Lambda Research Newsletter

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Research Accelerated

Contact Us

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

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

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Clinical Research NEWSletter

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GLOBAL NEWS

1. Metformin can be used for pancreatic cancer

A new research has suggested that antidiabetic drug metformin can be used in the treatment of pancreatic cancer. Targeting a particular cell signaling pathway with metformin might offer a way to stop the progression and spread of pancreatic cancer.

Metformin is approved for the treatment of type 2 diabetes mellitus. Laboratory investigations have revealed several ways in which metformin interacts with cells and tissues that might explain its anti-cancer effects.

Previous studies have shown that metformin can be used as a potential treatment for pancreatic cancer. The current research by Rutgers Cancer Institute of New Jersey in New Brunswick, is the first to show that the underlying mechanism involves the metformin's effects on the REarranged during Transfection (RET) cell signaling pathway.

Researchers now claim that targeting RET with metformin may be an attractive and novel strategy for the prevention and treatment of pancreatic cancer progression and metastasis.

Source: medicalnewstoday.com

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GLOBAL NEWS

2. Obesity paradox is a myth: say scientists

A research published in the European Heart Journal has suggested that the obesity paradox may be a myth. Obestiy paradox is an idea that overweight or obese people are not always at an increased risk of heart disease.

The study conducted in nearly 300,000 patients showed an increased risk of blood vessel problems, heart strokes, high blood presser with the increased body mass index (BMI) of 22-23 and the deposition of fat around the waist. The study was conducted in 296,535 healthy white European adults who took part in the UK Biobank study.

The patients were recruited between 2006 – 2010 and participants were available for latest analysis in 2015. Researchers found that the people who have BMI index between 22 and 23 had a lower risk of heart diseases. The higher BMI above 22 was associated with an increased risk of cardiovascular diseases increased by 13% for every 5.2 increase in women and 4.3 in men. Researchers also observed that people with increased waist-to-height or waist-to-height ratios and percentage body fat mass have increased risk of cardiovascular diseases.

Researchers suggest that obesity has no effect on deaths, but even protective fitness should be maintained.Minimizing the risk of CVD should be possible by maintaining the BMI between 22 and 23.

Source: economictimes.Indiatimes.com

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GLOBAL NEWS

3. Suicidal risk is higher in patients with urological cancer

Indian scientists in a recent survey have found 3-times higher suicidal risk in patients who have prostate, bladder, or kidney cancers than in the general population. The incidence of commiting suicide was 5% in these patients in the years between 2001 and 2011. The proportion of attempted suicides was higher in cancer patients, with urological cancers being the most common cancer.

The main cause of suicides is severe psychological stress due to the cancer diagnosis and treatment. Depression affects 5% – 25% of cancer patients and many are affected by Post-Traumatic Stress Disorder (PTSD).

The research included 13.4 million-person years cancer patients; 162 suicides and 1,222 suicide attempts were identified. Overall, the results showed that suicide rate was 30 per 100,000 people with all-cancers, whereas it was 10 per 100,000 people in the general population. In the urological cancer patients, the suicide rates are: 36 per 100,000 people in kidney cancer, 48 suicides per 100,000 in bladder cancer, and 52 per 100,000 in prostate cancer. Median time to suicide varied substantially with 175 days from diagnosis for kidney cancer, 846 days for prostate cancer, and 1037 days for bladder cancer.

Source: economictimes.Indiatimes.com

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GLOBAL NEWS

4. Pentavalent vaccine led to double infant deaths versus DPT

Pentavalent vaccine (PV) was introduced in the immunization program by the Government of India six year ago. T Doubling of infant deaths were observed after vaccination as compared with Diphtheria-Pertussis-Tetanus (DPT). In total, there were 10,612 deaths following the vaccination (both PV and DPT) in the past 10 years.

A combination form of DPT vaccines and two other vaccines (hemophilus influenza type B [Hib] and hepatitis B), PV was introduced into India's immunization programme in December 2011 to replace DPT vaccine in a staged manner with a view to add protection against Hib and hepatitis B without increasing the number of injections given to infants.

There have been sporadic reports of unexplained deaths following PV immunization, hence, a study was conducted to identify if these deaths were vaccine-related or merely coincidental. Under the Right to Information (RTI) Act, the researchers obtained data from April 2012 to May 2016 of all deaths reported within 72 hours of administering DPT and PV from different states.

The researchers assumed that all deaths within 72 hours of receiving DPT are natural deaths, hence, they presumed that any increase in the number of deaths above this baseline among children receiving PV must be caused by this vaccine. The results showed 237 deaths within 72 hours of administering the PV, which is 2-fold than the death rate among infants who received DPT vaccine. Further, the researchers have extrapolated the data and estimated 122 additional deaths within 72 hours, due to the switch from DPT to PV in the vaccination of 26 million children each year in India.

The researchers concluded that despite this large cohort data, the evidence is merely circumstantial and not conclusive. "These findings of differential death rates between DPT and PV do call for further rigorous prospective population-based investigations," the study concludes.

Source: pharmabiz.com

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PHARMA INDIA

1. CDSCO creates forum to discuss issues regarding drug regulations

The Central Drugs Standard Control Organization (CDSCO) has decided to create a forum to meet with pharmaceutical associations regularly for solving the issues of drug regulations in order to improve ease of doing pharmaceutical business in the country.

Indian Pharmaceutical Alliance, Indian Drugs Manufacturers Association, Bulk Drugs Manufacturers Association, Federation of Pharmaceutical Entrepreneurs, Confederation of Indian Pharmaceutical Industry and Laghu Bhartiya Udyog are the participating associations in the forum.

The Drug Controller General of India will have a discussion every quarter with two representatives of each association. In these meetings, only the nominated personnel will be allowed. Furthermore, with prior permissions, the subject matter experts from the association may be allowed.

The discussions are expected to include any issues relating to the industry and the country's drug regulations. The meetings will further help CDSCO to assess the impact of its regulations on the industry and is also expected to help promote innovation.

Source: economictimes.Indiatimes.com

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PHARMA INDIA

2. Indian pharmaceutical market profit likely to weaken in Q4 2018

According to pharmaceutical industry analysts, the Indian pharma sector is expected to report weak numbers in Q4 2018 with PAT (Profit After Tax) likely to decline by 9% y-o-y. The Edelweiss research analysis estimated that revenue of pharmaceutical sector is likely to grow at 3% y-o-y. There is an expected dip in the US revenue to 2% y-o-y in constant currency resulting from sustained pricing pressure due to customer consolidation and rise in competition. Meanwhile, the appreciation of 4% y-o-y on rupee against the US dollar will put further pressure on realisations.

Several other factors have also affected the pharma market including additional documentation requirements for elemental impurities by the USFDA (US Food and Drug Administration) which has led to the deline in new products approvals during Q4FY18 to 109 from 249 in Q3FY18. Furthermore, the USFDA regulatory inspections made some observations for Aurobindo's Hyderabad unit-IV, Cipla's Goa, Dr Reddy's Telangana and Sun Pharma's Halol units.

Indian pharmaceutical sector is estimated to account for 3.1–3.6% of the global pharmaceutical industry in value terms and 10% in volume terms. The Indian pharmaceutical sector is estimated to grow to USD 55 billion by 2020 and USD 100 billion by 2025. By the year 2020, Indian pharmaceutical market is expected to emerge as the sixth largest pharmaceutical market globally by absolute size.

Source: firstwordpharma.com

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PHARMA INDIA

3. New diabetes management guidelines – not for India – say experts

The American College of Physicians (ACP), an organization of internal medicine physicians, has issued a new guideline on diabetes management. The new guideline has relaxed the long-term blood sugar control marker called hemoglobin A1C (HbA1c) from traditional 6.5-7% to between 7% and 8% for people with type 2 diabetes. According to the new guidelines, the goals for glycemic control should be personalized on the basis of a discussion regarding the benefits and harms of pharmacotherapy, patients' preferences, patients' general health and life expectancy, treatment burden, and costs of care. Generally, HbA1c 6.5% is indicative of diabetes.

Indian medical fraternity, however, has opposed the new guidelines and feels that such rules will only worsen the diabetes epidemic in India. According to Indian doctors, the new rules should be ignored for Indians as it can lead to serious complications in diabetics as well as confusion in the treatment protocol.

In India, the disease is more aggressive and the Indian doctors are of the opinion that the new guideline should not be applied in the country as these new norms can have serious impacts on patients. India has its own three advisory bodies - the ICMR (Indian Council of Medical Research), RSDDI (Research Society For The Study of Diabetes in India) and API (Association of Physicians of India).

Published in the *Annals of Internal Medicine,* the new guideline has also drew flak from the American Diabetes Association who said that the new guidance does not consider the positive legacy effects of intensive blood glucose control confirmed in multiple clinical trials and, therefore, are not reflective of the long-term benefits of lower A1C targets.

Source: economictimes.Indiatimes.com

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PHARMA INDIA

4. AIDAN plead DTAB to remove non-experts from FDC panel

The All India Drug Action Network (AIDAN) has approached the Drugs Technical Advisory Board (DTAB) to remove 'non-expert' members from the panel to examine the fixed dose combination (FDC) drugs. AIDAN has also requested the government to relax the deadline set to make submissions. DTAB gets ready to inspect more than 300 FDCs that are banned.

The FDCs, drugs containing two or more active ingredients, were banned by the health ministry last year upon finding them unsafe by an expert committee. The ban was challenged by the pharmaceutical companies across the nation. The health ministry filed a petition in the supreme court in January 2018 against the high court order of removing the ban. The supreme court has ordered to re-examine the issue, hence, the DTAB panel was constituted and instructed to finalize their reports within 3 months. To facilitate the same, DTAB has directed AIDAN and other industry stakeholders to make their submissions regarding the FDCs in question before April 7.

Aidan has raised questions against the involvement of non-expert representatives in the panel. The task assigned to DTAB is of the nature of an expert review so that an analysis is made in greater depth, therefore, the members in the expert panel have to be selected on the basis of their expertise in medicine, pharmacology, rational therapeutics and regulation of health care.

Currently, the members of the panel include representatives of the Indian Pharmaceutical Association (IPA) and Indian Medical Association (IMA), which do not represent any expert bodies, hence, do not meet the criteria of expertise and objectivity required. There is a risk of conflict of interest with these non-expert panel members; many of the IPA members are affiliated to pharma companies, and IMA is known for its conflict of interest with respect to commercial endorsements and vis-a-vis the pharma industry.

Source: pharmabiz.com

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REGULATORY ROUND-UP

1. CDSCO flags companies selling FDC drugs without approval

The Central Drugs Standard Control Organization (CDSCO) has flagged the pharmaceutical firms who are making and marketing certain combination medicines to treat ailments like fungal infections and diabetes without its approval.

Necessary regulatory approvals were not taken for these drugs from the CDSCO, hence, their safety and efficacy could not be established and they may pose a great risk to the patients. Over 70 fixed dose combination (FDC) medicine brands marketed by 16 pharma companies have been seized in an ongoing raid of two drug manufacturing facilities. The CDSCO may cancel the licences of these firms and may take legal actions too.

The regulator has so far seized Rs 3 lakh worth of an anti-fungal combination of itraconazole 100 mg and terbinafine 250 mg manufactured by Mascot Health Series and marketed by Wockhardt under the brand name ‘Itrawok-T’ and Bestchem Formulations under the brand name ‘Betawin-IT’.

Source: economictimes.Indiatimes.com

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REGULATORY ROUND-UP

2. Maharashtra FDA approaches NPPA for more pricing regulations

A huge profiteering in margins ranging from 50 – 1,000% for various surgical and nonsurgical equipments like intraocular lenses, heart valves, balloon catheters have been reported, and the Maharashtra Food and Drug Administration (FDA) is now attempting to introduce price control regulations for these devices.

The state FDA has submitted a report to the National Pharmaceutical Pricing Authority (NPPA) and Drugs Controller General of India (DGCI) to include 24 more surgical and nonsurgical equipments under the list of Essential Medicines. The FDA also suggested that salts used in various medicines can be replaced by other cheaper variants. The NPPA has already capped the price control of coronary stents.

NPPA also sent to the health ministry for approval and their final prices will be decided. There are drastic changes between the actual manufacturing price and charges when purchased by the patients.

Source: economictimes.Indiatimes.com

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REGULATORY ROUND-UP

3. Domestic components should contribute 25-50% of medical device cost: New draft guidelines

The Pharmaceutical Department, Govt. of India, has proposed that domestically sourced components have to contribute about 20-50% of cost of medical devices, depending on device type. Furthermore, preference should be given to the devices made in India.

However, a lobby group of domestic medical device manufacture companies claimed that the proposed guidelines lack measures to help the growth of domestic industry and enforces circumstances that may compromise the quality of medical devices obtained through these tenders.

According to this draft, there should be ~50% cost shares by the domestically sourced components of medical disposables and consumables and 40% of the cost of implants to be able to meet Govt. device procurement criteria. For medical electronics, hospital equipment, surgical instruments and diagnostic reagents/in-vitro diagnostics, local components should contribute 25% of the cost.

The value of Indian medical device market was ~34000 INR crore in 2016-2017; the Association of Indian Medical Device Industry (AiMeD) claimed the market size is >65000 INR crore. The government hospitals contribute ~15000 crore.

Source: economictimes.Indiatimes.com

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REGULATORY ROUND-UP

4. Fight against opioid outbreak: Pharma manufacturers to held responsible

The use of prescription opiates for non-medicinal purpose has increased, and Milwaukee County has filed a lawsuit against many major pharmaceutical manufacturers and distributors globally. A law firm Baron & Budd will act as the leading firm on behalf of Milwaukee County.

Milwaukee County alleges that many of the drug manufacturers knowingly misinformed doctors by claiming that patients using these drugs rarely experienced addiction and thus pushed their highly addictive, dangerous opioids. The companies included in their lawsuit are Purdue Pharma, Janssen Pharmaceuticals, Endo Health Solutions, Teva Ltd., Mallinckrodt, and Allergan PLC. The products includes OxyContin, Actiq, Fentora, Duragesic, Nucynta, Nucynta ER, Opana/Opana ER, Percodan, Percocet, Zydone, Kadian and Norco.

There are also allegations against three of the country's largest medicine distributors – Cardinal Health, McKesson Corp and AmerisourceBergen – that they failed to monitor, identify and report suspicious activity in the size and frequency of opioid shipments to pharmacies, in violation of the federal Controlled Substances Act.

Source: pharmpro.com

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MERGERS /ACQUISITIONS /COLLABORATIONS

1. Abbvie and Voyager collaborate for Alzheimer's gene therapy

Abbvie, an expert in monoclonal antibody therapy with global clinical development and commercial capabilities and voyager, an expert in gene therapy platform that enables generating adeno-associated viral (AAV) vectors, have collaborated to develop potential new treatments for Alzheimer's disease and other Tau-related neurodegenerative diseases. Abbvie's has an advance strategy towards innovative treatment of brain diseases.

Tau is an abundant protein in the brain that promotes the stability of axonal microtubules in healthy persons. But in diseased conditions, phosphorylation occurs in tau protein and forms microfibrilary tangles and tau aggregates resulting in altered brain functions, neuronal cell death and progression of neurodegenerative symptoms.

Under the agreement, voyager will perform preclinical trials of vectorized antibodies against Tau, after which Abbvie will select one or more antibodies to further IND-enabling studies in clinical development. Voyager will receive $69 million upfront payment and potentially ~$155 million in preclinical and Phase 1 option payments as well as development and regulatory milestone payments and royalties. Voyager is eligible to receive $895 million in development and regulatory milestones for vectorized tau antibody compound.

Source: news.abbvie.com

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MERGERS /ACQUISITIONS /COLLABORATIONS

2. Recipharm and Altus collaborate to offer NDDS for value added medicines

Recipharm, the contract development and manufacturing organisation (CDMO), has collaborated with Altus Formulation Inc., a Canadian drug development company, to allow its customers to access new drug delivery technologies and products for value added medicines.

Under the agreement, Recipharm will utilize Altus' patented INTELLITAB™ and FLEXITAB™ drug delivery platform to co-develop novel value added medicines.

INTELLITAB™ is a novel technology for the prevention of misuse, abuse and dangers of over exposure of opioids, which can occurr due to tampering with immediate and extended release narcotics deliberatley or inadvertently. INTELLITAB tablets are hardened to resist cutting, crushing, chewing, common methods to accelerate drug release, and spontaneously form hard, stable gels in a range of solvents to deter injection. FLEXITA is an extended release technology enabling alcohol resistant tablets that maintain their performance after breaking to generate bio-equivalent lower strength tablets.

Source: WorldPharmatoday.com

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MERGERS /ACQUISITIONS /COLLABORATIONS

3. Lundbeck Pharma to acquire Prexton

Danish Pharma Company Lundbeck will acquire Prexton Therapeutics for an upfront payment of EUR 100 million and the deal terms also include up to EUR 805 million in development, regulatory and sales milestones.

Lundbeck will obtain global rights of an attractive compound (foliglurax), a first-in-class treatment which entered clinical phase II testing for symptomatic treatment of OFF-time reduction in Parkinson's disease and dyskinesia including Levodopa Induced Dyskinesia (LID).

There remains a large unmet need for effective treatments for Parkinson's patients to sustain the utility of dopaminergic therapies. Foliglurax stimulates a specific glutamatergic target point (mGluR4), which activates a compensatory neuronal system in the brain which is largely unaffected in Parkinson's disease.

Initial results from the clinical phase 2 trial of foliglurax are expected to be available in early 2019.

Source: WorldPharmatoday.com

MERGERS /ACQUISITIONS /COLLABORATIONS

4. Research on Chinese traditional medicines: Elsevier collaborates with Beijing University

Traditional Chinese Medicine (TCM) market is in the growing and developing phase, and the pharmaceutical companies are becoming more interested in developing and verifying the benefits of TCM as they carry no harm or appear to have minimum side effects. TCM is continuously being practised form a thousand years ago and now research work is continued with modern medical changes.

Elsevier, the global information analytics business specializing in science and health, announced a collaboration with Beijing University of Chinese Medicine (BUCM) to create a new taxonomy for TCM in Embase - the world's most comprehensive biomedical literature database. BUCM expertise will help enrich and enhance existing Elsevier content; opening new resources up to users as research and evidence about traditional Chinese medicine grows.

The trend in the use of traditional and complementary medicine is growing globally, and as a result, the volume of published resources into this field is increasing at a rate of around 6% per year, with >10,000 scholarly research or review articles published in 2017 alone.

Source: WorldPharmanews.com

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DRUGS: APPROVALS AND LAUNCHES

1. European Commission approves Roche's Hemophilia A drug – emicizumab

The European Commission has approved Roche's Hemlibra® (emicizumab) to prevent bleeding episodes in patients suffering from hemophilia A with factor VIII inhibitors. Hemlibra® is the first new medicine in >20 years to treat people with hemophilia A. This drug can be used in all age groups.

Hemlibra demonstrated superior efficacy compared to prior treatment with bypassing agents in two phase III studies in adults, adolescents and children. This approval is on the basis of these two large pivotal clinical studies in patients suffering from hemophilia A with inhibitors.

In the HAVEN 1 study, a randomised, multicenter, open-label, phase III study in adults and adolescents (12 years of age or older) with haemophilia A with inhibitors, Hemlibra prophylaxis showed a statistically significant reduction in treated bleeds at 87% (risk rate [RR]=0.13, $p<0.0001$) compared to no prophylaxis. In a first-of-its-kind intra-patient analysis, Hemlibra prophylaxis resulted in a statistically significant reduction in treated bleeds at 79% (RR=0.21, p=0.0003) compared to previous treatment with bypassing agent (BPA) prophylaxis collected in a non-interventional study (NIS) prior to enrolment.

Interim results from the HAVEN 2 study in children aged <12 years with hemophilia A with inhibitors showed that 87% (95% CI: 66.4; 97.2) of children who received Hemlibra prophylaxis experienced zero treated bleeds. In an intra-patient analysis of 13 children who had participated in the NIS, Hemlibra prophylaxis resulted in a 99% (RR=0.01, 95% CI: 0.004; 0.044) reduction in treated bleeds compared to previous treatment with a BPA.

Very few adverse events (≥10%) were reported in the pooled data with majority of then being injection site reactions and headache.

Source: WorldPharmatoday.com

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DRUGS: APPROVALS AND LAUNCHES

2. Bio-Techne launches MIMEX™ GI: An accessible 3-D cell culturing platform

Bio-Techne has launched MimEX™ GI, a new product line for generating 3-dimensional (3-D) gastrointestinal tissue on a 2-D surface.

This 3-D cell culture and organoid models of GI epithelium are being used for drug discovery, disease modeling and toxicology studies. These models are very complex and exert huge advantage over cell line and primary cell based methods minimizing original cell generation and replication of physical properties of the intestinal tissue.

The MimEX™ GI system platform is a novel human tissue model systems that enables the use of distinctive properties of adult ground-state stem cells, and can generate 3-D GI epithelial tissue on a 2-D surface. This system contains specialized media and reagents, which allows the enlargement and divergence of ground state adult stem cell communities, derived from GI tract with maintaining their original properties.

This system which generates 3-D tissue shows an original organ cell generation, which includes almost all types of cells such as crypt-like structures, gut epithelial polarity, goblet cells, paneth cells, and endocrine cells. These are useful both for educational purpose as well as for industries, including licensing programs which allows using in commercial applications.

Source: bio-techne.com

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DRUGS: APPROVALS AND LAUNCHES

3. FDA's additional approval for Verzenio™

The U.S. FDA has provided additional approval to Verzenio™ (abemaciclib, a product of Eli Lilly and Company) that can be used as initial endocrine-based therapy in combination with an aromatase inhibitor (AI) for the treatment of postmenopausal women with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) advanced or metastatic breast cancer.

This additional approval depicts the third indication for Verzenio™ within five months. Verzenio is the first and only one cyclin dependent kinase (CDK) 4 & 6 inhibitor approved in September 2017 in combination as well as a single agent in metastatic breast cancer.

Abemaciclib was approved in combination with fulvestrant for the treatment of women with HR+, HER2- advanced or metastatic breast cancer with progression of disease followed by endocrine therapy; and as a single agent in the treatment in women who are previously treated with chemotherapy in the metastatic setting.

The prescribed dose in combination with AI is 150 mg oral twice daily, which can be continued until there is a progression of disease or undesirable toxicity. It is available in four strengths 50 mg, 100 mg, 150 mg, and 200 mg.

Source: prnewswire.com

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DRUGS: APPROVALS AND LAUNCHES

4. Tildrakizumab: USFDA approved drug for plaque psoriasis

The USFDA has approved the Sun Pharma's biologic drug ILUMYA™ (tildrakizumab-asmn) for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

Tildrakizumab-asmn selectively binds to the p19 subunit of IL-23 and inhibits its interaction with the IL-23 receptor leading to inhibition of the release of pro-inflammatory cytokines and chemokines. The dose of tildrakizumab-asmn is 100 mg subcutaneous injection administered every 12 weeks, after the completion of initial doses at weeks 0 and 4.

The approval was based on the data from the pivotal Phase-3 reSURFACE program (two multicenter, randomized, double-blind, placebo-controlled reSURFACE 1 and reSURFACE 2 trials). A total of 926 patients received either tildrakizumab-asmn (N=616) or placebo (N=310).

The resutls of both Phase-3 studies met the primary efficacy endpoints. A significant clinical improvement, as measured by ≥75% of skin clearance (Psoriasis Area Sensitivity Index or PASI 75) and Physician's Global Assessment (PGA) score of "clear" or "minimal", was demonstrated at week 12 after two doses of ILUMYA 100 mg compared to placebo.

Efficacy Primary Endpoint at Week 12 in Adults with Plaque Psoriasis (NRI*)				
	reSURFACE 1 Study (NCT01722331)		**reSURFACE 2 Study (NCT01729754)**	
	ILUMYA 100 mg n=309	Placebo n=154	ILUMYA 100 mg n=307	Placebo n=156
PGA of "clear" (0) or "minimal" (1)†	179 (58%)	11 (7%)	168 (55%)	7 (4%)
PASI 75†	197 (64%)	9 (6%)	188 (61%)	9 (6%)
PASI 90	107 (35%)	4 (3%)	119 (39%)	2 (1%)
PASI 100	43 (14%)	2 (1%)	38 (12%)	0 (0%)

*NRI = Non-Responder Imputation; †Co-Primary Endpoints; PASI = Psoriasis Area Sensitivity Index

Source: IndiaInfoline.com

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DRUGS: DEVELOPMENT & CLINICAL TRIALS

1. Increase in global clinical trial approval in India in 2017

Under the clinical trial rule 2018 of the Central Drugs Standard Control Organization (CDSCO), there has been a positive trend in the number of approvals of global clinical trials (GCTs) conducted in India in 2017; it was 99 as compared to 38 in 2016. Clinical trial experts have hailed the positive trend of approval of GCTs.

In 2015, a total of 107 studies were reviewed by the CDSCO and out of them 43 were approved, which was much below compared with 87 approved GCTs of 150 reviewed studies in 2014. In 2013, the growth of clinical research was negatively impacted in India with only 17 GCTs approved.

As per the latest data, out of 2,68,620 clinical studies done globally, 3,315 studies are being done in India, 4,050 in South Asia at studies, 17 in Afghanistan, 286 in Bangladesh, 2 in Bhutan, 86 in Nepal, 411 in Pakistan and 57 in Sri Lanka. The smaller countries like Korea, Japan, and Taiwan are ahead of India in conducting GCTs.

The experts in India feel there is a requirement to conduct more clinical research in India to meet emerging health concerns (i.e., antibiotic resistant pathogens, H1N1, dengue), entrenched diseases (i.e., HIV, malaria, tuberculosis), and rare diseases (i.e., Gaucher disease, Pompe disease, etc).

Source: pharmabiz.com

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DRUGS: DEVELOPMENT & CLINICAL TRIALS

2. New target identified for ALS drug development: KIF5A mutation

An international team of researchers from UMass Medical School and the National Institute on Aging at the National Institutes of Health (NIH), have identified a new gene 'KIF5A', which is associated with the development of amyotrophic lateral sclerosis (ALS).

The research is published in the journal '*Neuron*', and promotes the knowledge about how ALS is caused and further defines the role of cytoskeleton default in axon, which is a common cause for ALS. This attributes to cytoskeleton as a potential target for new drug development for the disease.

Amyotrophic lateral sclerosis is a progressive neurodegenerative disease affecting neurons of the central nervous system. The muscle movements are affected in patients suffering from ALS, which may lead to full paralysis and may even result in death too within two to five years from diagnosis. Familial origin because of a genetic defect accounts for ~10% ALS cases whereas ~90% are considered sporadic without a family history; however, a much larger percentage of ALS is likely to be contributed by direct or indirect genetics.

KIF5A functions within neurons to transport material up and down the axon, a process known as axonal transport. KIF5A accomplishes this by acting like a chairlift transporting people and moving along cables in the axon's cytoskeleton.

The mechanism of KIF5A involves axonal transportation and RNA processing. These mutations have been found in people having a rare form of hereditary spastic paraplegia (HSP). Patients with these mutations exhibit longer survival period (average 10 years) than any other mutations after diagnosis of this disease.

These mutations were identified via search for ALS risk with comparing genomes in more than 20,800 ALS cases having 59,800 controls. Also, a "rare variant burden analysis" was done for 19,494 controls and 1,138 hereditary ALS cases. The results showed KIF5A as a new gene relating to ALS.

Source: news-medical.net

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DRUGS: DEVELOPMENT & CLINICAL TRIALS

3. Positive Phase III results for Encorafenib and Binimetinib in Melanoma

Array BioPharma has announced the results of the Phase 3 COLUMBUS trial of encorafenib and binimetinib in the treatment of melanoma. The manuscript entitled "Encorafenib plus binimetinib versus vemurafenib or encorafenib in patients with BRAF-mutant melanoma (COLUMBUS): a multicentre, open-label, randomised phase 3 trial," was published online on March 21, 2018 in the journal '*Lancet Oncology*'.

The COLUMBUS trial, (NCT01909453), is a two-part, international, multicenter (over 2000 sties across North America, Europe, South America, Africa, Asia and Australia) randomized, open label Phase 3 trial evaluating the efficacy and safety of the combination of encorafenib and binimetinib compared to vemurafenib and encorafenib monotherapy. The study included 921 patients with locally advanced, unresectable or metastatic melanoma with $BRAF^{V600}$ mutation.

The trial results demonstrated that the combination therapy of encorafenib and binimetinib had a better median progression-free survival of 14.9 months for patients with BRAF-mutant advanced, unresectable or metastatic melanoma vs 7.3 months with single agent vemurafenib.

Encorafenib and binimetinib are small molecules, which are late-stage inhibitors, inhibiting BRAF and MEK respectively. BRAF and also MEK are important protein kinases in the MAPK signaling pathway (RAS-RAF-MEK-ERK).

Source: biospace.com

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DRUGS: DEVELOPMENT & CLINICAL TRIALS

4. Ammonia Oxidizing Bacteria (AOB) for Acne Vulgaris: Positive Phase IIb data

AOBiome Therapeutics, promoting its patented microbiome-targeted therapies portfolio, has published the clinical safety results of Phase 1b/2a trial (Part 1) of its first-in-class Ammonia Oxidizing Bacteria (AOB) product.

AOBiome's candidate is a first-in-class, topical formulation of a single strain of beneficial AOB, Nitrosomonas eutropha. The platform is designed to repopulate the skin or nasal microbiome with AOB normally found on the body. Once deployed, AOB convert ammonia to nitrite, which is known to have antibacterial properties, and to nitric oxide, a signaling molecule known to regulate inflammation and vasodilation.

In Part 1, of the double-blind, multi-dose, vehicle-controlled of Phase 1b/2a trial, the product has shown encouraging safety and tolerability results when supplied intranasally to healthy participants (N=24, randomized 1:1:1 high dose AOB, low dose, and vehicle) with a course of two weeks. The first-in-class therapy has demonstrated a statistically significant 2-point reduction (p=0.03) in the Investigator's Global Assessment (IGA) score. All adverse events were mild in severity, none of which were considered to be related to the study drug. Additionally, there were no serious adverse events and no discontinuations. Furthermore, there were no infectious or inflammatory complications nor local/systemic adverse events related to the study drug and no changes in nasal patency, anatomy, or architecture.

On the basis of these safety data, the firm has initiated Part 2 of Phase 1b/2a trial which will analyze primary efficacy in subjects presenting with seasonal allergic rhinitis (SAR).

Source: biospace.com

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PATENTS: NEW APPROVALS /LITIGATIONS /SETTLEMENTS

1. American Gene Technologies adds one more immuno-oncology patent

American Gene Technologies International Inc. (AGT), a leading company in gene and cell therapy, has been granted one more immuno-oncology patent for the stimulation of gamma delta T cells in the treatment of solid tumors in epithelial cancers.

The patent obtained on March 13, 2018, with U.S. Patent No: 9,914,938 further strengthens their intellectual property status, which is about their innovative gene therapy platform. The patent gives details about AGT's characteristic lentivirus vector, which allow reformation of tumors for potent trigger of naturally-occurring T cells in the immune system delivering an efficient immune response as well as to destroy tumors.

Gamma delta T cells specifically act as an active agent against solid masses of tumors by infilitrating the tumor and thus killing the tumor effectively. Its response does not require special surface markers for each of tumor type. These cells are also less sensitive to immune checkpoint inhibitors in comparison to other T cells.

Source: news-medical.net

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PATENTS: NEW APPROVALS /LITIGATIONS /SETTLEMENTS

2. Suven Life Sciences obtains 3 patents

Suven Life Sciences shares has been granted patents for 3 New Chemical Entities (NCEs) products. These 3 patents are permitted, one from Norway, second from South Korea and the third from Singapore to NCEs for treating disease related to neurodegenerative category. These patents are viable via 2027, 2034 and 2036, respectively.

These patents are permitted for the category of selective 5-HT6 and 5HT4 compounds, respectively. These therapeutic agents are developed for major depressive disorders as well as for the treatment for cognitive impairment related to neurodegenerative disorders such as attention deficient hyperactivity disorder (ADHD), Alzheimer's disease, Huntington's disease, Parkinson, Schizophrenia and Narcolepsy.

Source: moneycontrol.com

PATENTS: NEW APPROVALS /LITIGATIONS /SETTLEMENTS

3. Japanese Patent Office permits protection for BioArctic patent

BioArctic AB has declared that the Japanese Patent Office (JPO) has permitted its patent application in Japan, 2014-545410, for the medical device, which is one of the main components in the product candidate SC0806.

The product candidate is a combination of medical device (implant) and a medicinal product (FGF1) for the treatment of patients with complete spinal cord injury.

This product candidate SC0806 is under clinical Phase 1/2 study and will provide an option for the treatment of patients having complete spinal cord injury, for which there is no definitive treatment available. BioArctic has covered all of the major geographic trades including the US, EU, Japan and China via this active patent policy.

Source: aboutpharma.com

PATENTS: NEW APPROVALS /LITIGATIONS /SETTLEMENTS

4. PetVivo's two patents approved by U.S. Patent and Trademark Office

The U.S. Patent and Trademark Office (USPTO) has approved two patents of PetVivo Holdings, Inc., which is a subsidiary company of Gel-Del Technologies, Inc., for their signature products: protein-based biomaterials used for various beneficial medical applications, including drug delivery devices, coated medical devices (e.g., stents and valves), and tubular/vascular grafts.

The applications for the first patent and the second patent filed with the U.S. Pat. App. Ser. No. 14/827,513 and U.S. Pat. App. Ser. No. 13/131,083, are entitled under "Protein Biomaterials and Biocoacervates and Methods of Making and Using Thereof" and "Protein Biomaterial and Biocoacervate Vessel Graft Systems and Methods of Making and Using Thereof", respectively.

The first patent provides description related to "amorphous biocoacervate materials that are cross-linked with one or more than one crosslinking agents" and the second one provides description related to "vessel graft system comprising: one or more than one tubes including, a first biomaterial formed from one or more precipitated amorphous thermoplastic biocoacervates."

Source: petvivo.com

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TECHNOLOGY /NDDS

1. Artificial heart developed using rocket technology

Scientist have developed an artificial heart using rocket technology, and the research is currently undergoing in the preclinical phase. The artificial heart was developed jointly by the China Academy of Launch Vehicle Technology (CALT) and the Teda International Cardiovascular Hospital in Tianjin.

The mechanism of the artificial heart is based on magnetic and levitation from rocket science. This technology can reduce the friction of device and increase the efficiency and extend the life span. It is also used to reduce damage to blood cells and it enables the blood pump to work longer.

In preclinical studies, scientists planted an artificial heart in a sheep, which survived for 120 days in good health. Then hearts were then placed in six other sheep, and all survived 100 days or longer, which proved that the artifical heart is qualified for batch production.

Source: economictimes.indiatimes.com

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TECHNOLOGY /NDDS

2. Male contraceptive pill: successful results from Phase I clinical trials

A new male contraceptive pill has been found successful in Phase I human studies. This new male contraceptive pill is ‘dimethandrolone undecanoate (DMAU)’. The DMAU contains a specific long-chain fatty acid that slows its clearance from the body making it a perfect "once-a-day" pill unlike other forms of oral testosterone, which classically are cleared from the body quickly.

The Phase 1 study recruited 100 healthy male subjects. Three different dosages including a placebo control were evaluated in three different goups. The highest dose group displayed the most effective results showing "marked suppression" of testosterone levels and specific hormones related to sperm production. Two primary side effects- decrease in HDL cholesterol and minor weight gain, were reported to be mild in severity.

Source: economictimes.indiatimes.com

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3. New target identified for untreatable blood cancer

Scientists from QIMR Berghofer Medical Research Institute's Immunology in Cancer and Infection have discovered a new biomarker that could help to unlock the medical mystery behind untreatable multiple myeloma.

In their study, researchers found that cytokine IL-18 suppressed the immune system to help create a bone marrow environment where the cancer was more likely to grow. The study analysed the impact of IL-18 on 152 patients with multiple myeloma. The results showed a strong evidence that high levels of the molecule were associated with poorer survival.

In the bone marrow, IL-18 was responsible for inhibition of a particular kind of white blood cell (granulocyte) in the bone marrow, and ultimately suppressed the immune system. This suppression was interrupted by the T cells.

Source: economictimes.indiatimes.com

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4. Big Pharma using artificial intelligence for improving drug discovery

Artificial intelligence (AI) can help analyze large data sets from clinical trials, health records, genetic profiles, and preclinical studies. It can recognize patterns and trends within this data, and can develop hypotheses at a much faster rate than researchers do.

Major pharmaceutical companies like Merck, Sanofi, and Astra-Zeneca are already taking AI to the laboratory. In 2017, AstraZeneca partnered with BERG, a Massachusetts startup, to use the latter's AI platform on promising biological targets and possible agents against neurological diseases such as Parkinson's.

Source: fortune.com

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WHAT'S NEW AT LAMBDA

1. New LCMS machines at Lambda

Looking at the continuous business flow for small molecule evaluations, Lambda has added six new Liquid Chromatography - Mass Spectrometer (LCMS) Systems in the Bioanalytical department. These machines have middle level sensitivity and have the capacity to detect drugs at nano grams/mL. Additionally, these machines have bigger autosampler capacities and can accommodate more than 580 samples at a time for evaluations, which would reduce the efforts involved in loading and un-loading of samples during the run and eventually help in expediting the analysis.

Sl No	Machine	Company	Type	No
1	Liquid Chromatography - Mass Spectrometer System	Shimadzu	Nexera + LCMS-8045	4
2	Liquid Chromatography - Mass Spectrometer System	Waters	UPLC + QPXE	2
3	Electrochemiluminescence System	Meso Scale Diagnostic	MESO Quick Plex SQ 120	1

2. Procedure update at Lambda Canada

As a part of quality system harmonization, e-Form system implementation has been extended to our Canada location for Deviation and Change Control Reporting.

As learning is a continuous process, Lambda Ahmedabad has software-based e-Form system in place which is functioning smoothly. This e-form system allows the user to create and send the user access, deviation and change control request in the software to a different designated person who provides approval in the software and the entire process occurs online without the need for paper documentation.

The e-Forms move through various stages in the process of submission and approval. Harmonization between the different locations in the same system has been implemented at our Canada facility.

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