For reprint orders, please contact: reprints@future-science.com

Industry update covering August 2018

Louise Rosenmayr-Templeton^{*,1}

¹Tower Pharma Consulting, Bellakreuzstrasse 21, Berndorf 2560, Austria

*Author for correspondence: louise.templeton@towerpharmacon.com

First draft submitted: 17 September 2018; Accepted for publication: 8 October 2018; Published online: 16 November 2018

Keywords: acquisitions • clinical trials • collaborations • competitive intelligence • intellectual property • regulatory approvals

This article is a round-up of industry news for the month of August 2018 mainly based on information from company press releases and websites. This month's biggest news from a therapeutic delivery perspective was the US FDA and the EU Commission granting regulatory approval for the RNAi product, Onpattro™ (patisiran) lipid complex injection from Alnylam Pharmaceuticals. Onpattro is indicated for the treatment of patients with polyneuropathy due to hereditary transthyretin-mediated (hATTR) amyloidosis. Its licensing is a first for a RNAi approach in both the USA and Europe. In addition, in the USA Onpattro is the first specific medicine for the treatment of this debilitating condition caused by a rare, inherited, genetic defect. It is hard to believe that just a few years ago, the formulation and delivery of these types of compound represented a major obstacle to progress in the field of silencing RNA and that having overcome this, the first product will soon be on the market in the USA and Europe.

Mergers & acquisitions

Emalex purchases Psyadon

On 14 August 2018 Emalex Biosciences (IL, USA), a Paragon Biosciences LLC portfolio company, made public, that it had acquired Psyadon Pharmaceuticals (MD, USA) and the rights to develop, register and market ecopipam, Psyadon's investigational drug, which has potential for the treatment of pediatric Tourette syndrome in children less than 16 years of age [1,2].

Tourette syndrome is a condition characterized by motor and vocal tics which becomes evident in childhood. It is estimated to affect 1 in 160 children between 5 and 17 years in the USA alone [3] and often occurs alongside other conditions such as attention-deficit/hyperactivity disorder and obsessive compulsive disorder. There is no cure for the condition and its treatment is associated with a number of unmet needs.

Ecopipam is a potent, selective dopamine D1 receptor antagonist which has been granted orphan status in the USA. Its development is based on evidence that the tics associated with Tourette's are caused by super-sensitivity of the D1 receptors. This theory was supported by initial Phase IIb study results in 40 pediatric patients which showed that ecopipam had the potential to reduce symptom severity based on a statistically significant reduction in the mean Yale Global Tic Severity Score Total Tic Score, a validated method for measuring medication effectiveness in Tourette syndrome [4]. The clinical program for ecopipam set in motion by Psyadon will continue at Emalex with the Illinois firm planning a larger Phase II trial in 2019 involving 150 children with Tourette's.

Novo Nordisk acquires Ziylo to support next-generation insulin development

On 17 August 2018, it was announced that Novo Nordisk (Bagsværd, Denmark) had acquired Ziylo Ltd. (Bristol, UK), a Bristol University spin-out company developing glucose-binding molecules for therapeutic and diagnostic uses [5]. The deal, which is structured in stages, potentially could be worth in excess of \$800 million and enables Novo Nordisk to exploit Ziylo's platform technology for the development of glucose-responsive insulins. Such biomimetic therapeutics could potentially negate the incidence of hypoglycemia in diabetic patients and improve metabolic control with a subsequent reduction in secondary complications associated with long-term diabetes treatment such as neuropathy and kidney damage.

newlands
press

Ziyo's technology is based on the work of the research group of Anthony Davis, Professor of Supramolecular Chemistry at the University of Bristol [6]. It involves synthetic, stable molecules which bind glucose in a highly selective manner in biological fluids such as blood. Novo Nordisk hopes to exploit this technology in combination with their extensive in-house insulin engineering expertise to produce the first insulin able to adapt to glucose levels in the blood.

As a result of the purchase, a new company, Carbometrics Ltd. (Bristol, UK), has been formed which will take over some of Ziyo's previous research activities. It has signed an agreement to collaborate with Novo Nordisk on the further development and optimization of the glucose-binding molecules for use in glucose-responsive insulins. Carbometrics has also in-licensed the rights for nontherapeutic applications of the technology and will focus on its use in continuous insulin monitoring.

Emergent takes over Adapt & its antinarcotic abuse spray

Emergent BioSolutions Inc. (MD, USA) announced on 28 August 2018 that it had agreed to take over Adapt Pharma Inc. (PA, USA) including its US and Canada approved product, Narcan® (naloxone HCl) Nasal Spray for the emergency treatment of opioid overdose and suspected overdose [7]. Subject to certain adjustments under the agreement, the deal is projected to be worth up to \$735 million and includes an upfront payment of \$575 million cash and \$60 million Emergent shares and up to \$100 million in cash for potential sales-based milestones until the end of 2022.

Narcan is the only naloxone product licensed as a nasal spray and was approved by the FDA in 2015 [8]. In addition, Adapt has a pipeline of four products in development for opioid overdose and one for opioid addiction [9], which also form part of the agreement. As a result of the purchase, Adapt Pharma will become part of Emergent's device business.

The acquisition fits with Emergent's strategy of building a portfolio of products for the treatment of public health threats and enables the company to broaden its drug offering and pipeline in opioid abuse and overdose, a key area of public health concern which is estimated to have claimed the lives of 42,000 people in 2016 in the US alone. Emergent anticipates that the incremental revenue contribution in 2019 from the purchase of Adapt to be around \$200–220 million.

This is the second major deal for Emergent this month with its purchase of the PaxVax Corporation (CA, USA), a company developing cholera and typhoid vaccines, being announced on 9 August 2018 [10]. The company hopes that both acquisitions will lead to it achieving its goal of \$1 billion in revenue in 2020.

Collaborations

Consortium to develop first-in-class gene therapy for cystic fibrosis

On 6 August 2018, it was made public that the UK Cystic Fibrosis Gene Therapy Consortium (CFGTC) – consisting of Imperial College (London, UK) and the Universities of Oxford and Edinburgh will collaborate with Boehringer Ingelheim (Ingelheim am Rhein, Germany) and Oxford BioMedica plc (Oxford, UK) together with Imperial Innovations, the technology transfer office of Imperial College, to develop a novel, long-term gene therapy for cystic fibrosis [11,12]. The CFGTC has extensive research experience with both nonviral vectors and viral vectors for the transfection of lung tissue with the transmembrane conductance regulator gene [13]. It is mutations in this gene that are responsible for cystic fibrosis, a congenital disease which is thought to affect around 70,000 people globally, and for which there is no effective cure and current treatments only slow progress of the disease.

The collaboration will focus on developing an inhalation gene therapy for cystic fibrosis using a nonreplicating lentivirus vector which has been shown to result in high *CFTR* transfection rates and can be potentially used for repeat therapy. As part of the deal, the CFGTC is responsible for the preclinical studies to support a first-in-man trial. With respect to the other partners, Oxford BioMedica brings its lentivirus vector manufacturing capabilities to the collaboration [14], Boehringer Ingelheim, its expertise in the research and development of medicines for respiratory disease and Imperial Innovations, technology transfer support. The agreement is a part of Boehringer Ingelheim's Research Beyond Borders strategic program. In addition, the Pharma giant has signed option and license agreements with Imperial Innovations and Oxford BioMedica for the viral vector and the production technology. This option includes the exclusive worldwide rights to develop, manufacture, register and commercialize the cystic fibrosis therapy.

Bayer to collaborate with Haplogen

On 14 August 2018, Bayer AG (Leverkusen, Germany) and Haplogen GmbH (Vienna, Austria) issued a press statement that they had agreed to collaborate on the discovery and development of compounds for the treatment of chronic obstructive pulmonary disease [15]. Haplogen's research expertise is focused on the discovery and development of drug candidates for the treatment and prophylaxis of infection by viruses, plus other diseases [16]. Their functional genomics platform, based on haploid genetics in human cell lines, enables the identification of novel host cell factors that are essential for viral infection and which have potential as targets for drug development. The company, which is a spin-out of the Research Center for Molecular Medicine of the Austrian Academy of Sciences (Vienna, Austria), has a long-standing partnership with Evotec AG (Hamburg, Germany) which has provided medicinal chemistry, drug development expertise and funding to the Austrian company since 2012. It already has a lead candidate for the prevention of rhinoviral infections in chronic obstructive pulmonary disease patients in early development with the start of the clinical program planned for 2019.

Under the terms of the collaboration, both Haplogen and Bayer will evaluate the new drug candidates and jointly own the generated results. Bayer is responsible for the further development and commercialization of these compounds and will receive an exclusive global license to all results, including those developed through the work between Haplogen and Evotec. No financial details of this multiyear deal were released. However, the agreement foresees Haplogen receiving an upfront payment, research funding and potentially preclinical, clinical and sales milestones plus tiered royalties.

RXi Pharmaceuticals & Karolinska Institutet to collaborate on sd-rxRNA compounds

RXi Pharmaceuticals Corporation (MA, USA) and the Karolinska Institutet (Stockholm, Sweden) signed a research agreement on 15 August 2018 to investigate RXi's sd-rxRNA[®] compounds' ability to impact on T cell and NK cell differentiation and/or in the immune cell tumor-induced stress response [17]. RXi's sd-rxRNA technology results in proprietary hybrid oligonucleotide compounds [18]. These modified molecules have a single-stranded phosphorothioate region, a short duplex sequence and a number of modifications that protect them against nuclease activity and increase their lipophilicity to facilitate efficient cellular uptake. The company already has several of its compounds in clinical trials for topical and ocular indications such as hypertrophic scarring and retinal scarring.

For immune-oncology indications the company is investigating the use of sd-rxRNA to improve adoptive cell therapy (ACT) and this is the goal of its collaboration with the Karolinska Institutet. ACT involves T lymphocytes isolated from specific patients or obtained from allogeneic immune cell banks which are then expanded *ex vivo* and, in some cases, treated to express tumor-binding receptors, before being re-administered to the patient. This technique has resulted in positive results in previously considered untreatable cancers. RXi hopes to increase the efficacy of adoptive cell therapy further by using its sd-rxRNA compounds to switch off the expression of immunosuppressive receptors or proteins in the therapeutic immune cells and, hence, make the development of tumor resistance less likely.

RXi and the Karolinska Institutet have already collaborated in this area and a recent paper from Rolf Kiessling's group at the Institutet showed that an sd-rxRNA targeting programmed cell death protein 1 was effective in increasing tumor-infiltrating lymphocytes activity against melanoma cells *in vitro* and that the compound could be easily loaded into tumor-infiltrating lymphocytes *ex vivo* using clinically relevant protocols [19].

Regulatory approvals

Galafold[™] adds USA to existing marketing authorizations

Amicus Therapeutics Inc. (NJ, USA) announced on 10 August 2018 that it had gained FDA approval for its Galafold[™] (migalastat) oral capsule product [20,21] under the regulatory authority's accelerated approval program. The approved indication is the treatment of adults with a confirmed diagnosis of Fabry disease and an amenable galactosidase α gene (*GLA*) variant based on *in vitro* assay data [22].

Fabry disease is caused by defects in the *GLA* gene which carries the genetic information for the manufacture of the enzyme, α -galactosidase A, which is responsible for the degradation of α -galactosidase A in lysosomes [23]. The absence or malfunctioning of this enzyme results in the build-up of globotriaosylceramide in cells, with those of the skin capillaries, kidney, heart and nervous system being particularly affected. It results in a variety of symptoms including burning and tingling in the hands and feet, angiokeratoma (clusters of red spots on the skin), hypohidrosis and corneal opacity and can lead to kidney damage, cardiovascular disease and premature death. It is

a rare, inherited condition affecting approximately 3000 people in the USA. As it is carried on the X-chromosome, it affects males with mutated *GLA* genes more than females who may have a milder version of the condition.

Galafold can be used to treat the estimated 35–50% of diagnosed patients who have one of 348 amenable *GLA* variants based on *in vitro* data from Human Embryonic Kidney (HEK-293) cell lines transfected with specific *GLA* variants producing α -Gal A mutants [20]. Migalastat's mechanism of action relies on these misfolded and less stable proteins still having some enzymatic activity. It binds reversibly to the proteins to increase their stability, enabling their transportation from the endoplasmic reticulum into the lysosome, where the complex dissociates enabling the enzyme to catalyze the breakdown of globotriaosylceramide and globotriaosylsphingosine.

Galafold is formulated as a capsule containing 123 mg migalastat with a dose of one capsule at the same time every other day with fasting 2 h before and 2 h after administration [22]. Approval was based on the results of a placebo-controlled Phase III study in 45 treatment-naïve patients which showed that administration of migalastat resulted in a reduction in levels of kidney interstitial capillary cell globotriaosylceramide substrate. As Galafold was approved via the FDA's accelerated approval pathway; the product's continuing approval is contingent on positive results in a confirmatory clinical study.

Galafold is already approved in the EU, Japan, Canada and a number of other countries.

FDA & EU give marketing approval for first RNAi therapeutic

On 10 August 2018, following a priority review, the FDA granted regulatory approval to Onpattro™ (patisiran) lipid complex injection, an RNAi product from Alnylam Pharmaceuticals Inc. (MA, USA) for the treatment of polyneuropathy due to hATTR amyloidosis in adults [24]. Similarly on 30 August 2018, the product received a marketing license in Europe for Stage 1 and 2 neuropathy in hATTR adult patients [25], following a positive opinion from the EMA's Committee of Human Medicinal Products in July 2018 [26]. The granting of both licenses is a first for an RNAi therapeutic but Onpattro is also the only specific medicinal treatment for this rare indication to gain approval in the USA.

hATTR amyloidosis is caused by mutations in the *TTR* gene which encodes for the TTR protein which functions as a carrier for Vitamin A in the body. These mutations lead to the progressive accumulation of amyloid in the body which subsequently causes damage to peripheral nerves and cardiac tissue. This damage results in intractable peripheral sensory neuropathy, autonomic neuropathy and/or cardiomyopathy, disability and eventually morbidity. The median survival rate for patients after diagnosis is 4.7 years.

Patisiran is a small double-stranded interfering RNA. It functions to reduce or switch off synthesis of the TTR protein in the liver by binding to the mRNA involved in both wild-type and mutant protein translation causing its degradation. As a result, levels of both the native protein and the damaging amyloid are diminished. It is formulated as a lipid complex 10 mg in 5 ml (2 mg/ml) injection and dosed at 0.3 mg/kg every 3 weeks by intravenous infusion to patients less than 100 kg following pretreatment with a corticosteroid, paracetamol and antihistamines (both H1 and H2 receptor blockers). The dose for patients heavier than 100 kg is 30 mg. The main side-effects seen in clinical trials are infusion-related reactions and upper respiratory tract infections. Unsurprisingly given the TTR protein's function, Vitamin A levels in the serum are reduced by therapy with Onpattro and supplementation is recommended [27].

Approval was based on the results of the placebo-controlled Phase III APOLLO study. It involved hATTR amyloidosis patients in 19 countries with a diverse range of *TTR* gene mutations (39 in total) who were treated with either Onpattro or placebo every 3 weeks for 18 months.

The results showed that patisiran therapy met the primary endpoint for the study which was improvement in the modified Neuropathy Impairment Score +7 compared with placebo. This score assesses motor strength, reflexes, sensation, nerve conduction and postural blood pressure. Treatment also showed positive benefits with respect to other measures of polyneuropathy including life quality, mobility and level of activity.

Clinical trials

Positive top-line Phase III results for rilpivirine & cabotegravir combination in HIV

On 15 August 2018, Janssen Sciences Ireland UC (Dublin, Ireland), one of the Janssen Pharmaceutical Companies of Johnson and Johnson (NJ, USA), made public initial positive results from a Phase III trial to investigate the safety and efficacy of a prolonged release injection combination of two drugs, rilpivirine and cabotegravir, for the treatment of HIV-1 infection [28].

Rilpivirine is a non-nucleoside reverse transcriptase inhibitor, originally developed by Janssen as an oral tablet and already approved for the treatment of HIV in combination with other antiretrovirals. It is currently being developed by Janssen Ireland as a nanoparticle suspension for intramuscular injection (Rilpivirine LA) but this formulation has not yet been approved by any regulatory authority.

Cabotegravir is being developed by ViiV Healthcare (Brentford, UK) for the treatment and prevention of HIV. It is an integrase inhibitor and is being formulated both as a controlled release nanosuspension formulation for intramuscular injection and a once-daily oral tablet. It is foreseen that the tablet would be used as an induction to therapy prior to administration of the long-acting injection.

The objective of the Antiretroviral Therapy as Long Acting Suppression study was to investigate whether HIV-1-infected adults with viral suppression currently receiving two nucleoside reverse transcriptase inhibitors daily plus a third agent (current standard of care) retained their viral-suppression status when their medication was changed to a two-drug prolonged release regimen of rilpivirine and cabotegravir. The noninferiority study involved 618 HIV positive patients (both male and female) at sites worldwide and had an open-label, active-controlled, parallel-group design. The study showed that monthly injections of long-acting rilpivirine and cabotegravir gave similar results to the oral regimen, and at week 48 met the primary study endpoint for non-inferiority which was the proportion of patients having plasma HIV-1 RNA levels ≥ 50 copies per milliliter using the FDA Snapshot algorithm. The top-line results from the Antiretroviral Therapy as Long Acting Suppression study are good news for people living with the HIV as the injection regimen if approved, would expand their treatment options and reduce dosing from daily to 12-times per year. The results of a similar study, FLAIR, which compares the daily three drug tablet regimen with the two drug injection therapy in treatment-naïve HIV-1 positive individuals, are also expected in 2018.

Positive Phase II data for Fasinumab in chronic osteoarthritis pain

On 16 August Regeneron Pharmaceuticals, Inc. (NY, USA) and Teva Pharmaceutical Industries Ltd. (Jerusalem, Israel) released positive initial data from a Phase III clinical trial to investigate the safety and efficacy of their investigational candidate, fasinumab, in the treatment of chronic osteoarthritic pain in the hip and knee [29]. Fasinumab is a human antibody against NGF, a regulatory molecule involved in pain signaling whose levels are elevated in the synovial fluid of osteoarthritis patients. It was discovered by Regeneron using the firm's proprietary VelocImmune® technology [30]. This technology is a critical part of Regeneron's VelociSuite® platform and results in the production of fully humanized antibodies to identified therapeutic targets. The VelociSuite platform includes technology for the replacement of genes encoding for mouse antibody variable regions with those encoding for human variable regions in mice embryonic stem cells. The modified stem cells are injected into mouse embryos at a very early stage so that when the embryos are implanted into a surrogate mother, the progeny mice produce only antibodies with human variable regions and a mouse constant region. Injection of the target protein into these genetically modified mice results in the production of antibodies to the target protein. Regeneron then identifies and isolates the cells producing antibody with high specificity to the target. The genetic coding from these cells is then transferred into mammalian cell lines capable of producing fully humanized antibodies in quantities sufficient for early development through clinical to commercial scale.

The 16-week clinical trial investigated fasinumab administered subcutaneously 1 mg every 4 or every 8 weeks against placebo in over 600 patients, 85% of whom had osteoarthritis in the knee. It is a substudy of a longer 52-week of active treatment study to determine the safety and tolerability of fasinumab, in patients suffering pain due to radiographically confirmed osteoarthritis of the knee or hip. The primary efficacy results after 16 weeks of therapy showed that fasinumab met both primary endpoints with patients treated with active reporting significantly less pain using the Western Ontario and McMaster Universities Osteoarthritis Index pain subscale score (scale 0–10) and an increase in functional ability from baseline compared with placebo. The drug was found to be well tolerated in general with similar side-effects being reported as in previous clinical studies of fasinumab. The trial now continues with the participants receiving a further 36 weeks of treatment, followed by a further 20 weeks of safety assessment.

Regeneron and Teva have planned three further studies as part of their development program for fasinumab which are at the enrollment stage, one investigating long-term safety and two comparing their investigational candidate to treatment with standard pain therapy. The two companies are developing fasinumab for global registration and commercialization, with the exception of Japan and some other Asian counties where this right is exclusively held by the Mitsubishi Tanabe Pharma Corporation (Osaka, Japan) [29].

Disappointing Phase III results for AstraZeneca's anifrolumab in lupus

On the last day of the month, AstraZeneca (Cambridge, UK) and MedImmune (Cambridge, UK), its biologics research and development division, made public that its investigational drug candidate, anifrolumab, which is being developed for the treatment of adults with moderate-to-severe systemic lupus erythematosus (SLE), had disappointed in the first of two Phase III clinical trials [31]. Anifrolumab, which is a fully human monoclonal antibody, targets the subunit 1 of the type I interferon receptor, thus, switching off the activity of all type I interferons including IFN- α , IFN- β and IFN- ω . Elevated levels of type I interferon gene expression have been demonstrated in peripheral blood and target tissues of 60–80% of SLE patients and the extent of elevation has been shown to correlate with disease activity [32]. It was therefore hoped that anifrolumab would be effective in this systemic, autoimmune, inflammatory disease which is associated with symptoms such as pain, rashes, joint swelling and, more seriously, organ damage and increased morbidity.

The first 'Treatment of Uncontrolled Lupus via the Interferon Pathway' (Tulip-1 trial) was a double-blinded, 52-week, placebo-controlled study involving 460 SLE patients with a primary endpoint of a statistically significant reduction in disease activity as measured by the SLE Responder Index 4 (SRI4) at 12 months. Neither of the two doses of anifrolumab (150 mg or 300 mg every 4 weeks by intravenous infusion) resulted in the endpoint being achieved. More detailed results of trial will be released later [31].

Patents

Patent granted for cannabinoid formulations

It was good news for Teewinot Life Sciences Corporation (FL, USA) and its Irish subsidiary, Teewinot Technologies, Ltd (Dublin, Ireland) on 21 August 2018 when the United States Patent and Trademark Office (VA, USA) granted a patent, U.S. Patent No. 10,052,303, for its liquid liposomal and micelle formulations of one or more cannabinoids or cannabinoid analogs [33,34]. The company, which has patents in several countries for the biocatalytic production of cannabinoids at industrial scale [35], now has three US patents for its formulations. The formulations have been developed for pharmaceutical and nutraceutical applications and are designed principally to overcome the poor oral bioavailability of cannabinoids due to their poor water solubility.

Financial & competing interests disclosure

The author has no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

References

1. Emalex Biosciences acquires Psyadon Pharmaceuticals to develop novel treatment for pediatric Tourette syndrome. www.prnewswire.com/news-releases/emalex-biosciences-acquires-psyadon-pharmaceuticals-to-develop-novel-treatment-for-pediatric-tourette-syndrome-300696350.html
2. Emalex Biosciences website. <https://emalxbiosciences.com/>
3. The Tourette Association of America. www.tourette.org/
4. Psyadon announces positive results from Phase 2b clinical study of Ecopipam for the treatment of Tourette's syndrome in children. www.psyadonrx.com/images/Psyadon_Tourette_s_Phase_2b_results_FINAL.pdf
5. Novo Nordisk acquires Ziylo Ltd to accelerate its development of glucose responsive insulins. www.novonordisk.com/media/news-details.2211063.html
6. University spin-out Ziylo acquired by global healthcare company in \$800 m deal which could transform the treatment of diabetes. www.bristol.ac.uk/news/2018/august/ziylo-deal.html
7. Emergent BioSolutions joins effort to combat national public health threat from opioid overdose through acquisition of Adapt Pharma and its flagship product NARCAN® (naloxone HCl) nasal spray. <http://phx.corporate-ir.net/phoenix.zhtml?c=202582&cat=news&id=2365165&p=RssLanding>
8. Entry for Narcan® on Drugs@FDA. www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=208411
9. Adapt Pharma website. <http://adaptpharma.com/>
10. Emergent BioSolutions to acquire PaxVax from Cerberus Capital Management. <https://paxvax.com/media/press-releases/>

11. Boehringer Ingelheim, the UK Cystic Fibrosis Gene Therapy Consortium, Imperial Innovations and Oxford BioMedica announce new partnership to develop first-in-class gene therapy for cystic fibrosis.
www.boehringer-ingelheim.com/press-release/new-partnership-develop-gene-therapy-cystic-fibrosis
12. Oxford BioMedica, UK Cystic Fibrosis Gene Therapy Consortium, Boehringer Ingelheim and Imperial Innovations form partnership to develop a novel gene therapy treatment for cystic fibrosis.
www.oxfordbiomedica.co.uk/news-media/press-release/oxford-biomedica-uk-cystic-fibrosis-gene-therapy-consortium-boehringer
13. UK Cystic Fibrosis Gene Therapy Consortium website. www.cfgenetherapy.org.uk/
14. Oxford BioMedica website. www.oxfordbiomedica.co.uk/
15. Bayer and Haplogen collaborate to develop new treatments against pulmonary diseases. <https://media.bayer.com/baynews/baynews.nsf/id/Bayer-and-Haplogen-collaborate-to-develop-new-treatments-against-pulmonary-diseases>
16. Halogen website. www.haplogen.com/
17. RXi Pharmaceuticals and Karolinska Institute: enter into collaboration to develop sd-rxRNA compounds to improve functionality and persistence of T cells and NK cells for the advancement of immuno-oncology therapeutics for solid tumors.
<http://investors.rxipharma.com/news-releases/news-release-details/rxi-pharmaceuticals-and-karolinska-institutet-enter>
18. RXi Pharmaceuticals website. www.rxipharma.com/
19. Ligtenberg MA, Pico de Coaña Y, Shmushkovich T *et al*. Self-delivering RNAi targeting PD-1 improves tumor-specific T cell functionality for adoptive cell therapy of malignant melanoma. *Mol. Ther.* 26(6), 1482–1493 (2018).
20. FDA approves new treatment for a rare genetic disorder, Fabry disease.
www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm616598.html
21. FDA approves Galafold™ (migalastat) for the treatment of certain adult patients with Fabry disease.
<http://ir.amicusrx.com/news-releases/news-release-details/fda-approves-galafoldtm-migalastat-treatment-certain-adult>
22. Entry for Galafold™ on Drugs@FDA. www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=2.08623
23. The Fabry International Network website. www.fabrynetwork.org
24. Alnylam announces first-ever fda approval of an RNAi Therapeutic, ONPATTRO™ (patisiran) for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.
<http://investors.alnylam.com/news-releases/news-release-details/alnylam-announces-first-ever-fda-approval-rnai-therapeutic>
25. Alnylam Receives Approval of ONPATTRO™ (patisiran) in Europe.
<http://investors.alnylam.com/news-releases/news-release-details/alnylam-receives-approval-onpattrotm-patisiran-europe>
26. Meeting highlights from the Committee for Medicinal Products for Human Use (CHMP) 23–26 July 2018
www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2018/07/news_detail_002994.jsp&mid=WC0b01ac058004d5c1
27. Entry for on Drugs@FDA for Onpattro™.
www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=210922
28. Janssen reports positive topline results for ATLAS Phase III study of a novel, long acting injectable two-drug regimen for the treatment of HIV-1. www.janssen.com/janssen-reports-positive-topline-results-atlas-phase-iii-study-novel-long-acting-injectable-two-drug
29. Regeneron and Teva announce positive topline Phase 3 fasinumab results in patients with chronic pain from osteoarthritis of the knee or hip. <https://investor.regeneron.com/news-releases/news-release-details/regeneron-and-teva-announce-positive-topline-phase-3-fasinumab?releaseid=1074989>
30. Regeneron website. www.regeneron.com/
31. Update on TULIP 1 Phase III trial for anifrolumab in systemic lupus erythematosus. www.astrazeneca.com/media-centre/press-releases/2018/update-on-tulip-1-phase-iii-trial-for-anifrolumab-in-systemic-lupus-erythematosus-31082018.html
32. Lauwerys BR, Ducreux J, Houssiau FA. Type I interferon blockade in systemic lupus erythematosus: where do we stand? *Rheumatology* 53(8), 1369–1376 (2014).
33. Teewinot Life Sciences Corporation announced today grant of a U.S. patent with claims to cannabinoid formulations.
www.prnewswire.com/news-releases/teewinot-life-sciences-corporation-announced-today-grant-of-a-us-patent-with-claims-to-cannabinoid-formulations-300703030.html
34. Teewinot Technologies Ltd. US Patent 10,052,303.
35. Teewinot Life Sciences. <https://tlscorp.com/>