Lambda Research Newsletter

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Volume 5 / May 2017

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Contents

LAMBDA
Research Accelerated
Volume 5 / May 2017

Clinical Research NEWSletter

www.lambda-cro.com

Contents

LAMBDA
Research Accelerated
Volume 5 / May 2017

Clinical Research NEWSletter

www.lambda-cro.com

GLOBAL NEWS

1. Drugs' prices increased, spending growth slowed in 2016

In the annual drug spending report of Quintiles IMS released on May 4, 2017, the institute has suggested a decline in pharmaceutical spending at 4.8% in 2016 compared with 8.9% in 2015. The net spending growth on drugs reached 4.9% in the U.S. last year at $323 billion. Overall, a 28% industry wide rebate and discounting level is also included in these figures. A slow spending growth was seen on an invoice basis from 15% in 2014 to 12.5% in 2015 and only 5.8% in 2016.

A continuous expansion in the overall growth and drug spending is seen in the U.S., in 2016, with an increase in net spending of 8.9% in 2015, and about 10% for 2014. The specialty medicine class now accounts for $384 of the $895 per person per year spent on pharmaceuticals in the U.S.

The average invoice price increases also slowed down from 13.7% in 2014 to 12% in 2015 and 9.2% in 2016; and lower average price increases were seen after discounts at 4.5% for 2014, 2.5% for 2015 and 3.5% for 2016.

It was observed that fewer than half the number of new medicines received US FDA approval in 2016 compared to 2014 and 2015, which led to downturn sales for medicines <24 months in the market to $13.9 billion in 2016 compared with $17.3 billion in 2015 and $20.6 billion in 2014. However, the trend seems to be reversing as the US FDA has approved more new medicines during the first quarter of 2017 than during the same period of any year in recent history.

Source: fiercepharma.com

LAMBDA
Research Accelerated
Volume 5 / May 2017

Clinical Research NEWSletter
www.lambda-cro.com

GLOBAL NEWS

2. 14 companies selling illegal cancer treatments get FDA warning letter

Warning letters were issued to 14 U.S. based companies, which were illegally selling cancer treatment drugs. More than 65 products were marketed and sold without FDA approval, most commonly on websites and social media platforms with fraudulent claims of prevention, diagnosis, treatment or cure of cancer.

A variety of product types marketed for use by humans or pets were included in these warning letters that includes pills, topical creams, oils, ointments, syrups, drops, teas and diagnostics (such as thermography devices). These products make illegal, unproven claims regarding preventing, reversing or curing cancer; killing/inhibiting cancer cells or tumors; or other similar anti-cancer claims.

Furthermore, prior to the FDA approval of the drugs stating that they are safe and effective for their labeled uses, the marketing and selling of products that claim to prevent, diagnose, treat, mitigate or cure diseases, is a violation of the Federal Food, Drug and Cosmetic Act. Hence, the 14 companies are asked to submit their responses as to how the violations would be corrected. Legal action including product seizure, injunction and/or criminal prosecution may result in case of failure to correct the violations.

Source: worldpharmanews.com

LAMBDA
Research Accelerated
Volume 5 / May 2017

Clinical Research NEWSletter
www.lambda-cro.com

GLOBAL NEWS

3. Merck sells its biosimilars business to Fresenius

In line with its strategy for its healthcare business sector to focus on its pipeline of innovative medicines, Merck has divested its biosimilars business to Fresenius.

An upfront payment of 170 million €, milestone payments of up to 500 million € plus royalties on future product sales will be awarded to Merck under this agreement. Furthermore, the supply and services agreements were also made by the companies, which include drug development support and manufacturing services.

Based on the regulatory approvals and other customary closing conditions, the deal is expected to be closed in the second half of 2017.

This divestment is a major step towards Merck's strategic alignment of R&D resources to healthcare priorities. This transaction will help focus on innovative drug development of high quality and first-to-market best-in-disease assets.

Source: thepharmaletter.com

LAMBDA
Research Accelerated
Volume 5 / May 2017

Clinical Research NEWSletter
www.lambda-cro.com

GLOBAL NEWS

4. New York appeals court revives NYU royalty case against Pfizer

A New York state appeals court has revived a lawsuit by New York University (NYU) seeking royalties on sales of Pfizer Inc's cancer drug Xalkori. Earlier the prospect of paying tens of millions in royalties on Xalkori (crizotinib) - its lung cancer drug, was presumed by Pfizer to have escaped; however, the NYU was awarded with a share of the Xalkori's sales by an appeals court, ruling that a lower court erred in tossing NYU's lawsuit against Pfizer.

The appeal court couldn't determine whether NYU is actually entitled to royalties on Xalkori, and only that the earlier dismissal was invalid. In a 3-2 decision statement, the court said that "to the extent Pfizer, on its own, discovered that crizotinib could treat" a specific lung cancer, "the discovery of crizotinib was still derived in part through NYU's research technology."

A 2.5% royalty was given to NYU for the medicine accounting for >$2 billion in sales since its launch in 2011, and $561 million just last year.

Source: fiercepharma.com

LAMBDA
Research Accelerated
Volume 5 / May 2017

Clinical Research NEWS letter
www.lambda-cro.com

PHARMA INDIA

1. Doctors and public health groups: Branded drugs should be phased out

Physicians and public health organizations are of the opinion that the government should develop a plan for gradually phasing out branded drugs and promote the prescription of generic drugs. This would also require the abolition of differential pricing under different brands.

India's Prime Minister, Mr Narendra Modi had recently made an announcement saying that doctors should mandatorily prescribe low cost generic medicines and that the government was looking to develop a legal framework to ensure that it is rigorously followed.

The Medical Council of India has issued a notice to all doctors to prescribe only generic medicines. This would only succeed if the branded drugs are removed from the market gradually in order to avoid pharmacists promoting specific brands.

The Indian Medical Association (IMA) has also recommended the abolition of differential pricing of different generic drugs.

Source: brandindiapharma.in

LAMBDA
Research Accelerated
Volume 5 / May 2017

Clinical Research NEWS letter
www.lambda-cro.com

PHARMA INDIA

2. Union Health Ministry to create an e-portal to track sale of quality medicines

Ministry of Health
Government of India

The Union Health Ministry is planning to develop a digital platform to keep a track of the sale of quality medicines and at the same time regulate it and keep the operations transparent. The "track and trace" mechanism which is currently in place to regulate the sale of quality drugs through the internet is applicable for the population, both in and outside India.

Presently, bar coding for medicine packs is done only for those that are exported. Quality of medicines manufactured in India have been found be substandard with nearly 3% being substandard as per a recent survey, hence the above move is very important.

The Health Ministry has issued a notice saying that all drug manufacturers have to register on the portal, and enter details of their sales along with quantity of the stock supplied with their batch numbers and expiry dates. This would be applicable to all stockists and wholesalers. They would also need to mention their dealings with their distributors or retailers. The portal would be accessible even through mobiles for ease of updation with an option to update once every 15 days.

The notice also mentions that medicines can be sold only with the prescription of a registered medical practitioner and the prescription should contain the doctor's registration number (MCI state medical council).

All these guidelines would be finalized by the government under the Drugs and Cosmetics Act, 1940 by April 15, 2017.

Source: brandindiapharma.in

LAMBDA
Research Accelerated
Volume 5 / May 2017

Clinical Research NEWS letter
www.lambda-cro.com

PHARMA INDIA

3. 7 Biologics in top 10 selling drugs

Biopharmaceuticals or Biologics have become best sellers with 7 out of the top 10 selling drugs being biologics. They have become an integral part of the management of many serious illnesses like rheumatoid arthritis, cancers and diabetes. The use of biologics has increased in the last decade and the sales have bypassed traditional drugs as they are considered high value therapeutics for many chronic diseases.

Biosimilars are copies of biologics and their market is valued at nearly 400 million USD and growing at a CAGR of 14%.

Indians are working on biosimilars for many biologics to capture and increase their share in the global market. A report by Assocham estimates the Indian contribution to the biosimilar market to reach US$ 40 billion by 2030, nearly 20% share in the global market.

Source: brandindiapharma.in

LAMBDA
Research Accelerated
Volume 5 / May 2017

Clinical Research NEWSletter
www.lambda-cro.com

PHARMA INDIA

4. FDA slams Indian API firm Sal Pharma for faking certificates of analysis

The US FDA issued a warning to Sal Pharma for using products of unapproved API manufacturers claiming that they had produced the same to US customers. The drugs included lansoprazole, a gastrointestinal API, and itraconazole, an antifungal API. The US FDA in its inspection in June/July noticed that Sal Pharma had removed the name of the original producers of the API and replaced with its name in the certificates of analysis (COA) from its own letterhead.

FDA says that "Omitting information from COA compromises supply-chain accountability and traceability, and may put consumers at risk."

Sal Pharma issued a statement saying that it would stop exporting these drugs to the US but the US FDA wants to understand from the company how exactly they would go about resolving this problem.

Earlier, the US FDA had identified a couple of Chinese companies involved in faking COAs and had issued warning letters.

A recent report says that FDA inspections have increased on Indian companies especially from 2010 to 2015 where it has tripled and the same trend continues in 2017.

Source: fiercepharma.com

LAMBDA
Research Accelerated
Volume 5 / May 2017

REGULATORY ROUND-UP

1. UK plans to finalize the Drug Pricing Bill ahead of elections

The lawmakers in UK plan to push through the Drug Pricing Bill before the parliament session closes for election. The decision to have the election has created a deadline for the politicians to resolve the differences between the two houses in the parliament and come up with a compromise amendment keeping in view the economic consequences of pricing decisions.

Before the election was declared, the draft legislation was passed back and forth between the two houses of the parliament, the House of Commons and the House of Lords, without any decision or consensus between them regarding the inclusion of a particular amendment.

These amendments aimed to address industry concerns regarding the bill showing support from the government.

Lawmakers from the ruling Conservative party in the House of Commons rejected both versions of the Lords' amendment with concerns regarding the wording of the text which they felt may hamper the government in controlling the cost of drugs effectively. Some senior politicians also opined that these proposed amendments may open the government for legal challenges if their decisions regarding the price of drugs do not support the life sciences industry.

Source: raps.org

LAMBDA
Research Accelerated
Volume 5 / May 2017

Clinical Research NEWSletter
www.lambda-cro.com

REGULATORY ROUND-UP

2. Revised erythromycin ethylsuccinate monograph by European Pharmacopoeia

A revised monograph was released by the European Pharmacopoeia for erythromycin ethylsuccinate. It was implemented from May 1, 2017, to allay fears that there would be a shortage of the drug due to the testing for related substances, ending five months of turbulence.

The version 9.0 of the monograph was implemented in January by the European Directorate for the Quality of Medicines (EDQM) but issues were raised regarding related substances test resulting in officials recognizing that the text may affect the stocks and supply of the drug.

In April, EDQM thought about reverting to the text in the previous version 8.0 of the monograph and has presently carried out in the new version implemented. The text is similar to version 9.0 except for the test of related substances. This has resulted in EDQM having some time to relook at the test in version 9.0 and assess its impact and think about the best way to resolve it in the long term.

Source: raps.org

LAMBDA
Research Accelerated
Volume 5 / May 2017
Clinical Research NEWSletter
www.lambda-cro.com

REGULATORY ROUND-UP

3. Biosimilar Interchangeability- Biosimilars Forum seeks more clarity in FDA Draft Guidance

Biosimilars Forum is a nonprofit group and represents companies such as Amgen, Pfizer, Teva and others. The Forum has sought clarity from the US FDA regarding their draft guidance ion biosimilar interchangeability. They want to know if "a demonstration of interchangeability represents a distinct requirement for additional data compared to a demonstration of biosimilarity."

The Forum also wants clarity regarding substitution and switching which are not clearly defined in the draft guidance. This FDA draft guidance was released in January 2017 and follows the release of comments from other stakeholders.

"The Forum believes industry and the public would benefit from the adoption of a glossary to define particular terms related to interchangeability that would supplement the definitions provided in the recently finalized FDA Guidance to Industry: Clinical Pharmacology Data to Support a Demonstration of Biosimilarity to a Reference Product," the comment says.

Source: raps.org

LAMBDA
Research Accelerated
Volume 5 / May 2017

Clinical Research NEWSletter
www.lambda-cro.com

REGULATORY ROUND-UP

4. WHO to invite biosimilar makers for Biosimilar Prequalification

The World Health Organization (WHO) made a statement on 3rd May 2017 inviting biosimilar makers for Biosimilar Prequalification pilot program in September for two of the top selling biologics. This is aimed to bring down the cost of treatment of the bisomilar versions of these two biologics to enable affordability in middle and low income countries.

The two biologics are Rituxan (rituximab) and Herceptin (trastuzumab) from Roche which cost many thousands of dollars for treatment in a year in the US.

"Innovator biotherapeutic products are often too expensive for many countries, so biosimilars are a good opportunity to expand access and support to countries to regulate and use these medicines," said Marie-Paule Kieny, WHO assistant director general for health systems and innovation.

Recnetly, EMA has approved biosimilars of rituximab from Sandoz and quite a few companies such as Mylan, Amgen and Samsung Bioepis and Pfizer are developing trastuzumab biosimilars.

Source: raps.org

LAMBDA
Research Accelerated
Volume 5 / May 2017

Clinical Research NEWS letter
www.lambda-cro.com

MERGERS /ACQUISITIONS /COLLABORATIONS

1. Japan's Sawai Pharma to acquire generics business of Upsher-Smith

UPSHER-SMITH
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Sawai Pharmaceutical Co. Ltd., a Japanese generic pharmaceuticals manufacturer, and Upsher-Smith Laboratories, Inc., an established generics manufacturer based in Minnesota, announced the signing of an agreement for Sawai to purchase the generic pharmaceuticals business of Upsher-Smith, from its parent, Acova, Inc.

Under the agreement signed, Sawai will purchase all the equity interest in the generic pharmaceuticals business of Upsher-Smith from Acova, for a consideration of $1.05 billion. The transaction will be financed by bank loans and available cash. It is expected to close near the end of June 2017, subject to customary regulatory approvals.

Upsher-Smith is a privately-held U.S. pharmaceutical company, owned by the Evenstad family through their company, ACOVA. Mark Evenstad is the CEO of Upsher-Smith, and his father, Ken Evenstad is the Chairman. Upsher-Smith has a diversified product portfolio of over 30 pharmaceutical products, mainly oral solid preparations, and a strong pipeline of over 30 products.

Source: pharmapro.com

LAMBDA
Research Accelerated
Volume 5 / May 2017

Clinical Research NEWSletter
www.lambda-cro.com

MERGERS /ACQUISITIONS /COLLABORATIONS

2. AstraZeneca enters respiratory diseases collaboration with Pieris

AstraZeneca today announced a strategic collaboration in respiratory diseases with Pieris Pharmaceuticals, Inc. to develop novel inhaled drugs that leverage Pieris' Anticalin® platform. Anticalin molecules are engineered proteins which can mimic antibodies by binding to sites either on other proteins or on small molecules. They are smaller than monoclonal antibodies, offering the potential of direct delivery to the lung.

Under the collaboration, Pieris will be responsible for advancing its preclinical lead candidate, PRS-060 into Phase 1 clinical trials in 2017. PRS-060 is an Anticalin agonist interleukin-4 receptor alpha (IL-4Ra) with potential in asthma. AstraZeneca will fund all clinical development and subsequent commercialization programmes and Pieris has the option of co-development and co-commercialization in the US from Phase 2a onwards. In addition, the parties will collaborate to progress four additional novel Anticalins against undisclosed targets for respiratory disease.

AstraZeneca will make upfront and near-term milestone payments to Pieris, about $57.5 million. Pieris has the potential to receive development-dependent milestones and eventual commercial payments for all products not exceeding $2.1 billion as well as tiered royalties on the sales of any potential products commercialized by AstraZeneca. The collaboration agreement is conditional upon the expiration or early termination of the applicable waiting period (and any extension thereof) under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended.

Source: worldpharmanews.com

LAMBDA
Research Accelerated
Volume 5 / May 2017

Clinical Research NEWSletter
www.lambda-cro.com

MERGERS /ACQUISITIONS /COLLABORATIONS

3. Servier and miRagen collaborate on microRNA-targeting therapeutics

Servier and miRagen Therapeutics have come together adding microRNA-92 as a new therapeutic target extending their collaboration in research upto September 2019. Both the companies plan to test MRG-110 in humans within one year. MRG-110 is an inhibitor of microRNA-92, which has been reported in many published articles to be associated with the regulation of new blood vessel creation. This can be useful in the management of of diseases such as cardiovascular disease, ischemic disease, and vascular flow-related diseases.

Servier R&D VP and cardiovascular and metabolism therapeutic innovation poles head Isabelle Tupinon-Mathieu said: “We are highly excited to pursue our collaboration with miRagen, with the ambitious goal to develop a first-in-class compound in the field of regenerative therapy with what we believe has the potential to restore the microvascular density. We really feel that, as a leader in cardiology, we have to use our expertise to find innovative answers to cover important medical needs.”

Source: biospace.com

LAMBDA
Research Accelerated
Volume 5 / May 2017

Clinical Research NEWSletter
www.lambda-cro.com

MERGERS /ACQUISITIONS /COLLABORATIONS

4. Novartis ties up with Conatus to develop new therapeutics for chronic liver diseases

Novartis released a statement that it has informed Conatus Pharmaceuticals that it would like to exercise its option to its exclusive license for the global development and commercialization of emricasan.

This collaboration and license agreement that has been signed between Novartis and Conatus on December 19, 2016 gives Novartis an exclusive license to develop novel medicines to treat liver disease after anti-trust approvals. This will also include Novartis to pay an option exercise fee to Conatus which is 7 million USD.

Source: pharmabiz.com

LAMBDA
Research Accelerated
Volume 5 / May 2017
Clinical Research NEWSletter
www.lambda-cro.com

DRUGS: APPROVALS AND LAUNCHES

1. US FDA grants accelerated approval for durvalumab

AstraZeneca's IMFINZI™ (durvalumab) has received US FDA accelerated approval for previously treated patients with advanced bladder cancer.

Durvalumab is an investigational anti-PD-L1 (programmed death ligand-1) human monoclonal antibody indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma (mUC) who have disease progression during or following platinum-containing chemotherapy, or whose disease has progressed within 12 months of receiving platinum-containing chemotherapy before (neoadjuvant) or after (adjuvant) surgery. The recommended dose is 10 mg/kg body weight administered as an intravenous infusion over 60 minutes every two weeks until disease progression or unacceptable toxicity.

The drug is approved under the FDA's accelerated approval pathway, based on tumor response rate and duration of response regardless of PD-L1 status. The approval is based on the data from Phase 1/2 Study 1108 that evaluated the safety and efficacy of IMFINZI in patients with locally advanced or mUC of the bladder. Results of the study are shown in below table.

	All Patients (N=182)	PD-L1 High (N=95)	PD-L1 Low/Negative (N=73)	PD-L1 Not Evaluable (N=14)
Objective Response Rate (ORR) by BICR*, n (%) (95% confidence interval [CI])	31 (17.0%) (11.9; 23.3)	25 (26.3%) (17.8; 36.4)	3 (4.1%) (0.9; 11.5)	3 (21.4%) (4.7; 50.8)
Complete Response (CR)	5	3	1	1
Partial Response (PR)	26	22	2	2
Median Duration of Response (DoR), months (range)	Not reached (0.9+; 19.9+)	Not reached (0.9+; 19.9+)	12.3 (1.9+; 12.3)	Not reached (2.3+; 2.6+)

*BICR=Blinded Independent Central Review
+ Denotes a censored value

Source: astrazeneca-us.com

LAMBDA
Research Accelerated
Volume 5 / May 2017
Clinical Research NEWSletter
www.lambda-cro.com

DRUGS: APPROVALS AND LAUNCHES

2. Abaloparatide: Approved for osteoporosis in postmenopausal women

The US FDA has approved Tymlos (abaloparatide) injection for the treatment of postmenopausal women with osteoporosis at high risk for fracture defined as a history of osteoporotic fracture, multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy.

Tymlos (abaloparatide) is a synthetic peptide analog of hPTHrP (human parathyroid hormone-related protein) for the treatment of postmenopausal women with osteoporosis. The investigational parathyroid-hormone–related protein (PTHrP) analog abaloparatide (Radius Health) significantly reduced fractures in high-risk postmenopausal women with osteoporosis, a key Phase 3 study has shown. The FDA's approval of Tymlos was based on results from an 18-month randomized, double-blind placebo-controlled Abaloparatide Comparator Trial in Vertebral Endpoints (ACTIVE) trial (>2000 women) and first six months of ACTIVExtend trial. The studies have demonstrated consistent significant and rapid reductions in the risk of vertebral and nonvertebral fractures regardless of age, years since menopause, presence or absence of prior fracture (vertebral or nonvertebral) and bone mineral density (BMD) at baseline. The results demonstrated significant reductions in the relative risk of new vertebral and nonvertebral fractures compared to placebo in the ACTIVE trial:

- 86% in new vertebral fractures
- 43% in nonvertebral fractures
- The absolute risk reductions were 3.6% and 2.0%, respectively.

Source: epgonline.org

LAMBDA
Research Accelerated
Volume 5 / May 2017
Clinical Research NEWSletter
www.lambda-cro.com

DRUGS: APPROVALS AND LAUNCHES

3. US FDA approved Brigatinib for ALK+ NSCLC

The US FDA has approved the ALK-inhibitor Alunbrig (brigatinib) of Japanese drug giant Takeda Pharmaceuticals for the treatment of patients with anaplastic lymphoma kinase-positive (ALK+) metastatic non-small cell lung cancer (NSCLC) who have progressed on or are intolerant to crizotinib.

The data used to approve brigatinib came from a phase 2 ALTA (ALK in Lung Cancer Trial of AP26113) trial in adults. In this ongoing, two-arm, open-label, multicenter trial in patients (n=222) with locally advanced or metastatic ALK+ NSCLC who had progressed on crizotinib, Alunbrig was given 90 mg once daily (n=112) or 180 mg once daily following a seven-day lead-in of 90 mg once daily (n=110) were given. The study results are presented in below table.

Efficacy parameter	IRC Assessment		Investigator Assessment	
	90 mg once daily (N=112)	90→180 mg once daily (N=110)	90 mg once daily (N=112)	90→180 mg once daily (N=110)
Overall Response Rate (95% CI)	48% (39-58)	53% (43-62)	45% (35-54)	54% (44-63)
Complete Response, n (%)	4 (3.6%)	5 (4.5%)	1 (0.9%)	4 (3.6%)
Partial Response, n (%)	50 (45%)	53 (48%)	49 (44%)	55 (50%)
Duration of Response, median in months (95% CI)	13.8 (7.4-NE)	13.8 (9.3-NE)	13.8 (5.6-13.8)	11.1 (9.2-13.8)

CI = Confidence Interval; NE = Not Estimable

Among the 23 patients who exhibited an intracranial response, 78% of patients in the 90 mg arm and 68% of patients in the 90→180 mg group maintained a response for at least four months. Overall, nausea, diarrhea, fatigue, cough, and headache were the most common adverse reactions (≥25%) reported.

Source: drugs.com

LAMBDA
Research Accelerated
Volume 5 / May 2017

Clinical Research NEWSletter
www.lambda-cro.com

DRUGS: APPROVALS AND LAUNCHES

4. Midostaurin is approved for newly diagnosed FLT3-mutated AML

The US Food and Drug Administration (FDA) has approved Rydapt (midostaurin, formerly PKC412) for the:

- treatment of acute myeloid leukemia (AML) in newly diagnosed patients who are FMS-like tyrosine kinase 3 mutation-positive (FLT3+), in combination with chemotherapy, and
- treatment of adults with advanced systemic mastocytosis (SM), which includes aggressive systemic mastocytosis (ASM), SM with associated hematological neoplasm (SM-AHN) and mast cell leukemia.

Earlier, a Breakthrough Therapy designation in FLT3-mutated AML, as well as Orphan Drug designation and Priority Review in both indications were granted by the FDA. This approval in newly diagnosed FLT3-mutated AML represents the first new treatment in more than 25 years. Rydapt is the first and only approved therapy for three types of SM collectively known as advanced SM, a group of ultra-rare, life-threatening conditions.

Rydapt is among a class of drugs called kinase inhibitors that are designed to block enzymes that foster cancer cell growth. It was evaluated in a clinical study of more than 700 people who hadn't been treated previously for AML. In FLT3-mutated AML, Rydapt treatment regimen demonstrated a significant improvement in overall survival with a 23% reduction in the risk of death. Low white cell count, fever, nausea, headache and muscular/bone pain were the common side effects.

Source: upi.com

LAMBDA
Research Accelerated
Volume 5 / May 2017

Clinical Research NEWSletter
www.lambda-cro.com

DRUGS: DEVELOPMENT & CLINICAL TRIALS

1. Altor BioScience's ALT-803 gets Fast Track designation for NMIBC

The US Food and Drug Administration (FDA) has granted Fast Track designation for Altor BioScience Corporation's investigational interleukin-15 (IL-15) agonist complex, ALT-803, in combination with bacillus Calmette-Guérin (BCG), for the treatment of patients with non-muscle invasive bladder cancer (NMIBC). The development and review of drugs to treat serious conditions and fill unmet medical needs are expedited by the FDA's Fast Track program.

The FDA Fast Track designation will apply to the clinical development of ALT-803 in combination with BCG for the treatment and prophylaxis of carcinoma in situ (CIS) of the urinary bladder, as well as for the prophylaxis of primary or recurrent stage Ta and/or T1 papillary tumors following transurethral resection (TUR) in patients with NMIBC.

ALT-803 of Altor BioScience Corporation - a leading developer of novel cytokine-based immunotherapeutics for cancer and infectious diseases, is currently being assessed in a Phase 1b/2 clinical trial. The objective of the study is to investigate the safety and efficacy of intravesical ALT-803 in combination with BCG in adult patients with BCG-naïve NMIBC. Furthermore, another Phase 2 study will investigate the safety and efficacy of intravesical ALT-803 in combination with BCG in adult patients with BCG-unresponsive NMIBC.

Results from the recently completed phase 1b NMIBC study will be presented at the American Urological Association Annual Meeting in Boston, in May, 2017.

Source: pharmabiz.com

LAMBDA
Research Accelerated
Volume 5 / May 2017

Clinical Research NEWSletter
www.lambda-cro.com

DRUGS: DEVELOPMENT & CLINICAL TRIALS

2. Positive results from NHP pilot study of PLX-R18 in acute radiation syndrome

Pluristem Therapeutics, a leading developer of placenta-based cell therapy products, announced promising results of its Non-Human Primates (NHP) pilot study for PLX-R18 as a treatment for Acute Radiation Syndrome (ARS).
The National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH) has conducted and funded the study with an aim to assess the safety and efficacy of PLX-P18 following intramuscular injection into irradiated and non-irradiated NHPs. The efficacy endpoints of the study were survival as well as level of bone marrow function, which is affected by exposure to high levels of radiation as may occur in a nuclear accident or attack.

All the cohorts treated with PLX-R18 showed improved survival compared to cohorts that received placebo, despite that this pilot study was not powered to demonstrate statistical significance. Two lower dosages 4 and 10 million cells/kilogram body weight resulted in higher survival rate in irradiated NHPs compared with the placebo treated control group (85% vs. 50%). A trend towards enhanced neutrophil and lymphocyte recovery was also observed. Overall, all PLX-treated groups showed improvements in survival rates compared to the untreated groups. There were no serious adverse reactions observed in non-irradiated NHPs. PLX-R18 cells did not increase leukocyte levels in non-irradiated NHPs, indicating no requirement to determine levels of radiation exposure prior to administration. This safety profile suggests that determination of an individual's level of radiation exposure would not be required prior to treatment in scenarios that require rapid treatment of large populations (i.e., in the case of a nuclear emergency).

Source: businesswire.com

LAMBDA
Research Accelerated
Volume 5 / May 2017
Clinical Research NEWSletter
www.lambda-cro.com

DRUGS: DEVELOPMENT & CLINICAL TRIALS

3. Pfizer's lorlatinib gets breakthrough therapy designation

The U.S. Food and Drug Administration (FDA) has granted Pfizer's investigational next-generation ALK/ROS1 tyrosine kinase inhibitor, a breakthrough therapy designation for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC), previously treated with one or more ALK inhibitors.

Based on the efficacy and safety data of an ongoing Phase 1/2 clinical trial, which includes patients with ALK-positive NSCLC who were previously treated with one or more ALK inhibitors, the Breakthrough Therapy designation is awarded to lorlatinib. Furthermore, the Phase 3 CROWN study (NCT03052608), an ongoing, open label, randomized, two-arm study comparing lorlatinib to crizotinib in the first-line treatment of patients with metastatic ALK-positive NSCLC has recently started enrolling patients.

Lorlatinib has been shown to be highly active in preclinical lung cancer models harboring chromosomal rearrangements of both ALK and ROS1. The drug was specifically designed to inhibit tumor mutations that drive resistance to other ALK inhibitors and to penetrate the blood brain barrier.

This breakthrough therapy designation recognizes the potential for lorlatinib to provide an important treatment option for patients with ALK-positive NSCLC whose cancers have progressed despite treatment. Pfizer's rapid development of lorlatinib reflects a commitment to developing biomarker-driven therapies to meet the evolving needs of patients

Source: pfizer.com

LAMBDA
Research Accelerated
Volume 5 / May 2017

Clinical Research NEWSletter
www.lambda-cro.com

DRUGS: DEVELOPMENT & CLINICAL TRIALS

4. Positive phase 2b results with Elagolix in women with uterine fibroids

The detailed results of a Phase 2b clinical trial were announced that evaluated the efficacy and safety of elagolix - a gonadotropin-releasing hormone (GnRH) receptor antagonist, alone or in combination with add-back therapy (estradiol/norethindrone acetate) for the treatment of women with heavy uterine bleeding associated with uterine fibroids.

The results of a 24-week, multicenter, double-blind, randomized, placebo-controlled, parallel group, Phase 2b uterine fibroids study (M12-813) showed that elagolix 300 mg BID, with and without add-back therapy, met the primary efficacy endpoint of reduced heavy menstrual bleeding in 567 premenopausal women (aged 18 to 51 years) as compared to placebo ($p<0.001$) at 6 months. A significant increase in hemoglobin concentration from baseline to six months was observed in women treated with elagolix compared to placebo.

Furthermore, the results showed decreased symptom severity and improved quality of life (assessed by the Uterine Fibroid Symptom and QoL [UFS-QoL] questionnaire) with uninterrupted elagolix treatment.

Elagolix is an orally administered, short-acting molecule that acts by competitively binding to GnRH receptors in the pituitary gland and blocks the endogenous GnRH signaling. This result in a rapid, reversible, dose-dependent inhibition of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) secretion. The decreased LH and FSH leads to reduced ovarian production of the sex hormones, estradiol and progesterone.

Elagolix is currently being investigated in diseases that are mediated by sex hormones, such as uterine fibroids and endometriosis. It has been studied in over 40 clinical trials totaling more than 3,000 subjects. Phase 3 trials of elagolix for the management of uterine fibroids are ongoing.

Source: drugs.com

LAMBDA
Research Accelerated
Volume 5 / May 2017

Clinical Research NEWSletter
www.lambda-cro.com

PATENTS: NEW APPROVALS /LITIGATIONS /SETTLEMENTS

1. US Court of Appeals reverses District Court's ruling on Aloxi patent

A panel of the United States Court of Appeals for the Federal Circuit has reversed the opinion of the District Court for the New Jersey for Aloxi (palonosetron hydrochloride) injection. The court has decreed that certain patent claims covering Aloxi are not valid or infringed by Teva's generic palonosetron product.

The ruling also stated that Teva can launch a generic version of Aloxi only if the Federal Circuit, the New Jersey Court and the Food and Drug Administration (FDA) take additional steps to allow such a launch.

Aloxi contains active substance palonosetron and is indicated for the use of patients undergoing chemotherapy to prevent nausea and vomiting and should be administered before chemotherapy.

Earlier in 2011, Helsinn and Roche filed patent infringement lawsuits in the US District Court for the District of New Jersey against Dr Reddy's, Sandoz and Teva, the first company to submit Abbreviated New Drug Applications (ANDAs) for Aloxi. Helsinn has already made settlements with Sandoz and Dr Reddy's, under which both companies cannot introduce a generic version of palonosetron hydrochloride through an ANDA before 30 September, 2018, except under certain circumstances.

Helsinn and Eisai have exclusive marketing rights of Aloxi in the US and Canada and stated their disappointment with the latest court verdict. Both companies stated that the patents protecting Aloxi are valid and they intend to pursue further legal options to validate and enforce such patents.

Source: pharmaceutical-technology.com

LAMBDA
Research Accelerated
Volume 5 / May 2017

Clinical Research NEWSletter
www.lambda-cro.com

PATENTS: NEW APPROVALS /LITIGATIONS /SETTLEMENTS

2. Amgen's legal battle with Sanofi and Regeneron

Dupixent, Sanofi and Regeneron's newly approved drug for severe eczema, is one of the top launches of 2017, and Amgen says it owns an underlying patent. Earlier this month, Amgen sued Sanofi and Regeneron for patent infringement. Amgen is complaining that Dupixent violates patent 487 on using antibodies that bind to IL-4R, which Amgen owns through its subsidiary Immunex, notably, Amgen has no competitive drugs in the market or in pipeline against Dupixent.

The patent battle between Amgen and Sanofi Regeneron continues from PCSK9 dispute in which Amgen won at the trial court level to force Sanofi and Regeneron to pull Praluent off market. However, Amgen is not pushing for an injuction to get Dupixent off market unlike PCSK9. It is very uncommon to use injunction to push a drug off-market and other drug makers and law experts had criticized Amgen's efforts in getting Praluent off-market.

Sanofi and Regeneron developed Dupixent (dupilumab) to block the IL-4 and IL-13 immune system pathways by binding to IL-4R. Amgen's subsidiary Immunex owns a patent—the '487 patent—on using antibodies that bind to IL-4R, and that patent identifies a particular antibody, 12B5, whose amino-acid sequences are specified in the '487 patent.

Meanwhile, Amgen had been trying to develop an asthma drug using the IL-4R binding approach, which failed in phase 2 study and is currently wiped off from Amgen's pipeline listing on its website.

Source: fiercepharma.com

LAMBDA
Research Accelerated
Volume 5 / May 2017

Clinical Research NEWSletter
www.lambda-cro.com

PATENTS: NEW APPROVALS /LITIGATIONS /SETTLEMENTS

3. AZ and BMS Face Suits Linking Onglyza to Heart Failure

A law suit was filed against AstraZaneca and Bristol Mayer Squibb in the District of New Jersey claiming that the companies failed to warn users on the possible cardiac arrest, congestive heart failure and death with Type 2 diabetes medicine Onglyza and related combo product Kombiglyza XR. Earlier, the US FDA had called for stronger heart-failure warnings on the label of Onglyza last year.

Onglyza was being marketed by the pharma pair in 2009 before evaluating patients' cardiac risks in clinical studies, which is required as per 2008 FDA guidance that urges companies to demonstrate that new therapies "will not result in an unacceptable increase in cardiovascular risk." Onglyza's heart risks most recently came into the spotlight last April, when the FDA insisted its label include a warning of increased heart-failure risk.

Source: pharmaletter.com

LAMBDA
Research Accelerated
Volume 5 / May 2017

Clinical Research NEWSletter
www.lambda-cro.com

PATENTS: NEW APPROVALS /LITIGATIONS /SETTLEMENTS

4. Johnson & Johnson loses $110 million verdict over talc-powder suit

Johnson & Johnson was ordered to pay over $110 million to a Virginia woman who claims that she developed ovarian cancer by using its talc-based products, for feminine hygiene, for almost 40 years. The plaintiff Lois Slemp, 62, was awarded $5.4 million in compensatory damages and punitive damages of $105 million against Johnson & Johnson and $50,000 against Imerys Talc America, the company which provides the product to J&J.

The $110 million verdict is the eighth-largest jury award in the U.S. so far in 2017; the largest was $500 million and awarded to ZeniMax Media Inc. over its claim that the virtual reality headset maker acquired by Facebook Inc. used stolen code.

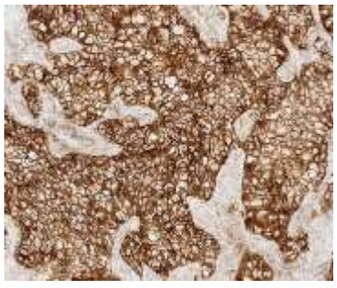
Source: health.economictimes.com

LAMBDA
Research Accelerated
Volume 5 / May 2017

Clinical Research NEWSletter
www.lambda-cro.com

TECHNOLOGY /NDDS

1. VENTANA PD-L1 (SP263) assay for bladder cancer



Roche introduced a new test VENTANA PD-L1 (SP263) assay for the detection of PD-L1 status, a protein involved in immunosuppression for patients with locally advanced or metastatic urothelial carcinoma (mUC) who are being considered for treatment with the FDA-approved anti- Programmed Death Ligand (PD-L1) immunotherapy IMFINZI™ (durvalumab, AstraZeneca).

VENTANA PD-L1 (SP263) Assay is a qualitative immunohistochemical assay using rabbit monoclonal anti-PD-L1 clone SP263 used for the assessment of PD-L1 protein in formalin-fixed, paraffin-embedded (FFPE) urothelial carcinoma tissue stained with OptiView DAB IHC Detection Kit on a VENTANA BenchMark ULTRA instrument.

VENTANA PD-L1 (SP263) is introduced for the qualitative detection of the PD-L1 in various cancer indications. The test evaluates patient PD-L1 status using both tumor and immune cell staining and scoring within the tumor microenvironment, providing clinicians with information that may guide treatment decisions.

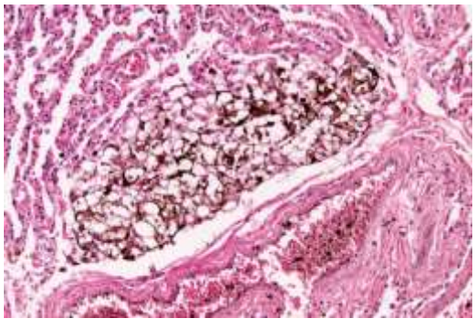
Source: ventana.com; epgonline.org

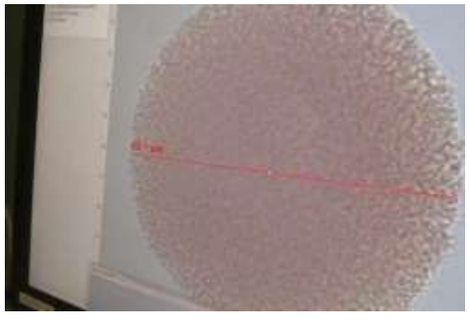
LAMBDA
Research Accelerated
Volume 5 / May 2017

Clinical Research NEWSletter
www.lambda-cro.com

TECHNOLOGY /NDDS

2. New microscopic technique to diagnose metastatic melanomas





For a long time, melanoma researchers have studied various samples of melanoma, which were uniform in size and color making them easier to study by various conventional means. But melanomas always don't come in similar shapes, sizes, and colors; often melanomas are irregular in shape, dark in color which makes them difficult to investigate. Now melanoma researchers at the University of Missouri, United States, have developed a new tool for the detection and assessment of single melanoma cells which are more representative of the skin cancers developed by most patients.

The team at the University included Gary Baker, an assistant professor of chemistry in the MU College of Arts and Science and Gerardo Gutierrez-Juarez, a professor and investigator at the University of Guanajuato in Mexico, introduced an emerging technique called photoacoustic (PA) spectroscopy, a specialized optical technique that is used to probe tissues and cells non-invasively. Present systems use the formation of sound waves followed by the absorption of light which shows that the tissues must adequately absorb the laser light. Hence, the researchers have focused only on strong-light-absorb cells melanoma cells until now. The researchers modified a microscope that was able to merge light sources at a range conducive to observing the details of single melanoma cells. Using the modified system, human melanoma and breast cancers as well as mouse melanoma cells were diagnosed with greater ease and efficiency. The researchers also noted that as the cancer cells divided, they grew paler in color but the system was able to detect the newer, smaller cells as well.

Source: technology.org; medicalxpress.com

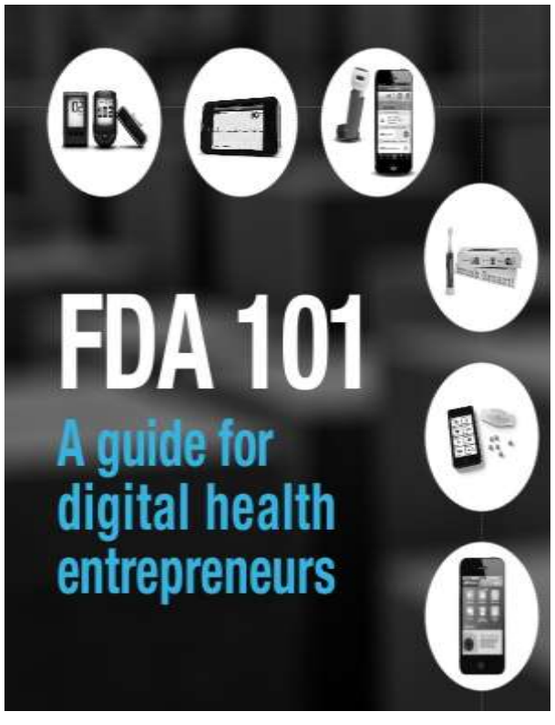
LAMBDA
Research Accelerated
Volume 5 / May 2017

Clinical Research NEWSletter
www.lambda-cro.com

TECHNOLOGY /NDDS

3. FDA to create digital health unit

Present world is completely digitalized with latest gadgets and applications. Now FDA is connecting these advanced gadgets and software advancements with the health units. Patients and normal citizens can use digital health units for their better health and to trace their health and wellness related activities.



The present technology like smart phones, social networks and internet applications are not only the way to communicate but are also providing complete new ways to monitor our health and wellbeing. As well as also connecting people with the health care and health outcomes.

At present a number of medical devices have the ability to connect to and communicate with other devices or systems. Devices which are already FDA approved or cleared are being updated to add digital features. New types of devices that already have these capabilities are being explored.

Federal Trade Commission (FTC) Mobile Health Apps Interactive Tool is a mobile app that collects, creates, or shares consumer information.

Source: fda.gov

LAMBDA
Research Accelerated
Volume 5 / May 2017

Clinical Research NEWSletter
www.lambda-cro.com

TECHNOLOGY /NDDS

4. Tekni-Plex to launch latest thermoformable film, closure liner technology at Interpack 2017

Tekni-Plex, Inc., is a globally-integrated manufacturer company of closure liners and seals for glass, metal and plastic containers. Now Tekni-Plex is introducing a latest flexible packing material for pharmaceutical applications along with an extensive line of closure liners for a wide variety of products.

The latest product Flexapharm super-barrier coated (SBC) will be thermoformable, polyvinylidene chloride (PVdC) blister film line which will offer ultra-high moisture and an oxygen barrier, and economic attributes for pharmaceutical applications.

Flexapharm SBC is an alternative to cold formed foil or PCTFE based blisters for a wide range of tablets and capsules. It is created by applying a PVdC barrier coating to a film structure typically made from layers of polyvinyl chloride (PVC) and/or polyethylene. Multiple layers can be applied depending on the desired barrier attributes of the specific application. The technology offers a greater degree of customization and flexibility compared to laminated structures.

Source: tekni-plex.com

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