene ciloleucel) for the treatment of adult patients with relapsed or refractory B-cell lymphoma. This drug is approved as a third line agent.

Yescarta<sup>®</sup> is a chimeric antigen receptor (CAR) T cell immunotherapy; in which T cells are modified to produce CAR protein. CAR protein helps T cells for the identification and elimination of CD19-expressing normal and malignant cells.

The approval of Yescarta<sup>®</sup> was based on a single-arm multicenter trial conducted on 108 adult patients with aggressive B-cell non-Hodgkin's lymphoma. The selected patients had refractory disease to their recent therapy or relapse within one year after stem cell transplantation.

During the trial, 101 patients were evaluated for efficacy in terms of objective response rate, which was found to be 72% with a complete remission (CR) rate of 51%.

Serious adverse reactions occurred in 52% of patients. The recommended dose of Yescarta<sup>®</sup> is a single intravenous infusion with the standard dose of  $2 \times 10^6$  CAR-positive viable T cells per kg.

Source: pharmaceutical-technology.com



**LAMBDA**

Research Accelerated

Volume 12 / December 2017

Clinical Research

**NE**

**S** letter

[www.lambda-cro.com](http://www.lambda-cro.com)

## ▶ DRUGS: APPROVALS AND LAUNCHES

### 4. Abbott receives European confirmation for Xience Sierra

Abbott has received Conformité Européene (CE) Mark for the sale of Xience Sierra in the European Union (EU). Xience Sierra is the newest gold standard Xience everolimus eluting coronary stent system. This approval will allow Abbott to sell the stent in all member states of the EU and various other countries recognizing CE mark.

New Xience is provided with new features and is much safer as compared to that of the other products; this will provide compliance during the complex procedure.

The new features include a thinner profile, increased flexibility, longer lengths, and small-diameters, which make it easier for cardiologists to access and unblock difficult-to-reach lesions.

Abbott has also submitted an application to the US Food and Drug Administration for Xience Sierra approval in the United States.

Source: [pharmabiz.com](http://pharmabiz.com)



Research Accelerated

Volume 12 / December 2017

Clinical Research

NE

S letter

www.lambda-cro.com

## DRUGS: DEVELOPMENT & CLINICAL TRIALS



### 1. New drug by Jazz Pharmaceuticals found promising for obstructive sleep apnea

Jazz Pharmaceuticals has developed a new drug Solriamfetol for wakefulness in patients with obstructive sleep apnea (OSA). The Phase 3 study has shown that the drug significantly improves wakefulness in patients with OSA during day time. In addition, Solriamfetol also reduces the tendency for subjective sleepiness.

Solriamfetol (JZP-110) is a selective dopamine norepinephrine reuptake inhibitor without life-threatening adverse events.

In the Phase 3 trial, 459 patients were assessed with OSA and excessive sleepiness. It was a 12 week randomized trial and patients were divided into 5 groups receiving one of four doses of solriamfetol - 300 mg, 150 mg, 75 mg, or 37.5 mg once daily or placebo. The results were presented at the 2017 Annual American College of Chest Physicians (CHEST) Meeting in Toronto, CANADA.

All the treatment groups aside from 75 mg reported a high rate of improvement. Patients in both 150 mg (89.7%) and 300 mg (88.7%) groups showed nearly 90% improvement in the patient global impression of change (PCI-G) scores at 12 weeks.

Change From baseline in maintenance of wakefulness test at 12 weeks and improvements in patient global impression of change

Treatment Group	n	Least Square Mean Change (Minutes)	P Value	Improvement, %	P Value
Solriamfetol 300 mg	115	13.0	<0.0001	88.7	<0.0001
Solriamfetol 150 mg	116	11.0	<0.0001	89.7	<0.0001
Solriamfetol 75 mg	58	9.1	<0.0001	72.4	<0.05
Solriamfetol 37.5 mg	56	4.7	<0.5	49.1	NS
Placebo	114	0.2	NS		

Source: medscape.com, mdmag.com





LAMBDA

Research Accelerated

Volume 12 / December 2017

Clinical Research

NE

S letter

www.lambda-cro.com

## DRUGS: DEVELOPMENT & CLINICAL TRIALS

### 2. AstraZeneca to run a new pivotal trial with Incyte for lung cancer



AstraZeneca is going to run a pivotal trial for Incyte's second-generation immunotherapy drug epacadostat with its Imfinzi. The combination of epacadostat and Imfinzi will be tested in patients with early stage cancer or up to stage 3.

Epacadostat is an Indoleamine 2,3-dioxygenase (IDO) inhibitor that helps the immune system to fight against cancer. IDO is an enzyme that protects tumors from the immune system. Imfinzi acts as programmed death-L1 (PD-L1) or PD-1 inhibitors that block a different mechanism that cancer cells use to prevent detection.

Incyte already has an agreement with Merck & Co and Bristol-Myers Squibb for separate Phase 3 trials. This Phase 3 trial will be cofunded by Merck & Co and Bristol-Myers Squibb, and conducted by AstraZeneca.

The enrollment of patients for the trial is expected to start from the first half of 2018. The combination is expected to work well, without added toxicity.

Source: reuters.com



**LAMBDA**

Research Accelerated

Volume 12 / December 2017

Clinical Research

**NE**

**S** letter

[www.lambda-cro.com](http://www.lambda-cro.com)

## ▶ DRUGS: DEVELOPMENT & CLINICAL TRIALS

### 3. Latest discovery to stop glaucoma in its tracks



Scientists from the University of California and the University of Toronto have discovered naturally occurring lipid mediators which have the potential to stop glaucoma at its initial stages. Glaucoma is the second leading cause for blindness in the world. The complete research was published in the Journal of Clinical Investigation. This study can provide a very good treatment option for the treatment of glaucoma.

Researchers worked on a rodent model and found that the inflammation-regulating lipid mediators (which are termed as lipoxins and are secreted from star-shaped cells known as astrocytes) stopped the degeneration of retinal ganglion cells in rats and mice with glaucoma.

Researchers also found that astrocytes, which maintain brain function and form the nerve fiber layer of the retina and optic nerve, release therapeutic biological agents lipoxins A4 and B4. Commonly, astrocytes are activated by injuries and release stress signals that kill off ganglion cells in the retina, causing optic nerve damage. This research also explains that astrocytes that are triggered by injury actually turn off novel neuroprotective signals that prevent optic nerve damage.

Now, the researchers will further investigate the therapeutic benefits and mechanisms of lipoxins A4 and B4 and their potential to stop or reverse neural damage. The researchers have also filed a joint patent application for the use of lipoxins as drugs in humans for the treatment of glaucoma and neurodegenerative diseases.

Source: [medicalxpress.com](http://medicalxpress.com)



LAMBDA

Research Accelerated

Volume 12 / December 2017

Clinical Research

NE

S letter

www.lambda-cro.com

## ▶ DRUGS: DEVELOPMENT & CLINICAL TRIALS

### 4. Novartis brolocizumab shows superiority over aflibercept in nAMD



Brolocizumab of Novartis Pharmaceuticals has shown positive results against aflibercept in the treatment of neovascular age-related macular degeneration (nAMD) in two Phase 3 studies. The results of these studies showed non-inferiority in the primary endpoint, superiority in key retinal health outcomes, and long-lasting effect in patients of nAMD. In nAMD, fluid leak into the eye from abnormal blood vessels causes damage to the eye and can lead to blindness.

The results from HAWK and HARRIER head-to-head trials were presented at the American Academy of Ophthalmology (AAO) 2017 Annual Meeting.

HAWK Trial:

At Week 16 and Week 48, relative to aflibercept, brolocizumab 6 mg patients showed 35% and 31% fewer presences of intra-retinal fluid (IRF) and/or sub-retinal fluid (SRF) respectively.

HARRIER Trial:

At week 16 and Week 48, relative to aflibercept, brolocizumab 6 mg patients showed 33% and 41% fewer presences of intra-retinal fluid (IRF) and/or sub-retinal fluid (SRF) respectively ( $P < 0.0001$  for all the values).

The absence of fluid in brolocizumab treated arm suggests long lasting effect and decreased treatment need. In addition to IRF and SRF, Brolocizumab 6 mg demonstrated superior reductions in central subfield thickness (CST).

Source: pharmpro.com



LAMBDA

Research Accelerated

Volume 12 / December 2017

Clinical Research

NE

S  
letter

www.lambda-cro.com

## ▶ PATENTS: NEW APPROVALS /LITIGATIONS /SETTLEMENTS

### 1. Teva files patent infringement lawsuit against Lilly for galcanezumab



TEVA PHARMACEUTICAL INDUSTRIES LTD.



Teva Pharmaceuticals has filed a patent infringement lawsuit against Eli Lilly to block the market entry of a new migraine drug from Lilly. Israeli-based Teva filed the patent infringement lawsuit in the federal court at Boston.

This patent suit alleges that Lilly's migraine treatment, galcanezumab infringes on five of Teva's patents. According to Teva, Lilly was aware of these patents for covering drug fremanezumab but was still working to launch the drug in the US market.

Galcanezumab is the member of the newest class migraine drugs which target a neurotransmitter called calcitonin gene-related peptide (CGPR). CGPRs have a potential market of \$8-\$10 billion.

After this lawsuit Lilly is expected to stop the manufacturing and sale of galcanezumab.

Source: pharmpro.com



**LAMBDA**

Research Accelerated

Volume 12 / December 2017

Clinical Research

**NE**

**S** letter

www.lambda-cro.com

## ▶ PATENTS: NEW APPROVALS /LITIGATIONS /SETTLEMENTS

### 2. Sanofi files a lawsuit against Mylan for patent infringement for Lantus



Sanofi filed a lawsuit against Mylan for the patent infringement of its top selling drug Lantus. Sanofi filed this lawsuit in the court mentioning that Mylan is infringing 18 patents of Sanofi on Lantus and asked the court to intervene in the launch of the generic.

A 70 page lawsuit filed by Sanofi in the federal court in New Jersey, in which Sanofi explains that initially they tried to gather information of Mylan's program but out-of-court negotiations proved "unsuccessful".

Sanofi's drug Lantus has a big market in the world with about €5.7 billion (\$6.7 billion) worth of sales last year. In 2015, Eli Lilly had already launched its drug Basaglar under a settlement with a market value of \$278 million so far in 2017. As there is only one market competitor for Lantus, discounting to the brand remain limited but if other competitors enter, then Sanofi's sales would be affected.

According to Sanofi's lawsuit, Mylan is working on its version of Lantus along with Biocon and filed for approval from FDA in September. According to the Orange Book of FDA, the patent expiry date for Sanofi's Lantus and SoloStar ranges between 2023-2028.

Source: fiercepharma.com



LAMBDA

Research Accelerated

Volume 12 / December 2017

Clinical Research

NE

S  
letter

www.lambda-cro.com

## ▶ PATENTS: NEW APPROVALS /LITIGATIONS /SETTLEMENTS

### 3. German Federal patent court grants compulsory license on HIV drug raltegravir



The German Federal patent court has granted a compulsory license (CL) to an HIV drug raltegravir. This license is provided for public interest and for benefit of the society. MSD provided prima facie evidence towards public interest and for grant of the compulsory license for raltegravir.

CL is provided by sovereign state authorizations, which enable a third party to make, use or sell a patented product without the consent of the patent holder. This grant is provided if no other alternative for the medicine is available.

The Federal Court of Justice (FCJ) of Germany affirmed a public interest in the continued availability of raltegravir for the treatment of infants and children up to 12 years of age. According to FCJ, raltegravir is the only integrase inhibitor which can be used in Germany for infants from the age of four weeks to three months as part of a combination therapy using two nucleoside reverse transcriptase inhibitors.

The grounds for granting a CL in India are insufficient availability of the patented drug, unaffordable pricing and non-working of the patent in the territory of India. Besides, the Central Government can grant a CL in circumstances of national emergency or extreme urgency or in the case of public non-commercial use. In Germany, the only ground is that of 'public interest'.

Source: spicyip.com



LAMBDA

Research Accelerated

Volume 12 / December 2017

Clinical Research

NE

S  
letter

www.lambda-cro.com

## ▶ PATENTS: NEW APPROVALS /LITIGATIONS /SETTLEMENTS

### 4. Canada provides additional guidance on diagnostic methods patent eligibility

Patent eligibility of diagnostic method claims always remained questionable in the United States. Now the Canadian Intellectual Property Office has issued some additional updated guidance on the types of diagnostic method claims that can or cannot be patented in Canada. As in this field, the stakeholders pursue patent protection internationally, it will be important to know the standards that will be applied in different jurisdictions.

In the US jurisprudence application, a two-step Mayo/Alice analytical framework is used for the analysis whereas in Canada there exists a different two-step analysis. In Canada, a problem-solution approach is used to determine whether the claimed diagnostic method pertains to patent-eligible data acquisition or patent-ineligible data analysis.

The guidance provided in Canadian Intellectual Property Office's (CIPO's) Manual of Operating Practice illustrates disclosures that "may indicate the existence of a data acquisition problem," including the following:

- disclosure of a novel or non- common general knowledge (CGK) analyte
- disclosure of a novel or non-CGK combination of biomarkers
- disclosure that a CGK means to identify or quantify an analyte is applied to a sample or subject population that is not standard to that means

This guidance also illustrates disclosures that may indicate the existence of a data analysis problem, including an emphasis on the discovery of an allegedly new correlation between a condition and an analyte that is CGK with a relative absence of technical details pertaining as to how to acquire the data about the analyte.

Source: [pharmapatentsblog.com](http://pharmapatentsblog.com)



LAMBDA

Research Accelerated

Volume 12 / December 2017

Clinical Research

NE

S letter

www.lambda-cro.com

## ▶ TECHNOLOGY /NDDS

### 1. Synthetic beta cells to secrete insulin for high blood sugar level

Researchers from the University of North Carolina and North Carolina (NC) State have developed patient friendly artificial beta cells. These cells will automatically release insulin into the blood stream in response to increased blood sugar levels.

Artificial beta cells (ABCs) will mimic the function of natural beta cells of pancreas. These ABCs can be inserted into the body of patients subcutaneously. Later, this subcutaneous injection could be replaced by painless and disposable skin patches.

The complete research report was published in the *Journal of Nature Chemical Biology* which shows that a single injection of ABCs in diabetic mice could normalize the animal's blood glucose level and keep them normal for upto five days.

ABCs are constructed with simplified cells of two layered lipid membrane containing specially designed insulin stuffed vesicles. Rise in glucose level leads to chemical changes in the vesicles' coating, causing the vehicle to release insulin. The ABCs showed a rapid responsiveness to high glucose level in diabetic mice without beta cells.

Source: medicalxpress.com



LAMBDA

Research Accelerated

Volume 12 / December 2017

Clinical Research

NE

S letter

www.lambda-cro.com

## ▶ TECHNOLOGY /NDDS

### 2. Synovial tissue analyzer for rheumatoid arthritis therapies



The National Institute of Health, the U.S. Food and Drug Administration, biopharmaceutical companies and not-for-profit organizations have developed a new diagnostic tool for analyzing the cellular and molecular profiles of synovial tissue and peripheral blood. This new tool may help in the detection of better treatment options for rheumatoid arthritis.

Rheumatoid arthritis (RA) is a chronic disease associated with pain, swelling, stiffness and limitation in the motion and function of multiple joints. The researchers have completed the first phase of development through cellular and molecular profiling of synovial tissue and matched peripheral blood from RA patients nationwide.



By using cytometry, mass cytometry and RNA sequencing, researchers studied 58 synovial tissues from 22 biopsies and from 36 electric surgical procedures. 30-40 cell types and several genes from the patient's samples were analyzed.

In the accelerated Medicines Partnership (AMP) RA, the researchers found that a robust cell from synovial tissues enables mass and flow cytometry data capturing.

Source: news-medical.net



**LAMBDA**

Research Accelerated

Volume 12 / December 2017

Clinical Research

**NE**

**S** letter

[www.lambda-cro.com](http://www.lambda-cro.com)

## ▶ TECHNOLOGY /NDDS

### 3. New optical biosensor for detection of dry eye syndrome



Researchers from the Universidad Politécnica de Madrid (UPM) have developed a new optical biosensor termed as Point-of-Care (PoC) Optical Reading Device for easy, fast and affordable detection of dry eye. This biosensor will help in the in-vitro detection of the biological material. The first trial was effective in the diagnosis of dry eye by assessing patient's tears. This technique could be used in various other therapeutic areas.

As dry eye syndrome (DES) is associated with eye irritation, redness and fatigue, and can lead to retinal detachment and vision loss, an early detection of the disease is required. These evidences of the disease can be confused with other eye diseases which are not related to DES. DES also affects tear composition by varying the protein concentration in tears which can be considered as a biomarker for detection.

This new device has several advantages over the traditional devices like portability, easy to use and label free as it does not require labeling agents such as enzymes, fluorophores, or gold particles to amplify the response, resulting in reduced cost. The PoC of this new device is based on the optical properties of the sensor when biological material is added. By monitoring the simple spectral response of reflected light through the new method, the amount of biological molecules on the surface can be detected.

Source: [phys.org](http://phys.org)



**LAMBDA**

Research Accelerated

Volume 12 / December 2017

Clinical Research

**NE**

**S** letter

[www.lambda-cro.com](http://www.lambda-cro.com)

## ▶ TECHNOLOGY /NDDS

### 4. First ever digital drug as antipsychotic pill



Otsuka Pharmaceutical Co. introduced their first digital drug, an antipsychotic pill for mentally ill patients. The US Food and Drug Administration (FDA) approved this product after the complete submission of safety results by Otsuka.

This digital chip contains minerals like silicon, magnesium and copper inside tablets of Abilify (Aripiprazole). Abilify is used for the treatment of schizophrenia, bipolar disorder and other mental illnesses.

Once swallowed, the chip mixes with the acids secreted by the stomach and sends a heartbeat like signal to the smart phone which indicates the time of ingestion. By this chip, doctors can monitor the patient and later the chip passes through the digestive tract normally.

This chip technology is provided by Proteus Digital Health Inc. This invention is intended for the mentally ill patients who don't take their medicine on time or forget to take medicine which affects their treatment. The digital drug may also solve the problem of missed doses.

Otsuka faces a number of fundamental questions like will insurers pay for this costly drug or what can be the advantages over its own conventional form of Abilify.

Source: [wsj.com](http://wsj.com)



LAMBDA

Research Accelerated

Volume 12 / December 2017

Clinical Research

NE

S  
letter

www.lambda-cro.com

## ▶ WHAT'S NEW AT LAMBDA

### 1. An Expansion of Excellence



At Lambda, we believe excellence is a continuous journey. Therefore, since inception, we have steadily evolved and grown in potential by adding new services to our portfolio, training our employees, upgrading our technologies and accelerating the journey of molecules to the market for the benefit of our clients globally.

As a testament to this progressive philosophy, we are proud to announce our most recent expansion with the launch of our state-of-the-art clinical facility in Mehsana, North Gujarat. This advanced 130 bed facility is approved by Indian regulatory body (DCGI) and brings our total tally of clinical beds to 700+ globally, reinforcing our status as one of the largest CROs in Asia.

This facility showcases Lambda's commitments to our clients and the clinical research domain in general with a single minded objective to excel on all fronts. As we continue to march towards a promising future with ambition and optimism, we look forward to your priceless patronage empowering our journey every step of the way.



**LAMBDA**

Research Accelerated

Volume 12 / December 2017

Clinical Research

NE

S  
letter

www.lambda-cro.com

## ▶ WHAT'S NEW AT LAMBDA

### 2. Regulatory Inspections and Approvals



Lambda Therapeutic Research Limited is a leading global Clinical Research Organization (CRO) conducting Early as well as Late Phase Clinical trials including BA/BE studies along with other support services such as Biostatistics and Data Management, Pharmacovigilance, Medical and Scientific Writing, and Central Laboratory. The CRO is headquartered at Ahmedabad - India, with facilities and operations in Mumbai (India), Mehsana (India), Toronto (Canada), Warsaw (Poland), London (UK) and USA.

Lambda offers the full spectrum of clinical trial solutions since its inception in 1998, to the biopharmaceutical industry. Lambda is regularly inspected by various regulatory authorities for the authentication of the numerous services provided. Lambda has an unblemished record with successful inspections/audits from various regulatory agencies across the world.

Similarly, in this year, 2017, 4 regulatory inspections were conducted by different regulatory authorities for different facilities/services of Lambda. The approvals by different agencies further demonstrate the quality provided by Lambda for all projects.

- Standards Council of Canada (SCC), Canada, conducted an inspection at Lambda's Canada facility for their Bioanalytical department in August, 2017, which was successful and retained the economic co-operation and development - Good Laboratory Practice (OECD GLP) certification. This certification by the agency will enable the CRO to perform sample analysis of GLP studies.
- National Pharmaceutical Regulatory Agency (NPRA), Malaysia, inspected Lambda's Ahmedabad site for their Clinical & Bioanalytical department in the month of August, 2017, which was also successful. This decision enables the sponsors to submit their data from studies conducted at Lambda Ahmedabad facility in Malaysian agencies.
- Central Drugs Standard Control Organization (CDSCO), India: Lambda established a new state of the art facility at Mehsana, Gujarat, India, and CDSCO inspected the new site in October, 2017. CDSCO has approved the site, and now clinical studies can be conducted at Mehsana site.



**LAMBDA**

Research Accelerated

Volume 12 / December 2017

Clinical Research

**NE**



**S** letter

[www.lambda-cro.com](http://www.lambda-cro.com)

- National GLP Compliance Monitoring Authority (NGCMA), India, inspection occurred in November 2017, and the decision is pending (expected soon). Lambda is authorized by NGCMA since 2014 and the inspection was conducted for the renewal of the certification. This is just a renewal process for the CRO to continue performing sample analysis of GLP studies



LAMBDA

Research Accelerated