Lambda Research Newsletter

July 2017

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Clinical Research NEWSletter

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GLOBAL NEWS

1. No six-month wait for biosimilars after FDA approval

The US Supreme Court has announced that biosimilar companies will not have to wait for additional six months for launching their new biosimilars after the US food and drug administration (FDA) approval.

The case setting competition between the 3 different biologics manufacturers Amgen, Novartis and Sandoz attempted to clarify the term “patent dance” for biosimilars. According to the patent dance process, companies must exchange and figure out the patent situation of a biologic and proposed biosimilar before the biosimilar comes to market.

According to the court, an applicant may provide notice of commercial marketing before obtaining a license. The statute’s use of the word ‘licensed’ entirely reflects the fact that, on the ‘date of the first commercial marketing,’ the product must be ‘licensed’.

The Supreme Court said that patent dance explains that a biosimilar applicant must provide the biologic reference product sponsor with its application and manufacturing information, enforceable by states.

The opinion also might set the stage for FDA to be more involved in the patent dance and interpreting the BPCIA (Biologics Price Competition and Innovation Act) further.

Source: raps.org

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GLOBAL NEWS

2. Generic recommendations started by Caribbean Regulatory System

The Caribbean Public Health Agency/Caribbean Regulatory System (CARPHA/CRS) begins its work of recommending generic drugs by introducing 4 generic drugs for the treatment of human immunodeficiency virus (HIV).

The recommendation follows approval from the World health organization (WHO). Recommendations included emtricitabine/ tenofovir and tenofovir tablets, which are generics of Viread and Truvada, recently approved by the US FDA.

This complete process aims to sign-off on marketing authorizations within 60 calendar days, which is remarkably faster than what the Caribbean countries can marshal independently.

Medicines which have prior approval from a trusted regulator, such as the FDA, Health Canada or Brazil's ANVISA will be examined by CARPHA/CRS.

Source: raps.org

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GLOBAL NEWS

3. FDA to remove Opana ER from the market

Endo Pharmaceuticals was ordered by the FDA to remove its analgesic drug oxymorphone hydrochloride extended-release tablets (Opana ER) from the market. With regards to opioid addiction crisis, FDA said its risks outweigh the benefits. If Endo does not remove the complete stock from the market, the FDA would take steps required for its removal from the market.

For the first time FDA has taken this kind of action which will be a warning for other companies to weigh the risk-benefit profiles of all approved opioid analgesic products.

This is one of the first policy decisions by the agency after recommendation of an advisory committee since Scott Gottlieb was appointed FDA commissioner by the US President Mr. Donald Trump, who had talked about the opioid crisis during his campaign.

An approximately $158 million sale was generated by Opana ER for the company last year, which was 10% less compared to the year before.

This decision by FDA comes as a result of a variety of lawsuits, by a number of states with high rates of mortality due to opioid overdose filled against Endo and other opioid makers.

Source: fiercepharma.com

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GLOBAL NEWS

4. Paracetamol may inhibit masculinity during pregnancy

Paracetamol is a popular pain reliving medicine, used worldwide. Researchers in a new study in an animal model found that paracetamol actually damages the development of male behaviours.

Studies are available which have shown that in male foetuses, paracetamol inhibit development of male sex hormone testosterone. This inhibition increases the risk of malformations of testicles in the infants and for adult male behaviours.

During a trial, mice which were exposed to paracetamol during foetal stages were unable to copulate like control animals. In the study, the dosages which were administered to mice were very close to that administered in pregnant women. The trials are restricted to animals only, so results cannot be transferred directly to the humans.

Reduction in testosterone in males
Testosterone helps in male body development along with the development of the brain. The masculine behaviours in mice observed were

- they did not attack other males
- unable to copulate
- behaved more like female mice when it comes to urinary territorial marking

The number of neurons was half in the area of the brain which control sex drive in the mice which were treated with paracetamol as compared to the control group.

Effects on female fertility
The study published in the scientific journal *Reproduction* in 2016, showed that female mice had fewer eggs in their ovaries if their mothers had paracetamol during pregnancy. This led to infertility of the mice more quickly.

Source: medicalxpress.com

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PHARMA INDIA

1. India introduces 12% GST for essential drugs

In India twelve percent Goods and Services Tax (GST) is going to be applied on the essential drugs from the month of July 2017. The government of India has fixed GST rate of 12% on most of the essential drugs as against the current rate of 9%. This will lead to increase in prices of drugs up to 2.29%.

Whereas there will be reduction in prices of some selected medicines like Insulin. Government is revising GST for these drugs downwards to 5% from the current 12%. The list of National Essential Medicines includes the likes of Heparin, Warfarin, Diltiazem, Diazepam, Ibuprofen, Propranolol and Imatinib for which prices are increased.

The Indian drug price regulator 'National Pharmaceutical Pricing Authority (NPPA)' has already notified that:

- excise duty levied on maximum retail price (MRP), will be calculated by applying a factor of 0.95905 to the existing ceiling price which will be exclusive of applicable GST rates
- those scheduled formulations which are exempted from excise duty, their existing notified ceiling price would also be the new ceiling price, exclusive of GST rates

If prices rise up >10% of MRP due to the 12 percent GST, companies would have to absorb the net increase whereas for the drugs like Insulin for which GST is reduced from 12 to 5%, companies will be required to reduce the MRP.

Source: health.economictimes.indiatimes.com

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PHARMA INDIA

2. Endoxifen clinical trial protocol approved by DCGI

Intas Pharmaceuticals Ltd., received Drugs Controller General of India-investigational new drug (DCGI-IND) committee approval for their clinical trial protocol for Endoxifen.

The study is going to be a double-blind, double-dummy, active-controlled, oral, multiple-dose, parallel, multicenter, randomized study to evaluate efficacy and safety of Endoxifen in bipolar I disorder patients with current manic or mixed episode.

A study of Endoxifen used for the treatment of mania has been published in the journal of *Clinical and Translational Science* in 2016. According to study, the protein kinase C (PKC) signaling system plays a role in mood disorders and PKC inhibitors such as endoxifen may be an innovative medicine for bipolar disorder (BP) patients.

Endoxifen is an active metabolite of tamoxifen with a higher affinity and specificity to estrogen receptors that also inhibit aromatase activity.

Source: ctri.nic.in

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PHARMA INDIA

3. Top five Indian companies spent over Rs 8,000 crore on R&D in FY17

To improve the standard of research in India and for future benefits, the top five pharmaceutical companies in India appear to have invested an amount of INR 8,025 crore for research and development (R&D) in FY17. This investment will be a potent cure for the present ills dogging the industry, as in India, a very less amount is spent for R&D. Research cost for generic business is somewhat similar for Teva, Mylan and Allergan in 2016. The R&D expenses constitute 9% of the cumulative revenues of the companies. The TOP five pharmaceutical companies in India spent more than INR 8,000 crore, which is higher than the profit earned by the largest pharma company in FY 17. This also eclipses the total profit earned by the remaining four leading drug companies.

Besides the traditional generic product pipeline, now the companies are investing in:

- research of complex generics,
- specialty and differentiated products, and
- biosimilars

For the five companies, R&D expenditure has increased by six fold since FY10.

The increase in spent on R&D of top five India pharma companies.

	FY 10				FY 17			
Companies	**R&D Spent**	**Revenues**	**R&D Spent as % of revenue**	**Net Profit**	**R&D Spent**	**Revenues**	**R&D Spent as % of revenue**	**Net Profit**
Sun Pharma	208.2	3808.6	5.5	1351.1	2145.8	30264.2	7.1	6964.3
Lupin	343.8	4773.6	7.2	681.6	2310	17119.8	13.5	2557.4
Aurobindo Pharma	97.2	3575.4	2.7	563.4	543	14844.7	3.7	2301.6
Cipla	228.1	5359.5	4.3	1082.5	1071	14280.8	7.5	1006.3
Dr Reddys Labs	379.3	7027.7	5.4	106.7	1955	14080.9	13.9	1257.2
Total	1256.6	24544.8	5.1	3785.3	8024.8	90590.4	8.9	14086.8

Source: Bloomberg; INR crore

Source: economictimes.indiatimes.com

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PHARMA INDIA

4. Pharmacovigilance cells set up for monitoring ADRs in 70 pharma companies

For collection and forwarding adverse drug reactions (ADRs) to licensing authorities, 70 pharma companies in India have set up pharmacovigilance (PV) cells in their organizations. There has also been active participation of 30% from market authorisation holders (MAHs) for ADRs.

Government by gazette notification on March 8, 2016, mandated MAHs to set up PV cells in their companies in accordance with updated ADR rules emerging from the use of the drug manufactured or marketed by the respective MAH in the country.

In order to check the risk-benefit balances, exporting pharmaceutical companies are supposed to set up a PV system to fulfill its legal tasks in relation to pharmacovigilance. Risk-benefit assessment of the product can be done properly through signal detection.

A pharmaceutical company can meet their PV obligations by

- setting up in-house systems for PV or
- entering into contractual arrangements with Contract Research Organizations (CROs) specializing in pharmacovigilance function.

Standard operating procedures (SOPs) can vary from few in number to many, depending upon the length and complexity of the processes involved. SOPs ought to reflect the main requirements of the relevant legislation but should also be adapted to the technical and human infrastructure of the company.

Source: pharmabiz.com

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REGULATORY ROUND-UP

1. DCGI sets guidelines for FDC drug trials

To meet the regulatory demands for clinical data of fixed dose combination, the Drug Controller General of India (DCGI) has set up a guideline. The DCGI is providing flexibility in the design of clinical trials and asking manufactures to focus on the safety data.

A total of 18 months' time period was given to manufactures by the DCGI to submit the data on products which were marketed without the DCGI approval. Only a few companies have submitted the data for Phase 4 clinical trials.

Primarily DCGI committee wants to gather data for the safety of FDCs, while efficacy is a secondary objective. The recommendations by DCGI committee provide advice as to how FDC manufacturers can design trials to generate the necessary data. The advice also provides manufacturers a lot of flexibility.

According to these recommendations the trials can be open label, double blind, comparative, single arm or crossover studies and sized to ensure statistical significance. Sponsors were instructed to ensure their trials in geographically distributed study sites along with anticipated safety parameter and related monitoring.

Source: raps.org, cdsco.nic.in

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REGULATORY ROUND-UP

2. WHO to craft essential diagnostics list

Based on the recommendations of the expert committee for the development of Essential Diagnostics List (EDL), the World Health Organization (WHO) is creating a Strategic Advisory Group of Experts on In Vitro Diagnostics (SAGE IVD), which will advise on the development of the list as well as policies.

According to the committee, initially, WHO will focus on *in-vitro* diagnostics, with priority areas including tuberculosis, malaria, human immunodeficiency virus (HIV) and hepatitis B and C. The list will be further expanded to other areas including other antimicrobials and non-communicable diseases.

The EDL is intended to provide countries with evidence-based guidance for the development of their own national list for essential diagnostic tests and tools just like that of the essential medicines list for different countries.

It is expected to provide same benefits as that of the essential medicines list by facilitating access to diagnosis with affordable prices. It will be beneficial particularly in low-resourced countries, by prioritizing the most important diagnostic tests.

This is considered as "a landmark decision" by Global Health Technologies to guide governments on the vital diagnostic tools that should be made available through healthcare systems.

Source: raps.org

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REGULATORY ROUND-UP

3. Upcoming pilot study by FDA to sign-off lower-risk digital health products without premarket review

The US Food and Drug Administration (FDA) is planning to run a pilot study program which would create a third-party certification program. Under this pilot study, lower-risk digital health products could be marketed without the FDA premarket review whereas higher-risk products could be marketed with a streamlined FDA review.

This pilot study will form a new approach for the regulations of digital health tools. This could reduce the time and cost of market entry for digital health products by employing a unique pre-certification program for softwares as medical devices.

The FDA will also provide guidance clarifying its stance on products which currently fall outside FDA regulations and that contain multiple software functions.

The FDA also mentioned that the postmarket collection of real-world data might support the new and evolving product functions.

Source: raps.org

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REGULATORY ROUND-UP

4. CDSCO releases revised draft guidelines on postmarketing surveillance of pharmaceutical products

In order to resolve uncertainty in the implementation of pharmacovigilance programmes, the Central Drugs Standard Control Organisation (CDSCO), in collaboration with Indian Pharmacopoeia Commission (IPC), released the revised draft guidelines on post marketing surveillance of pharmaceutical products in India.

These guidelines are mainly focused on identification of risk factors along with establishment of pharmacovigilance (PV) system for pharmaceutical products.

The CDSCO has ordered marketing authorisation holders (MAHs) of pharmaceutical products to establish PV system with medical officer or a pharmacist who will act as a pharmacovigilance officer-in-charge (PvOI) for collection and analysis of adverse drug reaction reports related to pharmaceutical products marketed by them in India.

Individual case safety report (ICSR) will be prepared by PvOI which will be submitted to National Coordination Centre Pharmacovigilance Programme of India (PvPI), by electronic transmission of individual case safety report (E2B).

Source: pharmabiz.com

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MERGERS /ACQUISITIONS /COLLABORATIONS

1. Janssen collaborates with Protagonist for the development of PTG-200

For the development, manufacture, and commercialization of PTG-200, Janssen Pharmaceutical has entered into a worldwide exclusive license and collaboration agreement with biopharmaceutical company Protagonist Therapeutics.

PTG-200 is an oral interleukin-23 receptor (IL-23R) antagonist drug candidate for the treatment of inflammatory bowel disease (IBD). PTG-200 can be also be used to treat patients suffering from Crohn's disease and ulcerative colitis (UC).

PTG-200 is currently in Investigational New Drug (IND) enabling studies. Protagonist Therapeutics will receive an upfront payment and is also eligible to receive development and commercialization milestone payments under this deal. A Phase 1 clinical trial will be slated to begin by this year for PTG-200.

The transaction under this deal is expected to conclude in the third quarter of this year. IBD currently affects five million people worldwide and the incidence is rising with a near three-time increase in the US according to a new report issued by the Centers for Disease Control and Prevention.

Source: pharmaceutical-technology.com

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MERGERS /ACQUISITIONS /COLLABORATIONS

2. CURE Pharmaceutical and CannaKids collaborate with Israel Institute of Technology for cancer-fighting cannabinoids

For the development of cancer-fighting cannabinoids, CURE Pharmaceutical along with CannaKids has entered into strategic research collaboration with Technion-Israel Institute of Technology.

CURE and CannaKids are collaborating with Israel Institute in order to:

- research how different cannabinoid compounds within cannabis strains can be used to treat various subtypes of cancer, and
- predict how to match a cancer subtype with an effective cannabis extract to optimize treatment efficacy

Aims of Technion team are to clarify:

- phytocannabinoids and terpenes antitumor role by various pathways, and
- mechanism of action of cannabinoid as an antitumor drug

Several studies are available which indicate that cannabinoids have antitumor effects. Collaboration with CURE will help Technion with their goal of determining which cannabis strains might be used to tackle different cancer cells and what cannabinoid compounds within the plant are responsible for the ability to kill these cells.

CURE aims to bring new cannabinoid molecules to the market through the FDA regulatory process.

Source: pharmpro.com

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MERGERS /ACQUISITIONS /COLLABORATIONS

3. Bristol-Myers Squibb collaborates with Novartis to evaluate combination therapy in colorectal cancer

For the investigation of the safety, tolerability and efficacy of Opdivo (nivolumab) and Opdivo + Yervoy (ipilimumab) regimen in combination with Mekinist® (trametinib), Bristol-Myers Squibb has entered into a clinical research collaboration with Novartis.

Companies are taking this regimen as a potential treatment option for metastatic colorectal cancer in patients with microsatellite stable tumors where the tumors are proficient in mismatch repair. The Phase 1/2 study is expected to:

- establish recommended dose regimens
- explore the preliminary anti-tumor activity of combining trametinib with Opdivo
- establish activity of trametinib in combination with the Opdivo + Yervoy regimen

Results will be used to determine optimal approaches to further potential clinical development of these combinations.

Opdivo is a first regulatory approved programmed death-1 (PD-1) immune checkpoint inhibitor that is designed to uniquely harness the body's own immune system to help restore anti-tumor immune response. Yervoy is a recombinant, human monoclonal antibody, which blocks the cytotoxic T- lymphocyte-associated antigen-4 (CTLA-4).

Source: worldpharmanews.com

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MERGERS /ACQUISITIONS /COLLABORATIONS

4. OBI Pharma acquires Threshold Pharmaceutical's anti-cancer drug TH-3424

OBI Pharma signed an agreement with Threshold Pharmaceuticals for the acquisition of TH-3424. The product will be renamed as OBI-3424. It is the first drug in the class of novel small-molecule prodrugs which selectively targets cancers overexpressing enzyme aldo-keto reductase 1c3 (AKR1C3).

According to this agreement, in exchange for an undisclosed, upfront one-time payment:

- Threshold will transfer its ownership rights to OBI Pharma
- Threshold will provide preclinical and manufacturing data for OBI-3424
- no further payments or future royalties are required
- OBI Pharma will obtain global intellectual property of Threshold along with the commercial, developmental, and manufacturing rights to OBI-3424

In the presence of the AKR1C3 enzyme, OBI-3424 selectively releases a potent DNA alkylating agent which distinguishes OBI-3424 from non-selective traditional alkylating agents, such as cyclophosphamide and ifosfamide.

OBI-3424 has demonstrated potent activity in preclinical models of hepatocellular carcinomas (HCC) which highly overexpress AKR1C3 in the majority of patients. AKR1C3 is also upregulated in response to castration; this is another logical unmet need population where OBI-3424 will be tested.

For the potential treatment of T-cell acute lymphoblastic leukemia (T-ALL), the US National Cancer Institute is also performing preclinical evaluations of OBI-3424.

Source: worldpharmatoday.com

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DRUGS: APPROVALS AND LAUNCHES

1. Approval for Aristada® by FDA for treatment of Schizophrenia

The U.S. Food and Drug Administration (FDA) approved Aristada® (Aripiprazole lauroxil) of Alkermes plc for the treatment of schizophrenia. Aristada® is an extended-release injectable suspension for the treatment of schizophrenia.

The FDA has approved four doses and three dosing regimens of Aristada®:

- 441 mg, 662 mg or 882 mg once monthly
- 882 mg once every six weeks
- 1064 mg once every two months

Aristada® provides a wide range of options for the treatment of patents according to their needs due to its only long-acting atypical antipsychotic activity. Being a long-acting injectable, Aristada® eliminates the burden of taking an oral antipsychotic medicine on a daily basis.

Accessibility of this kind of antipsychotic agent, which can be initiated prior to hospital discharge and provide therapeutic levels of medication for two months, will be beneficial for transitioning patients with schizophrenia from inpatient care to outpatient.

Source: drugs.com

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DRUGS: APPROVALS AND LAUNCHES

2. Strattera® (atomoxetine) receives approval from FDA for ADHD

The US Food and Drug Administration (USFDA) has approved the first generic Strattera® (atomoxetine) in multiple strengths for Apotex Inc., Teva Pharmaceuticals USA Inc., Aurobindo Pharma Limited and Glenmark Pharmaceuticals to treat attention-deficit/hyperactivity disorder (ADHD) in pediatric and adult patients.

Approval of Strattera® will be an important step for bringing another treatment to consumers which met the rigorous standards of FDA. Strattera® has similar high strength along with high quality as that of the innovator drug approved by FDA.

Upset stomach, decreased appetite, nausea or vomiting, dizziness, tiredness, and mood swings were the most common adverse drug reactions (ADRs) in children and adolescents. Whereas constipation, dry mouth, nausea, decreased appetite, dizziness, sexual side effects, and problems passing urine were the most common ADRs in adults during the clinical trials.

Patients prescribed with Strattera® should be closely monitored for clinical features like worsening, suicidality, and unconventional changes in behavior; these changes are mainly noted during the initial few months of a course of drug therapy, or at times of dose changes.

Strattera® may lead to severe liver damage, and also serious cardiovascular events.

Source: drugs.com

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DRUGS: APPROVALS AND LAUNCHES

3. EC approves Trumenba for prevention of MenB disease

Pfizer's Trumenba, a Meningococcal Group B Vaccine, has received approval from the European Commission (EC). The vaccine is used for the prevention of invasive meningococcal disease in persons aged ≥10 years.

Neisseria meningitidis serogroup B (MenB) is the causal agent for meningococcal disease, which may lead to the death of the patient within 24 hours. Disease is characterized by headache, nausea and vomiting.

Trumenba is a sterile suspension which may not be successful in preventing MenB in all vaccinated patients. This may be due to inherent environmental and social risk factors.

Trumenba is a combination of two recombinant lipidated factors H binding protein (fHBP):

- one from fHBP subfamily A (A05) and
- one from subfamily B (B01, respectively).

fHBP is present on the surface of *meningococci* and helps the bacterium to avoid host defenses. In the clinical development plan, more than 20,000 adolescents and adults were studied and around 15,000 received Trumenba. On the basis of these results, EC approved Trumenba.

Source: pharmaceutical-technology.com

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DRUGS: APPROVALS AND LAUNCHES

4. FDA approves first topical ocular formulation of cetirizine for allergic conjunctivitis

Zerviate, a cetirizine ophthalmic solution 0.24%, has received approval from the US Food and Drug Administration (FDA) for allergic conjunctivitis. Cetirizine is a second-generation antihistamine which reduces swelling, itching, and vasodilation by acting on histamine receptor sites. Zerviate is the first topical ocular formulation for the treatment of ocular itching associated with allergic conjunctivitis.

Efficacy of the Zerviate solution was demonstrated in three randomized, double-masked, placebo controlled, conjunctival antigen challenge clinical trials in patients with allergic conjunctivitis.

Two trials were conducted for evaluating the onset and duration of effect. Zerviate at 15 minutes and 8 hours after treatment showed statistically and clinically significant less ocular itching.

Zerviate is recommended as one drop every 8 hours. Some of the common reported adverse drug reactions (ADRs) associated with Zerviate are ocular hyperemia, instillation site pain, and reduction in visual acuity.

Source: pharmpro.com

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DRUGS: DEVELOPMENT & CLINICAL TRIALS

1. Gilteritinib shows promise in the treatment of AML

A new dug gilteritinib (ASP2215) has shown promise in targeting the mutations of acute myeloid leukemia (AML). The most common mutation associated with AML is Fms-like tyrosine kinase 3 (FLT3) gene mutations and is associated with short survival.

FLT3 gene is present in normal bone marrow cells and regulates growth of blood cells. When the gene is mutated in a leukemia cell, the mutated cells grow in an uncontrolled manner unless the function of FLT3 is turned off. Gilteritinib is an FLT3 inhibitor and was found to be well-tolerated in the first-in-human study. It is developed by Perelman School of Medicine at the University of Pennsylvania and Penn's Abramson cancer center and the complete research is funded by Astellas Pharma, National Cancer Institute and Associazione Italiana Ricerca sul Cancro.

In the Phase 1-2 trial, 252 adults with AML patients were enrolled with seven doses of gilteritinib being evaluated:20 mg, 40 mg, 80 mg, 120 mg, 200 mg, 300 mg, or 450 mg; while gilteritinib 120 mg/day is being tested in Phase 3 trials. Gilteritinib monotherapy was well-tolerated along with a high proportion of responses and effective survival results in patients with FLT3 mutations.

90% of FLT3 phosphorylation inhibition was noticed on day 8 in most patients receiving a daily dose of 80 mg or higher.

This study is published in *The Lancet Oncology*.

FLT3 mutations results in an aggressive disease with overall survival of around four months with available therapies. To avoid relapse, oncologists recommend a most aggressive chemotherapy, including marrow transplant.

Source: sciencedaily.com

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DRUGS: DEVELOPMENT & CLINICAL TRIALS

2. Neurotech declares phase 2 results for NT-501 in macular telangiectasia

Neurotech pharmaceutical in collaboration with Lowy Medical Research Institute (LMRI) announced results from a 24-month study of NT-501.

The study shows that NT-501 delivering Ciliary Neurotrophic Factor (CNTF) has beneficial effects in macular telangiectasia patients.

It was a multicenter, randomized clinical trial, which demonstrated that NT-501 significantly reduces the progressive loss of photoreceptors as compared to untreated individuals.

NT 501 uses Encapsulated Cell Therapy (ECT) platform to deliver specific therapeutic molecules. Significant results were recorded for NT 501 after a 24-month study. Increase in the MacTel lesion (0.065 mm^2) was statistically significant (p=0.030). Ellipsoid zone reduction was found to be significant (p = 0.045) and macular thickness was also significantly increased in the treated group (p=0.007).

NT 501 was found to be well-tolerated and the safety profile is consistent with previous studies of NT-501 in retinitis pigmentosa and dry AMD. No significant adverse drug reactions (ADRs) were noted. All the ADRs detected were due to the surgical procedure.

Source: centerwatch.com

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DRUGS: DEVELOPMENT & CLINICAL TRIALS

3. Monoclonal antibody-drug (brentuximab vedotin) in combination with common chemotherapy agent (gemcitabine) shows high response rate in Hodgkin's lymphoma

Researchers of Roswell Park Cancer Institute presented their research at the American Society of Clinical Oncology (ASCO) 53rd Annual Meeting, 2017. Their study shows high complete-response rate (58%) of monoclonal antibody-drug conjugate with a common chemotherapy agent in children and young adults suffering with Hodgkin's lymphoma.

Hodgkin's lymphoma is one of the most common type of cancer in young age people of 15-29 years. In the clinical trial AHOD1221 (NCT01780662), researchers evaluated the combination of brentuximab vedotin (Adcetris), a monoclonal antibody, along with the chemotherapy drug gemcitabine (Gemzar).

Researchers reported that these two drugs in combination show effective results in Hodgkin's lymphoma, which is not shown by the drugs alone. In the evaluable patients in the Phase 2 study, 23 (58%) achieved complete response to the combination within four cycles, and 6 (15%) had a partial response.

This drug combination shows a high response rate in combination which has some additional benefits of having a much reduced risk of long-term organ damage compared to the highly toxic chemotherapy agents.

Source: sciencedaily.com

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DRUGS: DEVELOPMENT & CLINICAL TRIALS

4. Tildrakizumab in the treatment of chronic plaque psoriasis

Tildrakizumab has been developed as a new biological agent which showed efficacy in the treatment of moderate to severe chronic plaque psoriasis in a Phase 3 trial.

Two three-part, parallel group, double-blind, randomised controlled studies, reSURFACE 1 and reSURFACE 2 were conducted on more than 1800 patients over 250 sites worldwide.

In Phase 3 study, 2 three armed studies were conducted. In both the studies one group received 200 mg tildrakizumab, one received 100 mg tildrakizumab and one received an inactive placebo.

Response rates were found to be 62%/59% for tildrakizumab 200 mg, 64%/58% (tildrakizumab 100 mg) and 6%/7% (placebo) respectively. For tildrakizumab 200 mg vs placebo, it was statistically significant p=0·0031; while for the 100 mg vs placebo, p=0·0663.

Tildrakizumab is a high-affinity, humanised, IgG1κ antibody targeting interleukin 23 p19 that represents an evolving treatment strategy in chronic plaque psoriasis and it was well-tolerated in the patients. Chronic plaque psoriasis, characterized by red scaly skin patches mainly affecting scalp, elbow and knees, is a very common disease affecting more than 6 million Americans. Disease usually appears in adolescence or mid-life but may require lifelong medication. Chronic plaque psoriasis can affect 10-100% of the skin surface.

The Phase 3 studies were funded by Merck & Co., Inc. and the results are published in journal *The Lancet*.

Source: medicalnewstoday.com

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PATENTS: NEW APPROVALS /LITIGATIONS /SETTLEMENTS

1. Lundbeck secures rights for Alzheimer's treatment of IBC's research

Lundbeck Pharmaceuticals and ImmunoBrain Checkpoint (IBC) signed an agreement for the rights of IBC's Alzheimer's disease treatment. The research is mainly on alteration of antibodies which are currently being used to treat cancer for use in Alzheimer's treatment.

The new approach is expected to yield potential treatments for the symptoms of the disease, as well as its progression. This agreement explains that the various studies for the determination of drug candidate and clinical evaluations of the drug will be conducted as well as funded by Lundbeck. Further along with that, Lundbeck will obtain a minority stake in IBC with the option of taking over all activities and rights.

The assessment of the drug will take a long time in the clinical trials as the present study is still in the early stages.

Lundbeck is mainly focused on psychiatric and neurological disorders. Alzheimer is mainly characterized by the degeneration of neurons leading to cellular loss along with the dysfunction leading to loss of memory, reasoning along with learning and language skills.

Source: pharmaceutical-technology.com

PATENTS: NEW APPROVALS /LITIGATIONS /SETTLEMENTS

2. USPTO grants patent to SYN-010 as a novel treatment for irritable bowel syndrome with constipation

Synthetic Biologics, Inc., received a patent by the U.S. Patent and Trademark Office (USPTO) for its new molecule SYN-010, as a novel treatment for irritable bowel syndrome with constipation (IBS-C).

SYN-010 is a modified-release formulation of lovastatin lactone for the treatment of constipation. Patent covers the intellectual property of SYN-010 in IBS-C till 2034.

The drug is intended to reduce methane production by certain microorganisms (*M. smithii*) in the gut while minimizing disruption to the microbiome to treat an underlying cause of IBS-C. It is intended to act primarily on intestinal lumen by avoiding systemic absorption. In a Phase 2 study, SYN-010 significantly reduced the abdominal pain and bloating. SYN-010 also improved the stool frequency and quality of life without any severe adverse drug reactions.

Source: biospace.com

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PATENTS: NEW APPROVALS /LITIGATIONS /SETTLEMENTS

3. GSK wins $235 million from Teva in Coreg patent trial

For infringing the patent covering blood pressure drug Coreg, the U.S. jury ordered Teva Pharmaceutical Industries Ltd to pay an amount of more than $235 million to GlaxoSmithKline Plc. (GSK).

The jury found that Teva willfully disobeyed the patent in connection with its sales of a generic version of the drug with a label indicating it could be used for treating chronic heart failure. Jury rejected Teva's argument that the patent was invalid.

Now Teva is ordered to pay $234.1 million to GSK in lost profits and the drug company will be awarded with additional $1.4 million in royalties.

Teva's generic version of Coreg, or carvedilol was approved by the U.S. Food and Drug Administration in 2007.

According to GSK, the generic drug maker changed its label in 2011 to add use for treating chronic heart failure which was not mentioned in the Teva's FDA application.

Source: finance.yahoo.com

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PATENTS: NEW APPROVALS /LITIGATIONS /SETTLEMENTS

4. AXIM Biotech files patent for controlled release chewing gum for opioid addiction treatment

AXIM Biotechnologies, Inc, filed an application for a patent that involves a chewing gum composition with controlled release of cannabinoids and opioid agonists or antagonists for opioid addiction. This chewing gum can be used for the treatment of chronic pain.

Opioid addiction is one of the leading global problems affecting health, social and economic conditions. By the AXIM chewing gum therapy, users may avoid adverse effects caused by injections, smoking and other delivery methods.

The chewing gum shows neuroprotective, distressing action along with the release of hormones such as dopamine and serotonin to improve oral health.

Cannabinoids, mainly cannabidiol (CBD), decreases craving for narcotics and may be given in microencapsulated form to improve the chewing gum's taste. Cannabinoids may prevent binding with the gum base and control cannabinoid release during mastication which may further improve bioavailability of the cannabinoids once they enter the gastrointestinal tract.

Source: biospace.com

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TECHNOLOGY /NDDS

1. Medtronic launches artificial pancreas in the U.S. market

Medtronic launched the world's first artificial pancreas in the U.S. market which is the only hybrid closed loop system. The system is a insulin pump that automatically delivers basal insulin to control blood glucose levels in people with Type 1 diabetes. The system is the only FDA approved insulin pump. Devices aren't implanted or surgically attached.

The system includes:

- a glucose sensor (measures glucose levels in the fluid just under the skin),
- the MiniMed 670G insulin pump and
- an infusion patch (delivers insulin through a catheter).

It uses an algorithm to self-adjust the delivery of basal, or background, insulin every five minutes based on real-time data gathered from the sensor. This system reduces the burden on patients who are constantly managing their glucose levels, but still requires patients to track their carbohydrates and manually request bolus insulin at mealtimes. Patients must also calibrate the sensor, which may be worn for seven days, from time to time.

The device was introduced in limited U.S sites in a Customer Training Phase earlier this year with 4 settings:

- target blood glucose range
- auto mode
- suspend on low (stops insulin delivery once a pre-set limit has been reached)
- suspend before low (stops insulin delivery before the limit is met).

Source: fiercebiotech.com

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TECHNOLOGY /NDDS

2. New biosensor developed for diagnosis of dengue

Brazilian scientists have developed a biosensor for the quick and cheap detection of dengue. A biosensor is an analytical device that converts a biological response into an electrical signal coated with a thin film of bacterial cellulose nanocrystals, which effectively detects a protein known as NS1 from blood samples. Simple tests such as testing blood from a finger prick are not available for dengue, and there is no dedicated treatment for the virus which is usually found in urban and semi-urban areas.

The complete development is published as “Biosensor for Dengue Virus Detection: Sensitive, Rapid, and Serotype Specific” in the journal *Biosensors and Bioelectronics*.

Scientist are looking to produce a testing kit that would cost clinics and hospitals around $30 and take about 15 minutes to analyze the blood samples for a key dengue protein.

Researchers want to explore ways to create cost-effective biosensor components that could be used to analyze multiple blood samples. The technology could potentially be adapted to detect proteins from viruses such as Zika, which is also transmitted by the Aedes aegypti mosquito.

Source: health.economictimes.indiatimes.com

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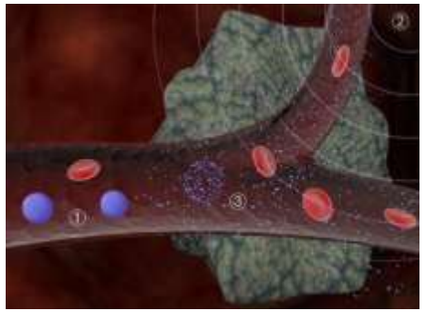
TECHNOLOGY /NDDS

3. Ultrasound activates nanoparticle aggregates for selective drug delivery



Researchers at the Harvard Wyss Institute have developed a new nanoparticle aggregate system by which drug can be delivered directly to the site of action. This nanoparticle aggregate (NPAs) system releases a drug when it is dispersed using ultrasound.

Normally tumors are treated using chemotherapy drugs that travel throughout the body and result in many side-effects. For these kinds of situations this new technology can be used to deliver toxic chemotherapy drugs directly to the tumor while reducing side-effects in healthy tissues.

In this technique, chemotherapy-loaded nanoparticle aggregates are injected into the bloodstream. An external ultrasound (US) activation system is energized at the tumor site, causing the aggregates passing through the blood to be disrupted and release their drug payload in the tumor. This system was tested in a mouse model of breast cancer and the nanoparticle aggregates combined with ultrasound delivered nearly five times the number of nanoparticles to the tumor, compared with aggregates without ultrasound.

When the nanoparticles were loaded with a common chemotherapy drug doxorubicin (Dox), only 10% of the normal dose of doxorubicin was required to reduce the tumor size by half, showing that this system can be used for highly specific drug delivery which can significantly improve drug effectiveness.

The complete mechanism is published in the journal *Biomaterials* which explains that when the Dox-loaded NPAs were injected and exposed to US energy locally, it resulted in a significantly greater reduction in tumor volume compared to tumors treated with a 20-fold higher dose of the free drug.

Source: health.economictimes.indiatimes.com

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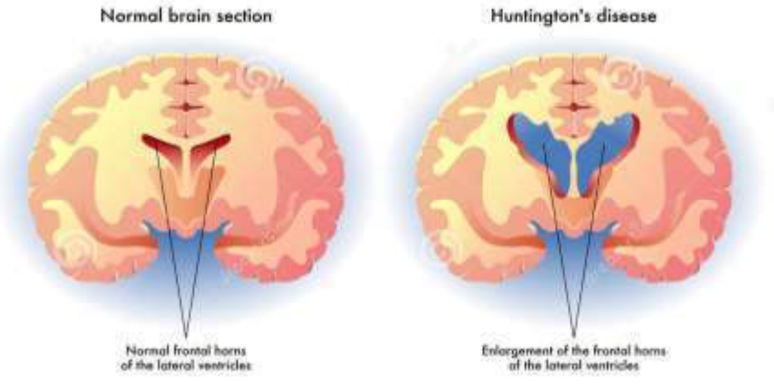
4. Neurofilament to help the detection of Huntington's disease

For the first time, a blood test has been developed for the detection of Huntington's disease. This test can predict the onset and track progression of Huntington's disease by measuring the levels of biomarker neurofilament.

This test may be helpful for identifying new treatments for the genetic brain disorders which are fatal and presently incurable.



Huntington's disease is an inherited disorder in which nerve cells in the brain break down with time. Protein neurofilaments are released by damaged cells of the brain. By measuring the amount of protein neurofilaments, doctors can predict the onset of the disease as well as its progression.

A study published in the journal *Lancet Neurology* showed that the neurofilament concentrations were 2.6 times in patients with genetic mutations as compared to the controlled participants. These levels further rise with stages of the disease.

Source: health.economictimes.indiatimes.com

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