Orphan Diseases / Drugs

Trend Chart On Orphan Diseases / Drugs

Date : November 2017, 27th

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-Insights on animal models to investigate inhalation therapy: Relevance for biotherapeutics
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-Ceritinib: an orphan drug for ALK positive non-small cell lung cancer with robust clinical evidence
-*De novo* mutations implicate novel genes in Systemic Lupus Erythematosus
-lysosomal diseases and therapeutic strategies
-Orchard Therapeutics: collaboration with Manchester University to Include MPSIIIB

Basic Science

Acute and chronic respiratory diseases account for major causes of illness and deaths worldwide. Recent developments of biotherapeutics opened a new era in the treatment and management of patients with respiratory diseases. When considering the delivery of therapeutics, the inhaled route offers great promises with a direct, non-invasive access to the diseased organ and has already proven efficient for several molecules. To assist in the future development of inhaled biotherapeutics, experimental models are crucial to assess lung deposition, pharmacokinetics, pharmacodynamics and safety. This review describes the animal models used in pulmonary research for aerosol drug delivery, highlighting their advantages and limitations for inhaled biologics.
The results appeared in November 24th online issue of Int J Pharm.

Related Informations / Publications

Reference	Title	Authors	Location (Last Author)	Results / Comment	Link to Abstract
J Asthma Allergy. 2017 Nov 7;10:293-301	Animal models of asthma: utility and limitations	Aun MV	Clinical Immunology and Allergy Division, Department of Internal Medicine, University of São Paulo School of Medicine, São Paulo, Brazil	The present review analyzes the animal models of asthma, assessing differences between species, allergens and routes of allergen administration	abstract

Gene Therapy

Nucleic acid therapeutics are an established class of drugs that enable specific targeting of a gene of interest. This diverse family of drugs includes antisense oligonucleotides, siRNAs, and mRNA replacement therapies, which can elicit both gene repression and activation, primarily at the RNA level. Recent advances in medicinal chemistry have increased drug potency and enhanced delivery and distribution to a broad array of tissue and cell types. A key advantage of nucleic acid therapeutics is in their application to monogenic diseases. Cystic fibrosis is one such disease that affects ~70,000 people globally. This severe disease is an excellent candidate for nucleic acid therapies, as it is due to a genetic defect in a single

epithelial chloride channel. Although CF affects many tissues, the primary cause of patient mortality is lung disease.
The review appeared in November 21st online issue of Nucleic Acid Ther.

Related Informations / Publications

Reference	Title	Authors	Location	Results / Comment	Link to Abstract
Expert Opin Ther Targets. 2017 Nov 23	TGFβ as a therapeutic target in cystic fibrosis	Kramer E	Cincinnati Children's Hospital Medical Center , 3333 Burnet Avenue, Cincinnati (US)	Future directions for research into TGFβ focused therapeutics are discussed	abstract
Curr Opin Pharmacol. 2017 Oct 18;34:83-90	Correcting CFTR folding defects by small-molecule correctors to cure cystic fibrosis	Mijnders M	Utrecht University (NL)	Combination therapy with correctors may also improve functional CFTR mutants and benefit patients on potentiator therapy.	abstract

Orphan Drus

Crizotinib is approved for the first line treatment in ALK+ lung adenocarcinomas due to the results of the PROFILE 1001 and PROFILE 1005 trials. Unfortunately, as in all targeted therapies, patients will inevitably experience disease progression over time. Mechanisms of resistance to ALK inhibitors include gatekeeper mutations (L1196M and G1269A), increase the number of copies of the fusion gene and the development of alternative routes to ALK, like EGFR, KRAS, cKIT, among others.
The review appeared in November 24th online issue of Exp Opin Orphan Drugs.

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Cologne, Germany: Institute for Quality and Efficiency in Health Care (IQWiG); 2015 Sep 29.	Institute for Quality and Efficiency in Health Care	IQWiG	Cologne, Germany: Institute for Quality and Efficiency in Health Care (IQWiG)	The assessment was conducted based on patient-relevant outcomes and on the data provided by the company in the dossier	abstract
Intern Med. 2017 Nov 20. doi: 10.2169/internalmedicine.9368-17. [Epub ahead of print]	A Case of Large Cell Neuroendocrine Carcinoma Harboring an ALK Rearrangement with Response to Alectinib	Hayashi N	Department of Respiratory Medicine, Sapporo Minamisanjyou Hospital, Japan	After seven cycles of cytotoxic chemotherapy, her genotype testing demonstrated ALK rearrangement. Subsequently, she was administered alectinib and exhibited a partial response	abstract

Rare Diseases

The omnigenic model of complex disease stipulates that the majority of the heritability will be explained by the effects of common variation on genes in the periphery of core disease pathways. Rare variant associations, expected to explain far less of the heritability, may be enriched in core disease genes and thus will be instrumental in the understanding of complex disease pathogenesis and their potential therapeutic targets. Recently, using complementary

whole-exome sequencing, high-density imputation, and *in vitro* cellular assays, British researchers have identified candidate core genes in the pathogenesis of Systemic lupus erythematosus.
The results appeared in November 21st online issue of Hum Mol Genet.

Related Informations / Publications

Reference	Title	Authors	Location	Results / Comment	Link to Abstract
Semin Arthritis Rheum. 2017 Oct 5. pii: S0049-0172(17)30469-9	Environmental triggers in systemic lupus erythematosus	Gulati G	Univiersity of Cincinnatti College of Mediciene (US)	Reaesrchers focus on the available literature to explore the role of environmental factors in SLE disease onset	abstract

Lysosomal storage disorders (LSDs) — designated as 'orphan' diseases — are inborn errors of metabolism caused by defects in genes that encode proteins involved in various aspects of lysosomal homeostasis. For many years, LSDs were viewed as unattractive targets for the development of therapies owing to their low prevalence. However, the development and success of the first commercial biologic therapy for an LSD — enzyme replacement therapy for type 1 Gaucher disease — coupled with regulatory incentives rapidly catalysed commercial interest in therapeutically targeting LSDs. Despite ongoing challenges, various therapeutic strategies for LSDs now exist, with many agents approved, undergoing clinical trials or in preclinical development.
The review appeared in November 17th online issue of Nat Rev Drug Discov.

Related Informations / Publications

Reference	Title	Authors	Location	Results / Comment	Link to Abstract
Transl Sci Rare Dis. 2017 May 25;2(1-2):1-71	Lysosomal storage diseases	Ferreira CR	Children's National Health System, Washington, DC (US)	The advent of treatment options for some of these disorders has led to newborn screening pilot studies, and ultimately to the addition of Pompe disease and Hurler disease to the Recommended Uniform Screening Panel (RUSP) in 2015 and 2016, respectively.	abstract

Clinical Trial

Galapagos NV Galapagos NV reported on November 19th positive topline results from its ALBATROSS phase II study in cystic fibrosis patients with C1 corrector GLPG2222. The ALBATROSS study included 37 cystic fibrosis patients with a gating (Class III) mutation on one allele and F508del (Class II) mutation on the other allele. All patients were on long-term stable Kalydeco treatment (150mg twice daily) at screening and continued their Kalydeco treatment throughout the study. The ALBATROSS study was fully recruited within five months. For further info.

Related Informations / Publications

Dtae	Title	Collaboration	Results / Comment	Link to Abstract / PR
November 2017		NA	Galapagos issued 41,000 new ordinary shares on	Press Release

			23 November 2017, for a total capital increase (including issuance premium) of €353,835.00.	
September 2017		Morphosys	The phase I study was a randomized, double-blind, placebo-controlled trial, evaluating single ascending doses (SAD) in healthy volunteers, and multiple ascending doses (MAD) in patients with moderate-to-severe atopic dermatitis. MOR106 was administered as an intravenous infusion.	Press Release

Industrial Landscape / Agreements

Orchard Therapeutics Limited, a clinical-stage biotechnology company dedicated to transforming the lives of patients with rare disorders through innovative gene therapies, announces on November 27th that it has acquired an exclusive license to develop lentivirus-based autologous *ex-vivo* gene therapy for Sanfilippo syndrome type B (or MPS-IIIB) from The University of Manchester, UK. The technology, developed in Professor Brian Bigger's laboratory, and recently published in the journal Brain, involves the use of a high-titre lentiviral vector to drive the expression of a codon-optimized *α-N-acetylglucosaminidase* (*NAGLU*) gene under the control of the myeloid-specific CD11b promoter (LV.CD11b.NAGLU). For further info.

Related Informations / Publications

Dtae	Title	Collaboration	Results / Comment	Link to Abstract / PR
September 2017	Bringing next-generation gene therapy to the clinic	NI	In this interview, Dr Andrea Spezzi, Orchard's Chief Medical Officer, discussed the challenges of translating pre-clinical ressearch from bench to bed side	Press Release