# Lambda Research Newsletter

June 2017


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# Clinical Research NEWSletter

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## GLOBAL NEWS

### 1. Eye drops could replace injections for AMD treatment

The scientists at Britain's University, Birmingham have developed a method of delivering the drug as an eye drop for the treatment of age-related macular degeneration (AMD) instead of previously used painful injections into the eye.

The AMD is a common painless condition in which people gradually lose their central vision, generally in both the eyes, which may result in blindness. The treatment of AMD consists of repeated administration of drug injections into the eye on a monthly basis for a longer duration of at least three years.

These researchers have developed an eye drop that uses a cell-penetrating peptide (CPP) to deliver the drug to the relevant part of the eye within a minute, and this revolutionizing drug-delivery option has the potential to significantly impact AMD treatment.

The laboratory research published in the journal *Investigative Opthalmology and Visual Science* has revealed that the eye drops provided similar treatment outcomes as compared to the injected drugs. Furthermore, the effective self-administration of the drug by means of eye drop is likely to have a significant reduction in the associated adverse outcomes and health care costs compared with the current treatment options.

Source: hindustantimes.com

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## GLOBAL NEWS

### 2. WHO to start pilot prequalification of biosimilars for two cancer drugs

The World Health Organization (WHO) is planning to launch a pilot project in 2017 to facilitate the availability of prequalifying expansive cancer biosimilar drugs in the low- and middle-income countries.

The WHO Assistant Director General for Health Systems and Innovation Marie-Paule Kieny, MD, said that the innovator biotherapeutic products are often too expensive for many countries; hence, biosimilars are a good opportunity for these countries to expand their access to use and regulate these medicines.

In the month of September 2017, the WHO will invite drug manufactures to submit applications for the prequalification of biosimilar version of 2 WHO essential drugs:

- rituximab - for non-Hodgkin's lymphoma and chronic lymphocytic leukemia
- trastuzumab - for breast cancer

Furthermore, the final decision will come after a two-day meeting in Geneva between the WHO and national drug regulators along with the pharmaceutical industry, patient and civil society groups, payers and policymakers on the discussion of the various possible methods to make the biotherapeutic medicines accessible to the low- and middle-income countries.

Source: who.int

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## GLOBAL NEWS

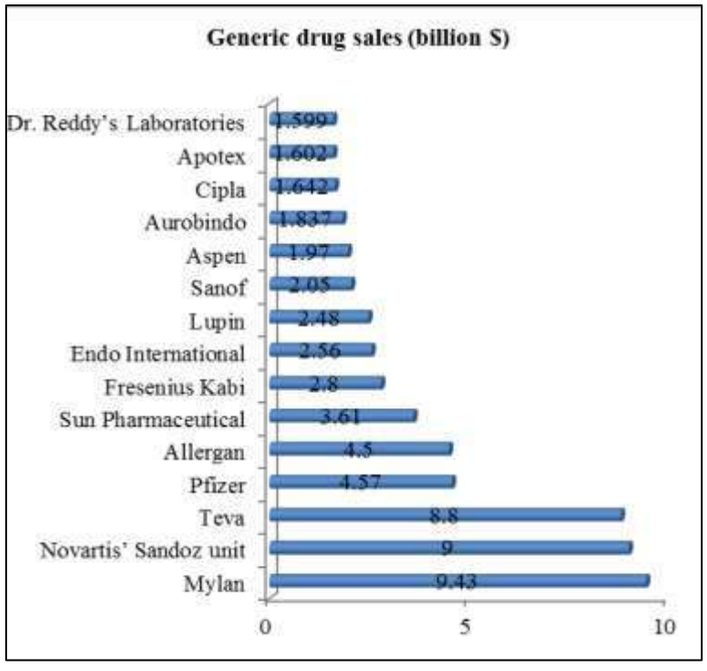
### 3. List of top 15 generic drug manufacturers by 2016 revenue

Companies manufacturing branded drugs was not only going through a tumultuous 2016, but generic drug companies were also facing the same pressure.

Where branded companies were suffering with the pain on costly cutting-edge therapies, generic companies suffered with already thin margins.

According to Fierce Pharma's 2016 ranking of pharma companies, Mylan is at the number one position in generic drugs with 2016 generic sales of $9.43 billion, followed by Novartis' Sandoz unit at 2nd position with sales of $9 billion and Teva at 3rd with $8.8 billion.

Generic drugs make up 89% of prescriptions but only 27% of drug costs, according to the industry, something the sector will continue to hammer out as lawmakers look to reduce drug costs in the U.S.




Source: fiercepharma.com

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## GLOBAL NEWS

### 4. Merck's Ebola vaccine candidate could see early action against new Congo outbreak

From a long time, Merck & Co. and various other biopharma players were trying to develop an Ebola vaccine. Now, before Merck's shot wins an official license, it could be used to combat a new outbreak in Congo.

A WHO advisory committee had recommended last month to deploy Merck's vaccine in the event of an outbreak.

An International Charity is in talks with the local government to implement a vaccine campaign, and WHO and local authorities are likely to approve the same. Aim of this vaccine is to create a protective barrier around the people at risk of Ebola infection. A Phase 3 trial demonstrated 100% efficacy of Merck's tested vaccine.

The international vaccine alliance Gavi has purchased and stockpiled 300,000 vaccine doses in case of an Ebola emergency. The current outbreak involves the Zaire strain of Ebola, which Merck's vaccine targets.

Source: fiercepharma.com

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## PHARMA INDIA

### 1. NRA of India for medicines commended by WHO

National Regulatory Authority (NRA) of India has been commended by the World Health Organization (WHO). In a letter to the Union Minister for Health & Family Welfare Mr. J. P. Nadda, WHO declared Indian NRA functional with a maturity level of 4, the highest level as per currently evolved definitions in respect of 5 functions.

Maturity level 4 indicates good results and sustained improvement trends, whereas level 3 reflects a systematic process based approach, early stage of systematic improvements, data availability regarding conformance to objectives and existence of improvement trends.

Due to the ability of low cost and high quality generic medicines manufacturing, India is being seen as a huge opportunity by domestic companies, and at the same time there exists growing concerns over the high prices of medicines worldwide.

Source: businesstoday.in

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## PHARMA INDIA

### 2. Pfizer's PCV 13 vaccine selected for India's immunization programme

According to latest announcement by Pfizer, its 13-valent pneumococcal conjugate vaccine (PCV 13) has been selected for the expansion of India's immunization programme. PCV 13 vaccine provides the broadest serotype coverage including the most prevalent one in India. PCV 13 is the most widely used pneumococcal conjugate vaccine in the world, with immunization program deployments in over 100 countries. Phase one of the programme will cover 20% (5.15 million) of about 26 million children of India's birth cohort.

PCV 13 will be introduced as a multi-dose vial in India. This presentation has been specially developed by Pfizer to enhance the efficiency of public immunization programmes.

Pneumococcal disease is one of the leading cause of deaths in children <5 years globally. According to a study published in 2015, approximately 1.05 lakh children died due to pneumococcal pneumonia in 2010. Epidemiological studies conducted in India have confirmed that the PCV 13 vaccine provides a higher coverage than any other PCV vaccine.

Source: pharmabiz.com

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## PHARMA INDIA

### 3. Generic blood cancer drug pomalidomide launched in India by Natco Pharma

Natco Pharma has launched the generic version of blood cancer drug pomalidomide as 1 mg, 2 mg, and 4 mg capsules in the domestic market.

Notco Pharma is a Hyderabad based pharmaceutical company, which is well known for making specialty medicines accessible to all. The company has released pomalidomide under the brand name 'POMALID' in India.

Pomalidomide is an analog of thalidomide, which is indicated in combination with dexamethasone for the treatment of patients with multiple myeloma who have shown disease progression on/within 60 days of at least two prior therapies, including lenalidomide and a proteasome inhibitor.

Source: health.economictimes.indiatimes.com

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## PHARMA INDIA

### 4. BE data submission to be mandatory for drug license

Now, the submission of the bioequivalence data is going to be a mandatory requirement for granting of licenses for the manufacturing of all drugs, including those in the market which have not submitted the data earlier.

According to the announcement of the Union Health Ministry, Biopharmaceutics Classification System (BCS) is going to be adopted for all drugs very soon. The BCS is a scientific framework for classifying drug substances from category 1 to IV based on their aqueous solubility and intestinal permeability. Drugs that fall under categories II and IV of the BCS would need to conduct bioequivalence studies mandatorily. Furthermore, a 3 year time window will be given to submit the BE data for the drugs which are already in the market.

The Drug Testing Advisory Board (DTAB) had recommended a group of experts to lay down the modalities related to the identification of the reference drug for the conduct of BE studies. According to DTAB, for those drugs which have completed four years in the market after first approval and are not considered as news drugs, the concerned State Licensing Authorities will grant the manufacturing license based on the submitted BE data.

Source: pharmabiz.com

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# REGULATORY ROUND-UP

## 1. EMA 2016 report with latest achievements

European Medicines Agency's (EMA) presented a report on outlining its successes from 2016 containing:

- approval of 27 new authorized medicines
- several new programs and schemes
- approval of 329 Orphan Drugs

EMA is quickly approving new drugs for those with unmet needs. Similar to US, a blooming number of applications are presented for approval to the EU regulator. EMA is also working on orphan medicines with its US and Japanese regulatory partners, and almost a third of applications for orphan designations were submitted to EMA and to another regulatory authority in parallel in 2016. In 2016, EMA launched a new clinical data website for the purpose of 'transparency', and since its introduction the site has 1,820 users, including 350 academics, with 6,474 documents viewed, 23,443 documents downloaded and about 330 downloads per day. EMA received 84 PRIME applications in 2016 including small and medium sized companies as well. Of those, 15 medicines were granted a PRIME designation, including:

- six for oncology treatments (out of 17 requested)
- 10 for advanced therapies

For speed and safety, EMA currently has a maximum time of 210 days to carry out an assessment for marketing authorization. If any further information or clarification is required during the assessment, the clock has to be stopped to give the company time to reply.

Source: raps.org

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## REGULATORY ROUND-UP

### 2. Congress calls on HHS to reverse biosimilar reimbursement policy

The Health and Human Services secretary, and administrator for the Centers for Medicare and Medicaid Services (CMS) received a letter from Sen. Pat Roberts (R-KS), and Reps. Joe Barton (R-TX) and Anna Eshoo (D-CA) as well as 52 other representatives and nine senators concerned with the biosimilar reimbursement policy from a recently issued final rule.

According to final rule by CMS issued on 30 October 2015 and later:

- same reference product of each biosimilar will be reimbursed at a single payment rate based on their average sales price under Medicare Part B
- each biosimilar should have its own Healthcare Common Procedure Coding System (HCPCS) code for reimbursement
- concerns from patient and physician groups, biosimilar manufacturers and others, have been raised particularly as the US Food and Drug Administration (FDA) is beginning to approve multiple biosimilars for the same reference product.

Source: raps.org

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## REGULATORY ROUND-UP

### 3. CFDA draft guidance for new drugs and devices

With the aim of reducing time consumed to set up a clinical trial and to accelerate the approval process, the China Food and Drug Administration (CFDA) released four draft documents, intended to encourage innovation in the drugs and medical devices industry.

The draft is focused on the:

- elimination of the need for sponsors to wait for the regulatory green light before starting a clinical trial
- sponsors can start the trial if CFDA fails to respond within 60 days

At 60 days, CFDA will still make companies wait longer than FDA, but the proposal makes timelines predictable for the first time. Existing approach with open ended nature made it difficult for companies to plan. CFDA signaled its interest in moving to a 60-day model when it proposed a cancer pilot project with that timeline in 2015.

Source: raps.org

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## REGULATORY ROUND-UP

### 4. Biogen escapes renewed fight over Tecfidera with court ruling

After the death of a patient taking Biogen's Tecfidera in 2014, a multiple sclerosis drug, Biogen was slapped with a warning from the FDA. This led to a total drop of Biogen in the market. Biogen also faced a securities lawsuit for hiding the negative fallouts. Now, Biogen has put that action to rest with a new ruling at the 1st Circuit Court of Appeals.

The plaintiffs said that Biogen executives knowingly concealed damage to Tecfidera's growth and didn't disclose the true damage to Tecfidera after the patient's death. Company's stock fell by more than 20% in one day when the drug maker finally lowered its sales guidance in 2015 for the blockbuster multiple sclerosis drugs.

A district court previously tossed the case which named Biogen's former CEO George Scangos, former EVP Stuart Kingsley and CFO Paul Clancy. The plaintiffs appealed. All those efforts turned out to be worthless as the appeals court agreed with the earlier ruling, stating that the plaintiffs' claims didn't meet a "rigorous standard" required of such securities suits.

Source: fiercepharma.com

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## MERGERS /ACQUISITIONS /COLLABORATIONS

### 1. Collaboration of Takeda with GammaDelta Therapeutics for T-cell therapy

For the development of T-cells therapy, Takeda Pharmaceutical has entered into a strategic collaboration with Abingworth portfolio company Gamma-Delta Therapeutics.

Concerning this collaboration, the two firms will jointly comprise an equity investment commitment up to $100 million to facilitate the GammaDelta Therapeutics led research and development.

The collaboration intends to develop GammaDelta Therapeutics' novel T cell platform, which is based on the unique properties of gamma delta (γδ) T cells derived from human tissues. The novel platform will facilitate to discover and develop new immunotherapies to treat multiple cancer diseases, including solid tumors and autoinflammatory diseases.

Source: takeda.com

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## MERGERS /ACQUISITIONS /COLLABORATIONS

### 2. Merger of INC Research and inVentiv Health

After the merger of Quintiles and IMS with a consolidated worth of $19 billion last year, this is going to be the 2nd largest merger with a combined worth of about $7.4 billion, with the two contract research organizations INC Research and inVentiv Health combining to form one major new company.

The announcement will result in the formation of:

- the second largest biopharmaceutical outsourcing provider in the world
- three contract research organizations (CROs) and contract commercial organizations (CCOs) are focused to improve customer performance and to accelerate market of new products
- reputed position in growing CROs and CCO.

Merged company will have commercial insights to inform the clinical trial process, designing studies to be more efficient and effective to address evolving patient and payer needs.

Source: spjnews.com

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## MERGERS /ACQUISITIONS /COLLABORATIONS

### 3. Pfizer and Sangamo collaborate to develop gene therapy programs for Hemophilia A

For conducting Phase 1/2 clinical study of their molecule SB-525, and to develop gene therapy programs for Hemophilia A, Pfizer and Sangamo have decided to collaborate in a deal worth up to $545 Million.

Under this collaboration, Pfizer will pay $70 million upfront to Sangamo for:

- conducting Phase 1/2 clinical trials of SB-525
- certain manufacturing activities

Pfizer will handle subsequent research, development, manufacturing and commercialization activities for SB-525 and additional products.

Sangamo will receive an estimated amount of $475 million from Pfizer, including:

- up to $300 million for the development and commercialization of SB-525
- up to $175 million for any additional hemophilia A gene therapy product candidates that get developed from Pfizer
- Sangamo will also be eligible for tiered double-digit royalties on net sales.

Source: biospace.com, connect.dcat.org

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## MERGERS /ACQUISITIONS /COLLABORATIONS

### 4. Definitive arrangement agreement between Merus Labs and Norgine

A definitive arrangement agreement is signed between Merus Labs and Norgine, according to which, Norgine will acquire all outstanding shares of Merus by cash at $1.65 per share with the total cost of approximately $342 million. All the transactions will be done by available cash and new credit facilities.

Clauses of agreement include:

- a non-solicitation bond on the part of Merus
- a customary "fiduciary out" provisions

In any circumstances if Merus terminates the agreement, Merus needs to pay an amount of $7.5 million to Norgine as termination fee.

- enters into an agreement with respect to a superior proposal or
- if the Board of Directors of Merus withdraws or modifies its recommendation with respect to the Arrangement

Source: biospace.com

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# DRUGS: APPROVALS AND LAUNCHES

## 1. Fast Track approval for C-Cure in heart failure by US FDA

Celyad receives Fast Track approval by the US Food and Drug Administration (FDA) for the development of its cardiopoietic stem cell therapy in heart failure (C-Cure® therapy). C-Cure® therapy is developed for:

- patients of chronic heart failure
- patents of ischemic cardiomyopathy
- reduction in mortality, hospitalization and improvement of quality of life in patients with chronic heart failure and ischemic cardiomyopathy. with cardiac diseases

C-Cure® is designated to enhance reparative capabilities in the failing heart by own cells of the patients. Cells are harvested from bone marrow, treated with a combination of cytokines and growth factors, and then re-injected into the heart. The 12 months data of CHART-1 trial were recently presented, which demonstrated that sizeable patient populations showed positive response to C-Cure®.

| **Safety data for cardiac events** | | | | | | |
|---|---|---|---|---|---|---|
| Timing Group | Prior control | Prior cell therapy | Post control | Post cell therapy | New event control | New event cell therapy |
| **Death** | **0 (0%)** | **0 (0%)** | **2 (8%)** | **0 (0%)** | **2 (8%)** | **0 (0%)** |
| **Elective transplant** | **0 (0%)** | **0 (0%)** | **0 (0%)** | **1 (5%)*** | **0 (0%)** | **1 (5%)*** |
| **Cardiac disorder** | **2 (8%)** | **5 (24%)** | **15 (62%)** | **16 (76%)** | **13 (54%)** | **11 (52%)** |
| SV arrhythmia | 1 (4%) | 3 (14%) | 7 (29%) | 9 (43%) | 6 (25%) | 6 (28%) |
| Ventricular fibrillation | 0 (0%) | 0 (0%) | 1 (4%) | 1 (5%) | 1 (4%) | 1 (5%) |
| Ventricular tachycardia | 1 (4%) | 2 (10%) | 8 (33%) | 6 (20%) | 7 (29%) | 4 (19%) |

*Death resulted as a complication following elective heart transplantation.

Source: pharmaceutical-technology.com, clinicaltrials.gov

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## DRUGS: APPROVALS AND LAUNCHES

### 2. FDA approves Kisqali® Femara® Co-Pack for cancer therapy

Two months after the intial approval of Kisqali®, Novartis has received the approval from FDA for the combination of Kisqali® and Femara®. Combination contains Kisqali® (ribociclib) and Femara® (letrozole) in the strengths of:

- Kisqali 600 mg plus Femara 2.5 mg,
- Kisqali 400 mg plus Femara 2.5 mg, and
- Kisqali 200 mg plus Femara 2.5 mg.

This co-pack is indicated for the treatment of:

- hormone receptor-positive advanced or metastatic breast cancer in postmenopausal women
- human epidermal growth factor receptor-2 negative (HR+/HER2-) advanced or metastatic breast cancer in postmenopausal women

After this approval, physicians prescribing Kisqali® and Femara® together can prescribe the combination in single co-pay.

Source: pharmaceutical-technology.com, bizjournals.com

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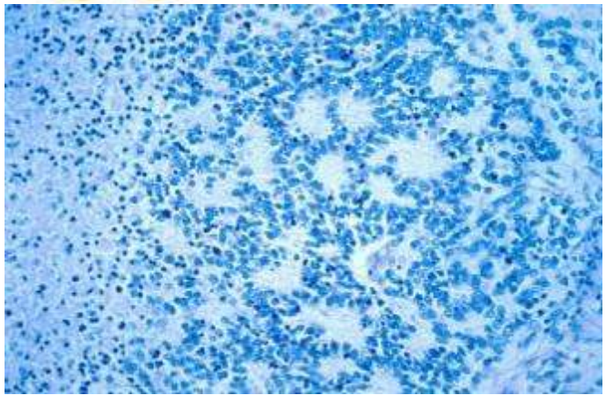
## DRUGS: APPROVALS AND LAUNCHES

### 3. EU approves dinutuximab-ß antibody for neuroblastoma

European Commission (EC) has approved a new antibody ch14.18/CHO (dinutuximab-ß) of EUSA Pharma for the treatment of high-risk neuroblastoma in patients older than a year. Dinutuximab-ß is the only permitted immunotherapy in Europe for high-risk neuroblastoma treatment. Up to 5 cycles of continuous infusion of ch14.18/CHO is administered at a dose of 10 mg/m$^2$/day over 10 days (total dose 100 mg/m$^2$/cycle) with a cycle duration of 35-days.



It is a monoclonal chimeric antibody, which acts on a specific antigen GD2 on neuroblastoma cells. This approval envisioned a hope for children suffering with neuroblastoma. Neuroblastoma is a most common form of solid tumors, primarily affects children under the age of 5 years. It arises from neural crest cells, responsible for fetal nervous system development.

Source: pharmaceutical-technology.com, clinicaltrials.gov

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## DRUGS: APPROVALS AND LAUNCHES

### 4. FDA approved avelumab for advanced bladder cancer treatment

Merck and Pfizer have received approval for the immunotherapy drug Bavencio (avelumab) injection from FDA for the treatment of patients with locally advanced or metastatic urothelial carcinoma (UC).


Bavencio belongs to a new drug of class called checkpoint inhibitors, which target a protein known as 'programmed cell death 1 ligand 1 (PD-L1)'.

PD-L1 is used by some cancer cells to evade the immune system. By blocking this protein, it helps immune cells recognize and attack the cancer cells and to kill them.

The indication for avelumab will be UC patients:

- who have exhibited progression during or following platinum-containing chemotherapy, or
- who have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

Source: pharmaceutical-technology.com

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## DRUGS: DEVELOPMENT & CLINICAL TRIALS

### 1. Novartis in-licensing for ECF843 with Lubris

A new treatment for the dry eye syndrome (DES) has been developed by Lubris and after in-licensing, Novartis has introduced it in the market. ECF843 is a recombinant human lubricin (rh-Lubricin) protein and works by:

- restoring the tear film function,
- reducing friction, and
- relieving associated symptoms.

ECF843 demonstrated its potential in a small Phase 2 study through instantly improving dry eye symptoms by increasing lubrication with no severe adverse events. Lubricin is an endogenous glycoprotein and acts on tear film where it binds to tissues of the ocular surface and protects them.

This in-licensing will build up Novartis's leadership in ophthalmology and DES treatment.

Source: novartis.com, pharmaceutical-technology.com

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## DRUGS: DEVELOPMENT & CLINICAL TRIALS

### 2. Eli Lilly scores Phase 3 migraine success with galcanezumab

Eli Lilly's calcitonin gene-related peptide (CGRP) monoclonal antibody, galcanezumab, showed positive results in a Phase 3 study. This calcitonin gene-related peptide is the second monoclonal antibody of the class calcitonin gene-related peptides for the prophylactic treatment of episodic and chronic migraine.

In patients suffering from episodic migraine, galcanezumab reduced the number of migraine headache days by 4.7 days with doses of 120 mg and 4.6 days with doses of 240 mg, respectively. This galcanezumab reduction was statistically significant compared to placebo which was 2.8 days.

Now, the company is planning to submit a Biologics License Application (BLA) to the FDA in the second half of 2017 and to other regulatory agencies for approval based on these studies.

Source: pharmaceutical-technology.com

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## DRUGS: DEVELOPMENT & CLINICAL TRIALS

### 3. Cannabidiol has shown efficacy for a severe form of epilepsy

Comprehensive Epilepsy Center at New York University (NYU) Langone Medical Center has introduced a new treatment for life-threatening seizures in children with a rare and devastating form of epilepsy. This randomized, controlled trial (Phase 1/2) showed that cannabidiol (CBD), a compound in marijuana, can be used for the treatment of epilepsy in children.

This study relies on Epidiolex, a liquid formulation of cannabidiol developed by the British company GW Pharmaceuticals. Epidiolex is not yet approved by the U.S. Food and Drug Administration. This study was funded by GW Pharmaceuticals and the company is planning to file for FDA approval this year.

The study was conducted on 120 children and teenagers, aged between 2 to 18 years, with Dravet Syndrome, which generally starts causing severe seizures within the first year of life. Liquid Epidiolex 20 milligrams or a placebo was given to patients, on top of their usual medication. Study was conducted at 23 sites in the United States and Europe for 14 weeks.

The results of the study are published in the May issue of the *New England Journal of Medicine*.

Source: drugs.com

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## DRUGS: DEVELOPMENT & CLINICAL TRIALS

### 4. Nasal spray therapy for treatment of tachycardia

A novel therapy comprising nasal spray of Etripamil was presented at Heart Rhythm 2017, the Heart Rhythm Society's 38th Annual Scientific Sessions. This nasal spray can be used at home for the treatment of paroxysmal supraventricular tachycardia (PSVT). This nasal spray can change the way patients are treated for a debilitating cardiac arrhythmia.

This was a multicenter, randomized trial that had enrolled over 100 patients from more than 35 centers across the U.S. and Canada. Etripamil established as a novel, potent, short-acting calcium channel blocker is being developed as a fast-acting nasal spray that can be self-administered by the patients to acutely terminate PSVT episodes.

Etripamil at doses of 70 mg, 105 mg and 140 mg yielded conversion rates of 87%, 75% and 95%, respectively that were all significantly better than the 35% conversion rate in the placebo group. The mean conversion time ranged from 2.60 minutes to 3.37 minutes in the Etripamil groups.

The most common adverse event that occurred to patients who used the Etripamil therapy was transient nasal congestion or irritation.

Source: medicalnewstoday.com

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## PATENTS: NEW APPROVALS /LITIGATIONS /SETTLEMENTS

### 1. Intec Pharma received patent for Accordion Pill™ comprising levodopa

United States Patent and Trademark Office granted a patent for Accordion Pill™ comprising levodopa to Intec Pharma Ltd. for the treatment of Parkinson's disease. The patent is scheduled to remain in force until November 2031 and belongs to the Company's IN-11 patent family to Intec Pharma Ltd.

Accordion Pill™ provides an improved treatment regimen, which is currently in a global Phase 3 clinical trial in patients with advanced Parkinson's disease.

Accordion Pill™ is an oral drug delivery system that is designed to improve the efficacy and safety of existing drugs and drugs in development by utilizing an efficient gastric retention and specific release mechanism.

Accordion Pill™ is being developed for:

- the prevention and treatment of gastroduodenal and
- small bowel Nonsteroidal Anti-Inflammatory Drug (NSAID)-induced ulcers.

AP-CBD/THC (Accordion Pill - cannabis sativa, cannabidiol/ tetrahydrocannabinol) is for:

- low back neuropathic pain
- fibromyalgia

Source: biospace.com

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## 2. Progenza patented by Regeneus (RGS.AX)

Regeneus received a patent for the composition, manufacture and use of Progenza stem cell technology from the Japanese Patent Office till 2032. Progenza is a allogeneic off-the-shelf stem cell technology platform for:

- the treatment of osteoarthritis,
- other musculoskeletal disorders and
- other inflammatory conditions.

Progenza acts by reducing the inflammation and promoting healing and repair in the damaged tissues. Progenza is made up from allogeneic mesenchymal stem cells (MSCs) from human adipose tissue and bioactive secretions of the cells with increased therapeutic benefit.

Progenza cells are adult stem cells not reprogrammed or genetically altered. Presently, Progenza is in a Phase 1 clinical trial for the treatment of knee osteoarthritis.

Source: abnnewswire.net

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## PATENTS: NEW APPROVALS /LITIGATIONS /SETTLEMENTS

### 3. Origenis receives patent for lead small molecule LRRK2 inhibitor

Origenis GmbH is a biopharmaceutical company that develops brain-penetrating small molecule medicines and diagnostics for a variety of neuro-inflammatory diseases.

Origenis GmbH has developed a novel agent to fight neurodegenerative and neuroinflammatory diseases known as a small molecule inhibitor of Leucine Rich Repeat Kinase 2 (LRRK2).

LRRK2 is associated with neurodegeneration of chronic and acute brain diseases including Parkinson‘s, Alzheimer’s, dementia, and traumatic brain injury among others.

The Patent Office has granted the company two important patents, US9,499,535 and US9,637,491, that protect the further development of small molecule inhibitor of LRRK2 within the Company´s CNS franchise.

Source: biospace.com

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## PATENTS: NEW APPROVALS /LITIGATIONS /SETTLEMENTS

### 4. InMed files provisional patent application for topical cannabinoid glaucoma therapy

InMed Pharmaceuticals Inc. filled a patent application for a novel, cannabinoid-based drug therapy INM-085 in the United States. INM-085 is a cannabinoid-based topical therapy for glaucoma.

Glaucoma is a second-leading cause of blindness in the world. It is a group of eye diseases which result in damage to the optic nerve and vision loss. Risk factors for glaucoma include increased pressure in the eye, a family history of the condition, migraines, high blood pressure, and obesity.

INM-085 preparation contains nanoparticle-laden vehicle for controlled delivery of ophthalmic drugs into the aqueous humor of the eye. This vehicle is used to reduce the intraocular pressure associated with glaucoma. It is used as a once-per-day eye drop, administered immediately prior to the patient's bedtime.

Source: pharmpro.com

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## TECHNOLOGY /NDDS

### 1. Dry powder inhalational device

H&T Presspart released new dry powder inhaler- PowdAir Plus. The device was developed by a Portuguese company Hovione Technology, a spinoff of Hovione. The PowdAir Plus uses capsule drug cartridges of gelatin and hypromellose (HPMC) and only four plastic parts.

One prominent inhalation therapy is the dry powder inhaler (DPI). Use of these devices is very simple. A device tray is opened to place the capsule inside and then closed. The device automatically punchers the capsule kept in the tray to make it ready for inhalation.

The most important DPI attributes are:

- a high respirable fraction (fine particle dose, FPD)
- breath triggered, with dose release at a consistent flow rate
- compatible with a range of formulations
- protection against low/high dosing in the hands of patients

Source: medgadget.com

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## TECHNOLOGY /NDDS

### 2. Calibrated tip wire guide for accessing pancreatic and bile ducts

A new technology in the form of Acrobat 2 calibrated tip wire guide for navigating pancreatic and bile ducts during cholangio-endoscopic procedures has been released by Cook Medical.

The Acrobat 2 is available in 0.025- and 0.035-inch diameters and 205 cm, 260 cm and 450 cm lengths, with straight and angled tips. Acrobat 2 can also be used during sphincterotomy. Other important attributes of the Acrobat 2 include:

- 29% greater pushability than the initial 0.035" version of the Acrobat wire guide.
- 1:1 torqueability for precise rotation of the wire when needed for selective cannulation and navigation of ducts.
- Mark V System® provides high-contrast visualization of movement and depth of insertion.

Source: medgadget.com, cookmedical.com

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## TECHNOLOGY /NDDS

### 3. A new blood test to detect pancreatic cancer

A new blood test has been developed for the earlier diagnosis of pancreatic cancer. Pancreatic cancer is a deadly type of tumor because it is often detected too late for effective treatment. This new experimental test detects a bundle of proteins churned out by pancreatic tumors.

This test appears to be more accurate than the available test for a protein called CA19-9 as a spike in the protein is not specific to the cancer; it can go up when the pancreas is inflamed. CA 19-9 is a biomarker to track the patients' progress during treatment.

The new test uses a chip technology that analyzes extracellular vesicles (EVs), which are churned out by cells into the bloodstream. EVs can come from both normal cells and cancer cells. Researchers found five specific proteins which were a good marker of pancreatic cancer, and testing for the five proteins detected 86% of the pancreatic cancer cases.

This study was published in the May issue of *Science Translational Medicine*.

Source: drugs.com

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## TECHNOLOGY /NDDS

### 4. Use of DC electricity to deliver drugs through skin


A New York based company named Soterix Medical, after FDA approval, introduced a new device - IontoDC iontophoresis medication delivery system. This device is mainly meant for the purpose of introducing soluble salt ions, but also used for fentanyl to control pain in the body.

This device relies on battery power to generate low current (up to 2 milliamperes) electricity, which can be adjusted between 1 and 2 milliamperes, depending on:

- the drug to be delivered in the body
- amount of time the current is activated

Current is required to move the drugs through the skin. The device constantly monitors and displays the electric current supplied, as well as the resistance of the body between the electrodes that indicates how well the skin is in contact with the cathode and anode.

Source: medgadget.com

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## WHAT'S NEW AT LAMBDA

### What is population pharmacokinetics (Pop PK)?

Population pharmacokinetics is the study of variability in drug concentrations between individuals (healthy volunteers or patients). It comprises the assessment of variability within the population and to account for the variability in terms of patient characteristics such as age, renal function or disease state.

**Differences between Pop PK and conventional pharmacokinetic evaluation?**

- The collection of relevant pharmacokinetic information in patients who are representative of the target population to be treated with the drug.
- Supports optimizing design for clinical studies and provide information for strategic drug development decisions.
- It helps to obtain integrated information on pharmacokinetics, even from sparse data obtained from patients with a target disease
- Relatively uses dense/rich data, or a combination of sparse and dense/rich data can also be used in Pop PK analysis.
- The identification and measurement of variability during drug development and evaluation.
- The explanation of variability by identifying factors of demographic, pathophysiological, environmental, or concomitant drug-related origin that may influence the pharmacokinetic behavior of a drug.
- Utilizes pool of data from a variety of clinical studies, such as from pediatric and elderly patients or data obtained during the evaluation of the dose-response and exposure-response relationships (i.e., comparison between dose or concentration and efficacy or safety).

All of these information is needed during the FDA's evaluation of a drug for marketing authorization (NDA or BLA).

**Why Pop PK is Important?**

Pop PK approach provides useful safety, efficacy, and dosage optimization information for the drug label. All drugs exhibit between-subject variability (BSV) in exposure and response, and many studies performed during drug development are aimed at identifying and quantifying this variability.

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A sound understanding of the influence of factors such as body weight, age, genotype, renal/hepatic function, and concomitant medications on drug exposure and response is important for refining dosage recommendations, thereby improving the safety and efficacy of a drug agent by appropriately controlling variability in drug exposure.
Population modeling is a tool to identify and describe relationships between a subject's physiologic characteristics and observed drug exposure or response.

Pop-PK is especially crucial when the clinical data is sparse such as in the cases of pediatrics or orphan (rare) diseases.

The efficacy and safety of a new chemical entity (NCE) is generally characterized in Phase 3 studies in a well-defined restricted patient population. The PK information is used to extrapolate the safety and efficacy findings to the wider patient population who may receive the NCE in question.

Today, Pop PK analyses are a regular part of the documentation of an NCE which provides supportive evidential information to queries which remain unanswered through conventional pharmacokinetics.

**How to perform Pop PK?**

Models provide a basis for describing and understanding the time-course of drug exposure and response after the administration of different doses or formulations of a drug to individuals, and provide a means for estimating the associated parameters such as clearance and volume of distribution of a drug. Population models can be developed using relatively few observations from each subject, and the resulting parameter estimates can be compared to previous assessments to determine consistency between studies or patient populations.

The non-linear mixed effects modeling approach has become increasingly used for population pharmacokinetics. Pop-PK models are complex mathematical equations describing the drug disposition in population or subpopulation with the targeted disease. Currently, various softwares like Phoenix NLME, NONMEM and Monolix are available for performing Pop

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PK analysis. Lambda Therapeutic Research Limited has the capability of performing Pop PK analysis by non-linear mixed effects modeling approach using Phoenix NLME™ software (Certara L.P., Version 7.0).

**Regulatory views for Pop PK**

Pharmaceutical industry scientists and the FDA have long been interested in the use of Pop PK/pharmacodynamics in the analysis of drug safety and efficacy among population subgroups.

The information on the variability that would occur during clinical use is critical, and it is obscured by restrictions kept during traditional PK studies

In Phase 1 and, perhaps, most of phase 2b, where patients are sampled extensively, complex methods of data analysis may not be needed. Two-stage methods can be used to analyze the data, and standard regression methods can be used to model the dependence of parameters on covariates. Alternatively, data from individual studies in Phases 1 and 2b can also be pooled and analyzed using the nonlinear mixed-effects modeling approach. The Pop PK approach can also be used in early Phase 2a and Phase 3 of drug development to gain information on drug safety (efficacy) and to gather additional information on drug pharmacokinetics in special populations, such as the elderly. This approach can also be useful in postmarketing surveillance (Phase 4) studies.

Currently, results from population analyses are most frequently used to characterize the PK in the target population, to provide PK data in special populations (elderly, children, renally impaired etc.) and to support dosing recommendations for these populations. To make the information resulting from a population analysis useful during the regulatory assessment, the report should include sufficient detail to enable a secondary evaluation by a regulatory assessor.
The analysis and report of the analysis need to be of sufficient quality so that the final model can be judged to be a good description of the data, and that the results and conclusions ensuing from the population analysis can be considered valid.

Written by: Chintan Bodiwala & Dr. Pradeep Sharma

Source: fda.gov; ema.europa.eu


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