^{6/15/2020} WikipediA

AstraZeneca

plc^[3] AstraZeneca is British-Swedish а multinational pharmaceutical and biopharmaceutical company with its global headquarters in Cambridge, England.^[4] Its R&D is concentrated in Cambridge, Gaithersburg, Maryland, and Mölndal in Sweden.^[5] AstraZeneca has a portfolio of products for major disease areas cardiovascular. gastrointestinal, including cancer. infection. neuroscience, respiratory and inflammation.^[6]

The company was founded in 1999 through the merger of the Swedish <u>Astra AB</u> and the British <u>Zeneca Group</u>^{[7][8]} (itself formed by the demerger of the pharmaceutical operations of <u>Imperial</u> <u>Chemical Industries</u> in 1993). Since the merger it has been among the world's largest pharmaceutical companies and has made numerous corporate acquisitions, including <u>Cambridge Antibody</u> <u>Technology</u> (in 2006), <u>MedImmune</u> (in 2007), Spirogen (in 2013) and Definiens (by MedImmune in 2014).

AstraZeneca has a primary listing on the London Stock Exchange and is a constituent of the FTSE 100 Index. It has secondary listings on the New York Stock Exchange and the OMX exchange.

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Controversies Seroquel Nexium	Revenue ▲ US\$24.384 bill (2019) ^[1]	lion
Bildman fraud, and faithless servant clawback Study	Operating income ▼ US\$2.924 b (2019) ^[1]	illion
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History		

AstraZeneca - Wikipedia

Astra AB was founded in 1913 in <u>Södertälje</u>, Sweden, by 400 doctors and <u>apothecaries</u>.^[9] In 1993 the British chemicals company <u>ICI</u> demerged its pharmaceuticals businesses and its <u>agrochemicals</u> and specialities businesses, to form <u>Zeneca Group plc</u>.^[10] Finally, in 1999 Astra and Zeneca Group merged to form AstraZeneca plc, with its headquarters in London.^[10] In 1999, AstraZeneca identified as a new location for the company's US base the "Fairfax-plus" site in North Wilmington, Delaware.^[11]

2000-06

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In 2002, its drug Iressa was approved in Japan as monotherapy for non-small cell lung cancer.^[12] On 3 January 2004 Dr Robert Nolan, a former director of AstraZeneca, formed the management team of ZI Medical.^[13]

In 2005, the company acquired KuDOS Pharmaceuticals, a UK biotech company, for £120M^[14] and entered into an anti-cancer collaboration agreement with Astex.^[15] It also announced that it had become a Diamond Member of the Pennsylvania Bio commerce organisation.^[16]

In 2006, following a collaborative relationship begun in 2004, AstraZeneca acquired Cambridge Antibody Technology for £702 million.^[17]

2007–12: The patent cliff and subsequent acquisitions

In February 2007, AstraZeneca agreed to buy Arrow Therapeutics, a company focused on the discovery and development of anti-viral therapies, for US\$150 million.^[18] AstraZeneca's pipeline, and "patent cliff", was the subject of much speculation in April 2007 leading to pipeline-boosting collaboration and acquisition activities.^[19] A few days later AstraZeneca acquired US company <u>MedImmune</u> for about US\$15.2 billion to gain flu vaccines and an anti-viral treatment for infants;^[20] AstraZeneca subsequently consolidated all of its biologics operations into a dedicated biologics division called MedImmune.^[21]

In 2010, AstraZeneca acquired Novexel Corp, an antibiotics discovery company formed in 2004 as a spin-off of the Sanofi-Aventis anti-infectives division. Astra acquired the experimental antibiotic NXL-104 (CEF104) (CAZ-AVI) through this acquisition.^{[22][23]}

In 2011, AstraZeneca acquired Guangdong BeiKang Pharmaceutical Company, a Chinese generics business.^[24]

In February 2012, AstraZeneca and Amgen announced a collaboration on treatments for inflammatory diseases.^[25] Then in April 2012, AstraZeneca acquired Ardea Biosciences, another biotechnology company, for \$1.26 billion.^[26] In June 2012, AstraZeneca and Bristol-Myers Squibb announced a two-stage deal for the joint acquisition of the biotechnology company Amylin Pharmaceuticals.^{[27][28]} It was agreed that Bristol-Myers Squibb would acquire Amylin for \$5.3 billion in cash and the assumption of \$1.7 billion in debt, with AstraZeneca then paying \$3.4 billion in cash to Bristol-Myers Squibb, and Amylin being folded into an existing diabetes joint venture between AstraZeneca and Bristol-Myers Squibb.^[28]

2013 restructuring and beyond

2013

In March 2013 AstraZeneca announced plans for a major corporate restructuring, including the closure of its research and development activities at Alderley Park and Loughborough in the UK and at Lund in Sweden, investment of \$500 million in the construction of a new research and development facility in Cambridge and the concentration of R&D in three locations: Cambridge, Gaithersburg, Maryland (location of MedImmune, where it will work on biotech drugs), and <u>Mölndal</u> (near <u>Gothenburg</u>) in Sweden, for research on traditional chemical drugs.^[5] AstraZeneca also announced that it would move its corporate headquarters from London to Cambridge in 2016.^{[29][30]} That announcement included the announcement that it would cut 1,600 jobs; three days later it announced it would cut an additional 2,300 jobs.^{[31][32]} It also announced that it would focus on three therapeutic areas: Respiratory Inflammation & Autoimmunity, Cardiovascular & Metabolic Disease, and Oncology.^[33] In October 2013, AstraZeneca announced it would acquire biotech oncology company Spirogen for around US\$440 million.^[34]

2014

On 19 May 2014 AstraZeneca rejected a "final offer" from Pfizer of £55 per share, which valued the company at £69.4 billion (US\$117 billion). The companies had been meeting since January 2014. If the takeover had proceeded Pfizer would have become the world's biggest drug maker. The transaction would also have been the biggest foreign takeover of a British company. Many in Britain, including politicians and scientists, had opposed the deal.^[35] In July 2014 the company entered into a deal with Almirall to acquire its subsidiary Almirall Sofotec and its lung treatments including the COPD drug, Eklira. The US\$2.1 billion deal included an allocation of US\$1.2 billion for development in the respiratory franchise, one of AstraZeneca's three target therapeutic areas announced the year before. In August 2014 the company announced it had entered into a three-year collaboration with Mitsubishi Tanabe Pharma on diabetic nephropathy.^[36] In September 2014 the company would join forces with Eli Lilly in developing and commercialising its candidate BACE inhibitor - AZD3292 - used for the treatment of Alzheimer's disease. The deal could yield up to US\$500 million for the company.^[37] In November 2014 the company's biologics R&D operation, MedImmune, agreed to acquire Definiens for more than US\$150 million. The company also began a Phase I/II trial collaboration with Pharmacyclics and Janssen Biotech investigating combination treatments.^[38] Also in November of the same year, the company agreed to sell its lipodystrophy treatment business to Aegerion Pharmaceuticals for more than US\$325 million.^[39] In December, the company received accelerated FDA approval for Olaparib in the

treatment of women with advanced <u>ovarian cancer</u> who have a <u>BRCA</u> genetic mutation. A major criterion governing the drugs approval was, on average, its ability to shrink tumours in patients for 7.9 months.^[40]

2015

In February, the company announced it would acquire the US and Canadian rights to Actavis' branded respiratory drug business for an initial sum of \$600 million.^[41] Later in the same month the company announced it would partner with Orca Pharmaceuticals to develop retinoic acid–related orphan nuclear receptor gamma inhibitors for use in the treatment of a number of autoimmune diseases, which could generate up to \$122.5 million for Orca.^[42] The company also announced their plan to spend \$40 million creating a new subsidiary focused on small molecule anti-infectives – primarily in the research of the gyrase inhibitor, <u>AZD0914</u>, which is currently in Phase II for the treatment of <u>gonorrhea</u>.^[43] The company underwrote twenty out of thirty-two seats of a new Cambridge-Gothenburg service by <u>Sun-Air</u> of Scandinavia.^[44]

In mid-March the company announced it would co commercialise naloxegol along with Daiichi Sankyo in a deal worth up to \$825 million.^[45] Towards the end of April the company announced a number of collaborations worth an estimated \$1.8 billion; firstly, to develop and commercialise MEDI4736, with Celgene, for use against non-Hodgkin's lymphoma, myelodysplastic syndromes, and multiple myeloma with AstraZeneca receiving \$450 million. The second of two-deals is an agreement to study a combination treatment of MEDI4736 and Innate Pharma's Phase II anti-NKG2A antibody IPH2201 for up to \$1.275 billion. The company's Medimmune arm also launched collaborative clinical trials with Juno Therapeutics, investigating combination treatments for cancer.^[46] The trials will assess combinations of MEDI4736 and one of Juno Therapeutics' CD19 directed chimeric antigen receptor Tcell candidates.^[47] In late June the company announced it has entered into a partnership agreement with Eolas Therapeutics on the Eolas Orexin-1 Receptor Antagonist (EORA) program for smoking cessation and other treatments.^[48] In July the company announced it would sell off its rights to Entocort (budesonide) to Tillotts Pharma for \$215 million.^[49] In July 2015, Genzyme announced it would acquire the rare cancer drug Caprelsa (vandetanib) from AstraZeneca for up to \$300 million.^[50] In August, the company announced it has acquired the global rights to develop and commercialise Heptares Therapeutics drug candidate HTL-1071, which focuses on blocking the adenosine A2A receptor, in a deal worth up to \$510 million.^[51] In the same month the company's MedImmune subsidiary acquire exclusive rights to Inovio Pharmaceuticals INO-3112 immunotherapy, currently in Phase I/II, under an agreement which could net more than \$727.5 million for Inovio. INO-3112 targets Human papillomavirus types 16 and 18.^[52] In September, Valeant licensed Brodalumab from the company for up to \$445 million.^{[53][54]} On 6 November it was reported that AstraZeneca acquired ZS Pharma for \$2.7 billion.^[55] In December the company announced its intention to acquire the respiratory portfolio of Takeda Pharmaceutical – namely Alvesco and Omnaris – for \$575 million^[56] A day later, the company announced it had taken a 55% majority stake in Acerta for \$4 billion. As part of the transaction the company will gain commercial rights to Acerta's irreversible oral Bruton's tyrosine kinase inhibitor, acalabrutinib (ACP-196), which is currently in Phase III development for B-cell blood cancers and in Phase I or II clinical trials in solid tumours.^[57] In 2015, it was the eighth-largest drug company in the world based on sales revenue.^[58]

2017

AstraZeneca - Wikipedia

In July 2017, the company's CEO Pascal Soriot said that <u>Brexit</u> would not affect its commitment to its current plans in the United Kingdom. However, it had slowed decision making for new investment projects waiting for post-Brexit regulatory regime to settle down.^[59] In September 2017, the company's chairman Leif Johansson planned in taking "first steps" in moving their research and manufacturing, operations away from the United Kingdom, If there is a hard Brexit.^[60] In 2017, it was the eleventh-largest drug company in the world based on sales and ranked seventh based on R&D investment.^[61] In January EVP Pam Cheng stated that AstraZeneca has ignited startup of duplicate QA testing facility in Sweden and has initiated hiring in Sweden.^[62]

2018

In February 2018, AstraZeneca announced it was spinning off six early-stage experimental drugs into a new biotechnology-focused company, to be known as Viela Bio, valued at US\$250 million.^[63]

2019

In March 2019, AstraZeneca announced it will pay up to \$6.9 billion to work with Daiichi Sankyo Co Ltd on an experimental treatment for breast cancer. AstraZeneca plans to use some of the proceeds of a \$3.5 billion share issue to fund the deal. The deal on the drug known as trastuzumab deruxtecan sent shares in Japan's Daiichi soaring 16%.^[64]

In September 2019, the company announced that it would cease drug production at its German headquarters in Wedel, leading to the loss of 175 jobs by the end of 2021.^{[65][66]}

In October 2019, AstraZeneca announced it would sell the global commercial rights for its drug to treat acid reflux to German pharmaceutical company Cheplapharm Arzneimittel GmbH for as much as \$276 million.^{[67][68]}

2020

In February 2020, AstraZeneca agreed to sublicense its global rights (except Europe, Canada and Israel) to Movantik (naloxegol) to Redhill Biopharma.^[69]

In June 2020, AstraZeneca Plc made a preliminary approach to rival drugmaker <u>Gilead Sciences Inc</u>. about a potential merger, worth almost \$240 billion.^{[70][71]} However, these plans were subsequently dropped because it would have distracted the company from its own pipeline and ongoing COVID-19 vaccine efforts.^[72]

Coronavirus (COVID-19) response

In March 2020, the company announced that it would be donating <u>PPE</u>, including 9 million face masks, to help support various international health organisations mitigating the COVID-19 pandemic.^[73]

In April, the Chief Executive, <u>Pascal Soriot</u>, reported that the company was working with <u>GlaxoSmithKline</u> and the <u>University of Cambridge</u> to develop a new laboratory capable of conducting <u>30,000 Covid-19</u> tests per day.^[74] The company also announced plans for a clinical trial to assess the potential use of Calquence in the treatment of Covid-19.^[75]

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In June 2020, the National Institute of Allergy and Infectious Diseases (NIAID) confirmed that the third phase of testing for potential vaccines developed by Oxford University and AstraZeneca would begin in August 2020.^[76]

In June 2020, AstraZeneca and Emergent BioSolutions signed a \$87 million deal to manufacture doses of the Oxford University's adenovirus-based COVID-19 vaccine specifically for the U.S. market. The deal was part of the President Trump administration's Operation Warp Speed initiative to develop and rapidly scale production of targeted vaccines before the end of 2020.^{[77][78]}

On 13 June 2020, AstraZeneca signed a contract with Europe's Inclusive Vaccines Alliance, a group formed by France, Germany, Italy and the Netherlands, to supply up to 400 million doses of its experimental COVID-19 vaccine to all European Union member states.^{[79][80][81]}

Acquisition history

The following is an illustration of the company's major mergers and acquisitions and historical predecessors:^[82]

AstraZeneca Acquisitions		
raZeneca		
AstraZeneca (Merged 1999)		
Astra AB (Founded 1913)		
└─ Tika (Acq 1939)		
Zeneca (Spun off from Imperial Chemical Industries, 1993)		
– Salick Health Care (Acq 1996)		
L Ishihara Sangyo Kaisha (US fungicide operations, Acq 199	7)	
KuDOS Pharmaceuticals (Acq 2005)		
MedImmune Biologics		
 Cambridge Antibody Technology (Acq 2006) 		
Aptein Inc (Acq 1998)		
MedImmune (Acq 2007)		
Definiens ^[83] (Acq 2014)		
Arrow Therapeutics (Acq 2007)		
Novexel Corp (Acq 2010)		
Guangdong BeiKang Pharmaceutical Company (Acq 2011)		
Ardea Biosciences (Acq 2012)		
Amylin Pharmaceuticals (Acq 2012 jointly with Bristol-Myers Squib))	
Spirogen (Acq 2013)		
Pearl Therapeutics ^[84] (Acq 2013)		
Omthera Pharmaceuticals ^[85] (Acq 2013)		
ZS Pharma (Acq 2015)		

Operations

AstraZeneca develops, manufactures and sells pharmaceutical and biotechnology products to treat disorders in the <u>oncology</u>, <u>respiratory</u>, <u>cardiovascular</u>, <u>neuroscience</u>, <u>gastrointestinal</u>, <u>infection</u> and inflammation areas.

AstraZeneca has its corporate headquarters in Cambridge, United Kingdom, and its main research and development (R&D) centers are in Cambridge (UK), Gaithersburg (Maryland, US), Gothenburg/Mölndal (Sweden) and Warsaw (Poland).^[86]

Products

The following products are found on the AstraZeneca website.^[87] <u>Generic drug</u> names are given in parentheses following the brand name.

– Anesthetics

- Carbocaine (mepivacaine)
- Citanest (prilocaine)
- Diprivan (propofol)
- EMLA (lidocaine/prilocaine)
- Marcaine/Sensorcaine (<u>bupivacaine</u>)
- Naropin (ropivacaine)
- Xylocaine (lidocaine)
- Xyloproct (lidocaine/hydrocortisone)
- Cardiovascular
- Atacand (candesartan cilexetil)
- Betaloc (metoprolol tartrate)
- Brilinta/Brilique/Possia (ticagrelor)
- Crestor (rosuvastatin; 2003 launch)
- Exanta/Exarta (ximelagatran; 2004 launch; not approved in the US, now withdrawn)
- Epanova (omega-3-carboxylic acids)
- Imdur (isosorbide mononitrate)
- Inderal (propranolol)
- Lexxel (enalapril/felodipine)
- Logimax (felodipine/metoprolol)
- Nif-Ten (nifedipine/atenolol)
- Plendil (felodipine)
- Ramace (ramipril)
- Seloken XL/Toprol-XL/Betaloc ZOC (metoprolol succinate extended-release)
- Tenoretic (atenolol/chlortalidone)
- Tenormin (atenolol)
- Unimax (felodipine/ramipril)
- Zestoretic (lisinopril/hydrochlorothiazide)
- Zestril (lisinopril)
- Diabetes
 - Bydureon (exenatide extended-release)



The AstraZeneca R&D facility in Mölndal, Sweden

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- Byetta (exenatide)
- Farxiga/Forxiga (dapagliflozin)
- Kombiglyze XR/Komboglyze (saxagliptin/metformin extended-release)
- Onglyza (saxagliptin)
- Symlin (pramlintide)
- Xigduo/Xigduo XR (dapagliflozin/metformin)
- Gastrointestinal
- Entocort (budesonide)
- Losec/Prilosec (omeprazole, Non-prescription variant sold under license by Procter and Gamble [Prilosec], and Bayer [Losec])
- Nexium (esomeprazole-(S)-stereoisomer of omeprazole, non-prescription variant sold under license by Pfizer)
- Vimovo (naproxen/esomeprazole magnesium delayed release)
- Infectious diseases
 - Apatef/Cefotan (cefotetan)
 - Avloclor (chloroquine)
 - Cubicin (daptomycin)
 - Foscavir (foscarnet)
 - Lexinor (norfloxacin)
 - Merrem/Meronem (meropenem)
 - Paludrine (proguanil)
 - Savarine (proguanil/chloroquine)
 - Synagis (palivizumab)
 - Fluenz/FluMist (Quadrivalent Live Attenuated Influenza Vaccine)
- Neuroscience
 - Heminevrin (clomethiazole)
 - Mysoline (primidone; handed over to Acorus Therapeutics Ltd. in July 2004)
 - Seroquel (quetiapine)
 - Seroquel XR/Seroquel Prolong (quetiapine extended-release)
 - Vivalan (viloxazine)
 - Zomig (zolmitriptan)
- Oncology
 - Arimidex (anastrozole)
 - Caprelsa (vandetanib)
 - Casodex/Cosudex (bicalutamide)
 - Imfinzi (durvalumab)
 - Faslodex (fulvestrant)
 - Iressa (gefitinib)
 - Lynparza (<u>olaparib</u>)

- Nolvadex/Istubal/Valodex (tamoxifen)
- Tagrisso (osimertinib)
- Tomudex (raltitrexed)
- Zoladex (goserelin implant)
- Respiratory and inflammatory diseases
- Accolate (zafirlukast)
- Bambec (bambuterol)
- Bricanyl (terbutaline)
- Daliresp (roflumilast)
- Fasenra (benralizumab)
- Oxis (formoterol)
- Pulmicort/Rhinocort (budesonide)
- Symbicort (budesonide/formoterol)

Orphan drugs

In April 2015, AstraZeneca's drug tremelimumab was approved as an <u>orphan drug</u> for the treatment of <u>mesothelioma</u> in the United States.^[88] In February 2016, AstraZeneca announced that a <u>clinical trial</u> of tremelimumab as a treatment for mesothelioma failed to meet its primary endpoint.^[89]

Senior management

As of 2008, David Brennan was paid \$1,574,144 for his role as chief executive officer.^[90]

On 26 April 2012 it was announced that Brennan was to retire early in the June of that year^[91] In August 2012, Pascal Soriot was named CEO of AstraZeneca.^[92]

It was also announced that Leif Johansson would succeed Louis Schweitzer as Non-Executive chairman on 1 June 2012, three months earlier than previously announced, and would become Chairman of the Nomination and Governance Committee after (the 2012) Annual General Meeting.^[91]

Controversies

Seroquel

In April 2010 AstraZeneca settled a *qui tam* lawsuit brought by <u>Stefan P. Kruszewski</u> for \$520 million to settle allegations that the company defrauded <u>Medicare</u>, <u>Medicaid</u>, and other government-funded health care programs in connection with its marketing and promotional practices for the blockbuster atypical antipsychotic, <u>Seroquel</u>. According to the settlement agreement, AstraZeneca targeted its illegal marketing of the anti-psychotic Seroquel towards doctors who do not typically treat schizophrenia or bipolar disorder, such as physicians who treat the elderly, primary care physicians, pediatric and adolescent physicians, and in long-term care facilities and prisons.^[93]

In March 2011, AstraZeneca settled a <u>lawsuit</u> in the United States totalling \$68.5 million to be divided up to 38 states.^[94]

Nexium

The company's most commercially successful medication is <u>esomeprazole</u> (Nexium). The primary uses are treatment of gastroesophageal reflux disease, treatment and maintenance of <u>erosive esophagitis</u>, treatment of <u>duodenal ulcers</u> caused by <u>Helicobacter pylori</u>, prevention of <u>gastric ulcers</u> in those on chronic <u>NSAID</u> therapy, and treatment of gastrointestinal ulcers associated with <u>Crohn's disease</u>. When it is manufactured the result is a mixture of two <u>mirror-imaged molecules</u>, R and S. Two years before the omeprazole patent expired, AstraZeneca patented S-omeprazole in pure form, pointing out that since some people metabolise R-omeprazole slowly, pure S-omeprazole treatment would give higher dose efficiency and less variation between individuals.^[95] In March 2001, the company began to market Nexium, as it would a brand new drug.^[96]

The (R)-enantiomer of omeprazole is metabolized exclusively by the enzyme CYP2C19, which is expressed in very low amounts by 3% of the population. Treated with a normal dose of the enantiomeric mixture, these persons will experience blood levels five-times higher than those with normal CYP2C19 production. In contrast, esomeprazole is metabolized by both CYP2C19 and CYP3A4, providing less-variable drug exposure.^[97] While omeprazole is approved only at doses of up to 20 mg for the treatment of gastroesophageal reflux,^[98] esomeprazole is approved for doses up to 40 mg.^[99]

In 2007, <u>Marcia Angell</u>, former <u>editor-in-chief</u> of the <u>New England Journal of Medicine</u> and a lecturer in <u>social medicine</u> at the <u>Harvard Medical School</u>, said in <u>Stern</u>, a German-language weekly newsmagazine, that AstraZeneca's scientists had misrepresented their research on the drug's efficiency, saying "Instead of using presumably comparable doses [of each drug], the company's scientists used Nexium in higher dosages. They compared 20 and 40 mg Nexium with 20 mg <u>Prilosec</u>. With the cards having been marked in that way, Nexium looked like an improvement – which however was only small and shown in only two of the three studies."^[100]

Bildman fraud, and faithless servant clawback

On 4 February 1998, Astra USA sued Lars Bildman, its former president and chief executive officer, seeking \$15 million for defrauding the company.^[101] The sum included \$2.3 million in company funds he allegedly used to fix up three of his homes, plus money the company paid as the result of the EEOC investigation. Astra's lawsuit alleged Bildman sexually harassed and intimidated employees, used company funds for yachts and prostitutes, destroyed documents and records, and concocted "tales of conspiracy involving ex-KGB agents and competitors. This was in a last-ditch effort to distract attention from the real wrongdoer, Bildman himself." Bildman had already pleaded guilty in US District Court for failing to report more than \$1 million in income on his tax returns; in addition, several female coworkers filed personal sexual-harassment lawsuits.^[102]

In *Astra USA v. Bildman*, 914 N.E.2d 36 (Mass. 2009), applying New York's <u>faithless servant</u> doctrine, the court held that a company's employee who had engaged in financial misdeeds and sexual harassment must "forfeit all of his salary and bonuses for the period of disloyalty."^[103] The court held that this was the case even if the employee "otherwise performed valuable services," and that the employee was not entitled to recover restitution for the value of those other services.^{[103][104]} The decision attracted a good deal of attention by legal commentators.^[105]

Study

AstraZeneca - Wikipedia

In 2004, <u>University of Minnesota</u> research participant <u>Dan Markingson committed suicide</u> while enrolled in an industry-sponsored pharmaceutical trial comparing three FDA-approved atypical antipsychotics: <u>Seroquel (quetiapine)</u>, <u>Zyprexa (olanzapine)</u>, and <u>Risperdal (risperidone)</u>. University of Minnesota Professor of Bioethics <u>Carl Elliott</u> noted that Markingson was enrolled in the study against the wishes of his mother, Mary Weiss, and that he was forced to choose between enrolling in the study or being involuntarily committed to a state mental institution.^[106] A 2005 FDA investigation cleared the university. Nonetheless, controversy around the case has continued. A <u>Mother Jones</u> article^[106] resulted in a group of university faculty members sending a public letter to the university Board of Regents urging an external investigation into Markingson's death.^[107]

Transfer mispricing

In 2010 AstraZeneca agreed to pay £505 million to settle a UK tax dispute related to transfer mispricing.^[108]

Doping in cycling

On 27 July 2015, <u>Fabio Taborre</u> (<u>Androni-Sidermec</u>) returned a positive doping test result for the banned blood-booster <u>FG-4592</u> in an out-of-competition control on 16 June 2015. FG-4592 (<u>Roxadustat</u>) is in phase 3 clinical trials and has not yet been commercialised. The drug was developed jointly by FibroGen and AstraZeneca. Unlike <u>Erythropoietin</u> (EPO), which directly stimulates the production of red blood cells, FG-4592 is taken orally, and stimulates natural production of EPO in a manner similar to altitude training.^[109]

See also

- Pharmaceutical industry in the United Kingdom
- List of pharmaceutical companies

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