REVA Pharma
Caring for Healthier Lives

NEWS LETTER
For Private Circulation only

Biogen Rises as FDA Panel Backs Alzheimer's Drug, Easing Safety Concerns

Biogen's (BIIB.O) shares rose 2% on Monday as a unanimous backing of its Alzheimer's drug by the U.S. health regulator's advisers strengthened the case for a traditional approval with no major new safety warnings.

The Food and Drug Administration's advisory panel unanimously agreed that a late-stage trial of the drug Leqembi, developed with partner Eisai (4523.T), verified the benefit of treatment for those at an early stage of the disease. The vote clears the way for a traditional approval by the agency, months after it gained an accelerated approval in January.

The advisers discussed the risk of using Leqembi in certain patients, like those taking drugs that prevent blood clots and those with a rare condition called cerebral amyloid angiopathy. The condition causes the protein amyloid, that Leqembi targets, to build up in the walls of arteries in the brain and can cause bleeding. But the advisers said that those concerns could be managed, and were balanced against the benefits provided by the drug.

"It seems unlikely that the updated FDA label will include additional contraindications," said Stifel analyst Paul Matteis, referring to the written information that accompanies an approved drug. Traditional approval by the FDA, which is expected by July 6, is likely to expand Medicare payment for the treatment. The FDA generally follows the advise of its independent experts.

The panel considered data from Eisai's confirmatory trial that showed the drug slowed cognitive decline by 27% in early Alzheimer's patients. At least three brokerages raised their price targets on Biogen's shares after Friday's vote. The company's shares trade at 4.71 times Wall Street's estimates for sales in the next 12 months, compared with 2.89 for rival Bristol Myers Squibb (BMY.N) and 3.61 times for Gilead Sciences (GILD.O). (Source: Reuters)

AstraZeneca's Tagrisso Slashes Death Risk in Certain Post-Surgery Lung Cancer

AstraZeneca's lung cancer therapy, Tagrisso, cut the risk of death by more than half in patients with a certain form of lung cancer who were diagnosed early enough to have their tumour surgically removed, trial data showed. Tagrisso is already the crown jewel in the Anglo-Swedish drugmaker's portfolio, raking in $5.4 billion last year.

The drug has regulatory approvals across multiple geographies for certain patients with so-called non small cell lung cancer (NSCLC) who have a mutation of the EGFR gene. The latest data, presented at the American Society of Clinical Oncology (ASCO) meeting, establishes Tagrisso as the backbone treatment for EGFR-mutated lung cancer, said Susan Galbraith, executive VP of oncology R&D at AstraZeneca in a statement. In a 682-patient trial called ADAURA, Tagrisso was evaluated against a placebo in earlier-stage EGFR-mutated NSCLC patients who had undergone surgery to remove their primary tumour. The majority of such patients eventually see their cancer return despite surgery and add-on chemotherapy. In the trial, Tagrisso or a placebo was given to patients to assess whether the AstraZeneca therapy could keep their cancer at bay.

Data showed Tagrisso slashed the risk of death by 51% compared to placebo. "This is a pretty dramatic and remarkable improvement," said Dave Fredrickson, executive vice president of oncology at AstraZeneca in an interview with Reuters. An estimated 88% of patients treated with Tagrisso were alive at five years compared to 78% on placebo, trial data also showed.

Outside of chemotherapy, there are no drugs apart from Tagrisso that have shown to help patients with EGFR-mutated lung cancer live longer, Fredrickson highlighted, adding that there are probably a third of eligible patients who are not yet being prescribed Tagrisso. "We would hope that we would be able to use these data to be able to close that gap," he said. AstraZeneca is also expecting to provide details on the impact of combining Tagrisso with chemotherapy in patients with advanced EGFR-mutated lung cancer later this year. (Source: Reuters)

A Saily Aspirin May Lead to Anemia In Older Adults, Study Says

Aspirin is one of the most commonly used medications in the US. Studies show that more than 40% of adults ages 60 or older take an aspirin every day to prevent dangerous blood clots that could lead to a heart attack or stroke. In recent years, experts have backed away from blanket use of aspirin therapy for all older adults, however, after studies showed that it carried an increased risk of major bleeding that most likely outweighed any benefit in preventing first heart attacks or strokes. However, it's still recommended in some cases for people who have had a heart attack or stroke, to prevent another.

Because aspirin can contribute to the danger of big bleeds like aneurysms, researchers wanted to know whether it might also be a factor in more subtle blood loss: the kind that may lead to anemia, or reduced oxygen in the blood. Anemia is another big problem in the elderly, though perhaps underappreciated compared with heart attacks and strokes. Studies show that 30% of adults 75 and older worldwide are anemic, and anemia is generally tied to worse health – including fatigue, memory and thinking trouble, depression and an increased risk of death. A study published Monday in the Annals of Internal Medicine followed more than 18,000 adults who were 65 and older from the US and Australia. Half took 100 milligrams of aspirin a day – a low dose – while the other half took a dummy pill. The researchers followed them for about five years. Study participants had yearly doctors visits and blood tests for hemoglobin and ferritin, a protein in blood cells that stores iron.

They saw a small but clear difference. Adults who took aspirin were 20% more likely to be anemic than those who didn't take it. Based on their results, the researchers estimated that 24% of seniors in the daily aspirin group would develop anemia within five years, compared with 20% of those in the placebo group. Those on aspirin regimens also had slightly lower levels of hemoglobulin and ferritin, which help blood cells carry oxygen. The difference remained even when the researchers adjusted their data to account for cancer and for major bleeding events during the study, and for other differences between the participants like age, sex, diabetes, kidney disease and the use of nonsteroidal anti-inflammatory medications, or NSAIDs.

The study didn't look at how aspirin may be contributing to anemia, but the authors have an idea about how it might happen. Aspirin makes it harder for blood to clot because it keeps platelets from sticking together. It also blocks and enzyme called Cox-1, which is important for the maintenance of the lining of the stomach and intestines. With this protective barrier damaged, it's easier for small amounts of blood to leak out of the gut over time, eventually causing anemia. The researchers wrote that because they saw this effect across many different groups, regardless of their underlying health, it's likely to be a bigger concern for people who have other risks for anemia, such inflammatory diseases like arthritis or chronic renal insufficiency. They say doctors should consider more closely monitoring their patients' hemoglobin levels if they have multiple risk factors, including aspirin use. (Source: CNN)

'Alarming' Rise in Diabetes Globally by 2050.

Scientists projected that the current number will more than double to around 1.3 billion people by 2050 The majority of the cases are type 2 diabetes, the form of the disease that is linked to obesity and largely preventable, the researchers said.

The increase in prevalence globally is not uniform: Some countries and regions are particularly badly hit. For example, prevalence rates are expected to reach 16.8 per cent in North Africa and the Middle East and 11.3 per cent in Latin America and the Caribbean by 2050, compared to an estimated 9.8 per cent globally. Currently, the prevalence is 6.1 per cent. But every country will be impacted, researchers said.

"The rapid rate at which diabetes is growing is not only alarming but also challenging for every health system in the world," said Liane Ong, lead author of the paper, pointing out that the condition is linked to a number of other heart conditions such as heart disease and stroke.

The growing numbers of people with diabetes is in part driven by rising obesity, and in part by demographic shifts: Prevalence is higher among older adults, the study showed. The data from 204 countries does not take into account the impact of the Covid-19 pandemic because those numbers were not yet available, researchers said. The study, funded by the Bill and Melinda Gates Foundation, is part of a wider series on diabetes published on Thursday in The Lancet medical journal. The series calls for more effective mitigation strategies and an awareness of inequality, with the majority of diabetes patients living in low- and middle-income countries and unable to access proper treatment. (Source: Reuters)

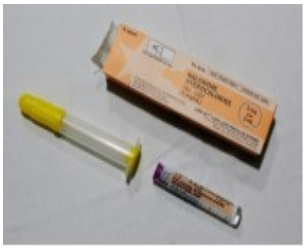
Prioritise Quality And Accountability, USFDA Officials Tell Pharma Industry

Quality concerns lead to drug shortages, said Patrizia Cavazzoni, the United States Food and Drug Administration's director of the Center for Drug Evaluation and Research, urging senior management of the pharmaceutical industry to prioritise quality and accountability. Calling on senior management to "walk the talk" on quality, Cavazzoni said in a recorded message to pharma industry representatives that quality compliance should be a top-down commitment and resources need to be allocated for the purpose. She called for "sustainable compliance" that involved a proactive response in terms of identifying a problem and undertaking remediation measures.

An ongoing dialogue can prevent shortages, she said, referring to the medicne shortages being witnessed in the US, in segments including cancer drugs. Listing about 16 oncology drugs in short supply (May 2023), she said, shortages included old generic drugs like Cisplatin and Carboplatin injections. This scenario was in part because a shut down due to quality issues, she said. Outlining reasons behind the shortages, she said, there was a shortfall in manufacturing capacities, and this could be from a lack of incentives. Critical segments like sterile injectibles are impacted. Sometimes, there are long periods of remediation that could also cause delays in supply. Unforeseen climate events, geo-political issues and financial pressures causing closure of a manufacturer could also impact supplies.

The USFDA has resumed on-site inspections of foreign facilities, she said, and some of the recurring issues seen, included microbial contamination, poor excepient quality, lack of data integrity and inadequate controls. Cavazzoni was addressing the Indian Pharmaceutical Alliance's quality summit (Mumbai). Speaking at a panel discussion, Sarah McMullen, Country Director (India) and Office of Global Operations, USFDA, pointed to data integrity issues still being found, and added, it was important to trust the data to be able to trust the product. Pointing out that compliance was a "shared goal", she said, there was a need for products from the industry. James Pound, Deputy Director Standards and Compliance with the United Kingdom's MHRA (Medicines and Healthcare products Regulatory Agency), echoed the USFDA official's view that sites were assessed on the ability to identify problems and address it. The European Directorate for the Quality of Medicines & HealthCare (EDQM) Inspector - Certification of Substances Department, Thomas Hecker added, international regulators did rely on each others assessment reports.Responding to a query on moving towards harmonised laws, the Central Drugs Standard Control Organisation (CDSCO) Deputy Drug Controller Rubina Bose said, India was on several of these international committees to harmonise technical requirements for certain segments of the industry. The concluding session of the IPA summit will see Union Health Minister Mansukh Mandaviya addressing the gathering on Friday. (Source: Business Line)

US Drug Overdose Deaths Top 109,000 In The Past Year



More than 109,000 Americans died from drug overdoses in the 12-month period ending January 2023, a slight increase from the previous year, according to provisional data from the U.S. Centers for Disease Control and Prevention (CDC) released on Wednesday. The figure is up 0.7% from 108,825 overdoses recorded in the 12-month period ending January 2022, according to U.S. data. The increase comes despite a push by President Joe Biden's administration for action to tackle drug addiction and overdoses. The Biden administration in May imposed sanctions on 17 people and entities based in China and Mexico it accused of enabling production of counterfeit fentanyl-laced pills. Illicit fentanyl has played an outsized role in the U.S. opioid crisis and drug overdoses.

The U.S. drug overdose death toll crossed the 100,000-mark for the first time in 2021, as the COVID pandemic disrupted medical care and increased mental health problems. The effect was exacerbated by the widespread availability of lethal drugs such as fentanyl, which is 50 times stronger than heroin and increasingly mixed in with other illegal drugs. During the pandemic, rates of mental illness, depression and anxiety went up dramatically, and people increasingly began to switch to substances, said Tom Britton, CEO of American Addiction Centers.

U.S. drug overdose deaths rose 13.7% between January 2021 and January 2022 and by 31.4% in the prior 12 months at the height of the pandemic. But the surge in overdose deaths began before the pandemic took hold due to abuse of prescription opioid painkillers and illegal drugs like heroin. Stacey McKenna, senior fellow at the R Street Institute, a Washington, D.C.-based independent think tank, said the crackdown on fentanyl and other addictive drugs could be having the opposite of the intended affect. There's this iron law of prohibition that the harder you crack down on the supply, the more likely you are to get a more potent supply or a more dangerous supply," McKenna said.

The CDC noted that the latest numbers represent an estimate to include underreporting and cases pending investigation. (Source: Reuters)

Zydus Lifesciences Initiates Phase-IV Trial For Saroglitazar Mg in NAFLD Patients

Zydus Lifesciences Limited announced the commencement of Phase-IV Real World Data registry trial Evidences-XI for Saroglitazar Magnesium (Mg) in Non-Alcoholic Fatty Liver Disease (NAFLD) patients with comorbidities. The Phase-IV Evidences-XI trial will enrol about 1,500 male and female NAFLD patients with comorbidities such as obesity, type 2 diabetes mellitus, dyslipidemia or metabolic syndrome- 200 patients each. The study duration is approximately 56 weeks. The primary endpoint is to measure the change in liver stiffness measurement performed by transient elastography from Baseline to Week 52, the company said in a statement.

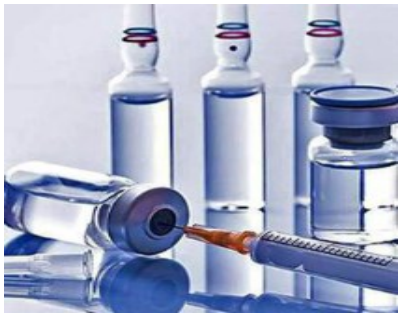
Saroglitazar Mg has been studied in two well-controlled Phase 3 clinical trials in patients with NAFLD and Non-Alcoholic Steatohepatitis (NASH) in India. The first Phase III trial was conducted in biopsy proved NASH patients, where Saroglitazar Mg demonstrated a significant difference of 28 per cent versus placebo in the primary endpoint NAFLD Activity Score with no worsening of fibrosis in greater proportion of patients.

In the second Phase III study, patients had a beneficial effect on primary end-point of change in liver fat content as measured by non-invasive magnetic resonance imaging and secondary endpoints, including liver stiffness as measured by transient elastography/FibroScan in patients with NAFLD at week 24. Rohit Loomba, MD, Professor of Medicine, Division Chief of Gastroenterology at the University of California, San Diego School of Medicine and Director of Hepatology at UC San Diego Health will lead the Steering Committee of the Phase-IV Evidences Real World Data Study. He termed this Phase 4 Evidences study as a landmark establishing one of the largest prospective registries of patients with NASH in the world. “It will help generate novel Real World Data (RWD) in NAFLD/NASH patients, especially lacking in Asian population. Real World Data is crucial to formulate clinical guidelines, to further support its use in clinical practice and this will add to our existing knowledge of Saroglitazar Mg and its role in the management of NAFLD/NASH,” he said.

Pankaj R. Patel, Chairman, Zydus Lifesciences Ltd. said, “NAFLD and NASH are serious life-threatening conditions and we have now studied Saroglitazar Mg in over ten different trials which have been completed and the ongoing EVIDENCES I to X series of clinical trials in patients with NAFLD and NASH across clinical sites in India, Mexico, USA and Europe.”

“We hope that this will be a big leap forward in managing and treating the unmet healthcare needs of NAFLD and NASH,” he added. In the USA, the EVIDENCES-X Phase 2b study of Saroglitazar Mg is currently ongoing in 240 patients with NASH with a 72-week biopsy driven endpoint. Saroglitazar Mg has been studied in patients with Primary Biliary Cholangitis (PBC), a rare liver disease with two separate EPICS-I and EPICS-II series of trials conducted in USA and Mexico. A third Phase 2b/3 adaptive trial is currently ongoing in patients with PBC, with sites in USA and Europe. The USFDA has granted Fast Track status and Orphan Drug Designation for Saroglitazar Mg in PBC. Saroglitazar Mg has also received Orphan Drug Designation in Europe for the treatment of PBC. Once approved, the Orphan drug designation will lead to 10 years of market exclusivity in Europe. Zydus Lifesciences shares traded nearly flat at ₹510.65 with 0.47 per cent gains at the afternoon trade on BSE Friday. (Source: Business Line)

Pandemic Learnings: Innovation Delivered, Partnerships Worked, But More Effort Needed On Equity, Says Pharma Makers



After three years of intensive work and collaborations between big and small pharma and the scientific community to bring out vaccines and medicines to tackle Covid-19, it’s clear that trust and early engagement played a key role, observed industry representatives whose companies were involved in these international partnerships.

However, equitable access still needed work, observed a representative with the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA), summing up the milestones and challenges in supplying Covid-19 vaccines and medicines globally in the shortest possible time. Pointing out that innovations had delivered and partnerships had worked, IFPMA Director-General Thomas Cueni added, that more work needed to be done on equity. Representatives from innovators and licensees shared their experiences on manufacturing products at risk and working on licensing out technology, even as lock-downs made it difficult for officials to travel to different regions to facilitate the smooth transfer of technology.

Participating in the Geneva Pharma Forum organised by the IFPMA were, among others, representatives from MSD, Johnson and Johnson, Gilead, AstraZeneca and Pfizer, alongside collaborators Dr Reddy’s Laboratories, Aspen Pharma and Biovac. Outlining learnings from the pandemic experience, DRL’s representative stressed the need for early engagement to help pave the way for products to low and middle income countries, as well.

Pointing to how partnerships helped, the representative from Gilead (US maker of remdesivir) and one of its licensees Ferozsons Laboratories Ltd (Pakistan) recalled the time when the Delta wave had hit India and some ingredients for the product fell short for another market. Licensees from Pakistan and Egypt stepped up to keep the flow of supplies, they said.

While representatives with innovator companies stressed the need for industry to have a seat at the table during multi-stakeholder discussions, others representing licensees also highlighted the need for regional manufacturing in Africa, for example, that bore the brunt of vaccine inequities during the pandemic, due to protectionist measures,