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FDA Orphan Drug Data Analysis

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Background

- Obtain data from FDA Orphan Drug Designations and Approvals and processed them into MyChem.info
- Source:
 - <https://www.accessdata.fda.gov/scripts/opdlisting/oopd>

The screenshot shows the FDA U.S. Food & Drug Administration website. The top navigation bar includes links for Home, Food, Drugs, Medical Devices, Radiation-Emitting Products, Vaccines, Blood & Biologics, Animal & Veterinary, Cosmetics, and Tobacco Products. A search bar is located at the top right. Below the header, a sub-navigation menu for 'Search Orphan Drug Designations and Approvals' is displayed, with options for 'FDA Home' and 'Developing Products for Rare Diseases & Conditions'. The main content area is titled 'Search Criteria' and contains fields for 'Product Name', 'Orphan Designation', 'Start Date' (01/01/1983), 'End Date' (04/09/2021), 'Search results' (set to 'All designations'), 'Output format' (set to 'Download Excel file'), and 'Sort results' (with options for 'Display condensed list' and 'Display detailed list'). A note below the output format field states: '(Note: The information contained in the downloadable Excel file for the "CF Grid Key" column is for FDA purposes only.)'. At the bottom left is a 'Run Search' button, and at the bottom right is a blue 'Download Excel file' button, which is highlighted with a yellow box.

Data Set (1/2)

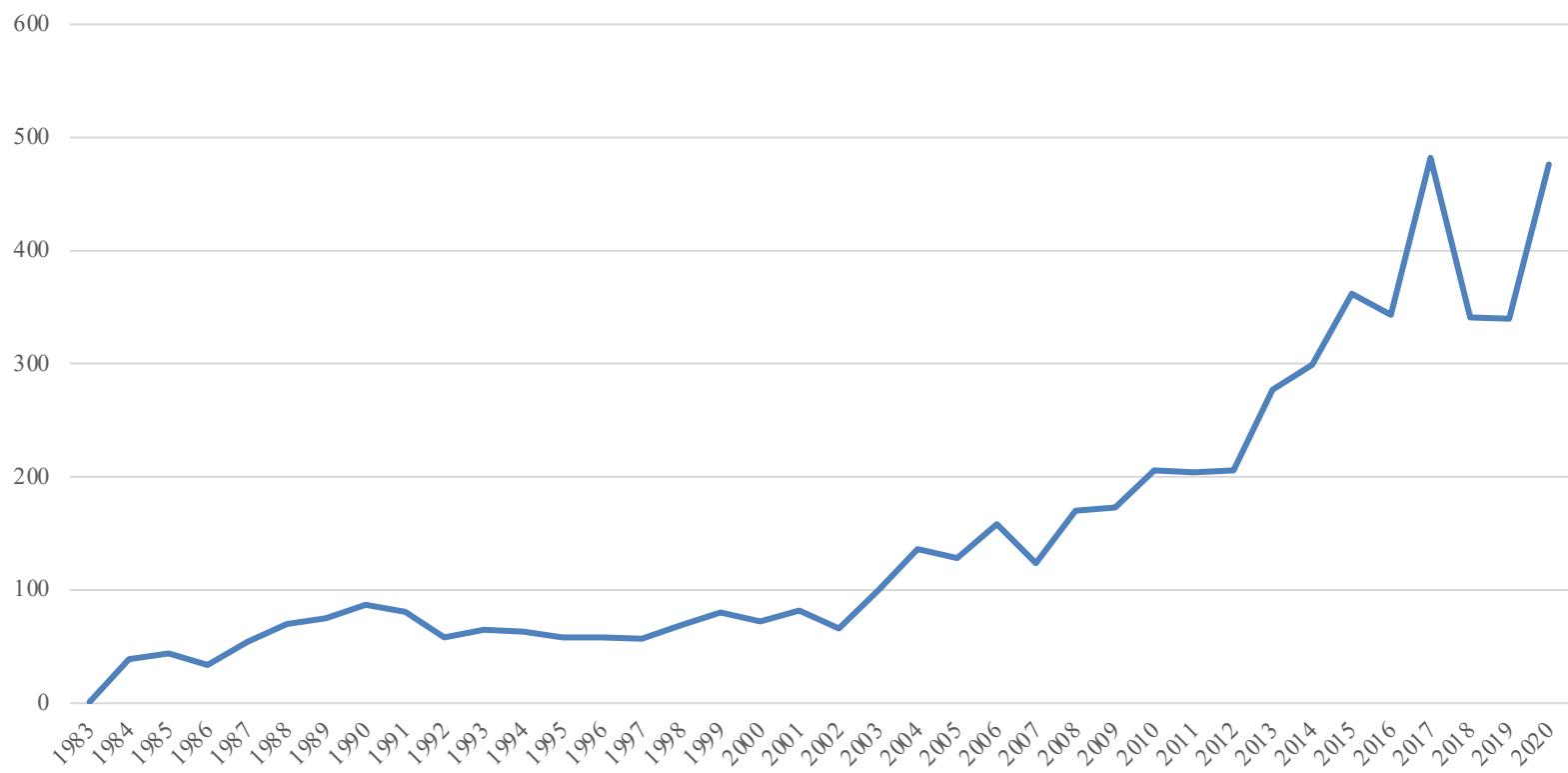
A	B	C	D	E	F
Generic Name	Trade Name	Date Designated	Orphan Designation	Orphan Designation Status	FDA Orphan Approval Status
(2S,3S,4E,6S,7R,10R)-7,10-Dihydroxy-3,7-dimethyl-12-oxo-2-[(2E,4E,6R)-6-(pyridin-2-yl)hepta-2,4-dien-2-yl]oxacyclododec-4-en-6-yl 4-methylpiperazine-1-carboxylate		6/22/17	Treatment of chronic myelomonocytic leukemia (CMML)	Designated	Not FDA Approved for Orphan Indication
(2S,4R)-1-(2-(3-acetyl-2-(methyl(pyrimidin-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridin-2-yl)-4-fluoropyrrolidine-2-carboxamide		11/2/17	Treatment of paroxysmal nocturnal hemoglobinuria	Designated	Not FDA Approved for Orphan Indication
(2-chloro-4-phenoxyphenyl)(4-(((3R,6S)-6-(hydroxymethyl)tetrahydro-2H-pyran-3-yl)amino)-7H-pyrrolo[2,3-d]pyrimidin-5-yl)methanone		12/8/20	Treatment of chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)	Designated	Not FDA Approved for Orphan Indication
1-(2-Nitro-imidazolyl)-3-[18F]fluoro-2-propanol;1H-1-(3-[18F]fluoro-2-hydroxypropyl)-2-nitroimidazole		1/6/16	As a diagnostic for clinical management of soft tissue sarcoma, including rhabdomyosarcoma.	Designated	Not FDA Approved for Orphan Indication
2-(2-((2-(1H-benzimidazol-2-yl)ethyl)amino)ethyl)-N-[(3-fluoropyridin-2-yl)methyl]-1,3-oxazole-4-carboxamide trihydrochloride		6/17/19	Treatment of beta-thalassemia	Designated	Not FDA Approved for Orphan Indication
37,6?,7,7,12?-tetrahydroxy-5?-cholan-24-oic acid		10/22/20	treatment of progressive familial intrahepatic cholestasis	Designated	Not FDA Approved for Orphan Indication
4-(4-((6-(4-Chlorophenyl)-spiro[3.5]non-6-en-7-yl)methyl)-piperazin-1-yl)-N-((3-nitro-4-((2S)-1,4-dioxan-2-ylmethyl)amino)phenyl)sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide		8/28/20	Treatment of Chronic Lymphocytic Leukemia	Designated	Not FDA Approved for Orphan Indication
a non-replicating, recombinant adeno-associated virus serotype 9 (AAV9) containing the human Methyl Cpg Binding Protein 2B (MECP2B) cDNA under the control of a segment of the murine MECP2 promoter.		4/17/19	Treatment of Rett Syndrome (RTT)	Designated	Not FDA Approved for Orphan Indication
A recombinant plasmid-derived DNA-based vaccine targeting the E6 and E7 antigens of both HPV6 and HPV11		7/28/20	Treatment of recurrent respiratory papillomatosis	Designated	Not FDA Approved for Orphan Indication
a self-complementary adeno-associated virus serotype 9 (AAV9) vector expressing codon-optimized human SURF1 DNA coding sequence		10/20/20	Treatment of Leigh Syndrome.	Designated	Not FDA Approved for Orphan Indication
allogeneic CRISPR/Cas9-mediated genetically modified CAR T cells targeting CD19 antigen		2/16/21	Treatment of acute lymphoblastic leukemia	Designated	Not FDA Approved for Orphan Indication
antibody drug conjugate comprised of an anti-B cell maturation (BCMA) IgG1 humanized antibody conjugated covalently to the dibenzocyclooctyne (DBCO) noncleavable linker maytansinoid warhead		2/23/21	Treatment of multiple myeloma	Designated	Not FDA Approved for Orphan Indication
apadmatase alfa		9/28/20	Treatment of Sickle Cell Disease	Designated	Not FDA Approved for Orphan Indication
ascorbic acid		5/11/09	Treatment of Charcot-Marie-Tooth disease type 1A.	Designated	Not FDA Approved for Orphan Indication

Data Set (2/2)

- Total: 5,849 records (treatment-disease)
- Generic Name (Column A)
 - Chemicals (substance and compound)
 - Medication, gene therapy or other therapies
 - Processed with mychem, pubchem and Google search
- Orphan Designation (Column D)
 - Processed with Medical NLP algorithms

Data Trend

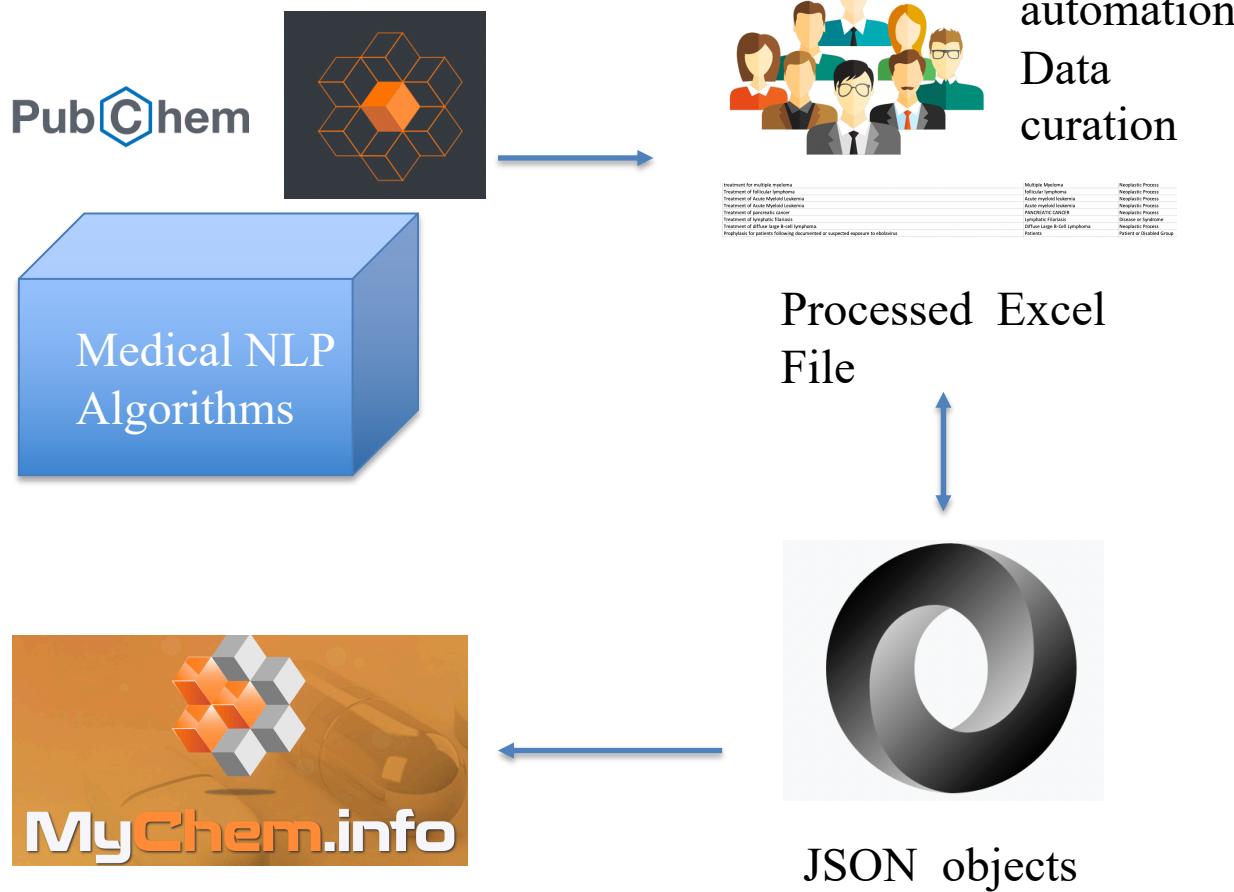
Disease-Treatment Summary Trend (1983-2020)



Process Flow



Original Excel File



Data Clean and Normalization (1/3) (column D)

- Example 1:
 - Treatment of paroxysmal nocturnal hemoglobinuria
paroxysmal nocturnal hemoglobinuria (C0024790;
Neoplastic Process)
- Example 2:
 - For immune reconstitution and prevention of graft
versus host disease following allogeneic hematopoietic
stem cell transplantation.
graft versus host disease (C0018133;Disease or
Syndrome)

Data Clean and Normalization (2/3) (column D)

- Example 3:
 - Intravenous treatment of patients presenting with moderate to severe acetaminophen overdose
[Acetaminophen overdose \(C0572025; injury or poisoning\)](#)
- Example 4:
 - For use in post-exposure prophylaxis for occupational exposure to human immunodeficiency virus
[Exposure to Human immunodeficiency virus \(C1096519; injury or poisoning\)](#)

Data Clean and Normalization (3/3) (column D)

- Processing Types:
 - Disease or Syndrome
 - Neoplastic Process
 - Pathologic Function
 - Injury or Poisoning
 - Gene or Genome
 - Congenital Abnormality
 - Finding
 - Sign or Symptom
 - Intellectual Product
 - Anatomical Abnormality
 - Bacterium
 - Virus
 - Body Space or Junction
 - Mental or Behavioral Dysfunction
 - Cell Component
 - Eukaryote

Result – Column A

- Group 1 (51.92%; 3,037 records): PubChem, MyChem and Google search
 - Key: InChI Key or Substance ID
- Group 2 (48.08%; 2812 records): Not directly related to chemicals or did not find any match

Result – Column D

- Group 1 (96.6%; 5,650 records): Processed with type support

Record Id	Original text	Parsed Text	Text Type
1	Treatment of chronic myelomonocytic leukemia (CMML)	Chronic Myelomonocytic Leukemia	Neoplastic Process
2	Treatment of paroxysmal nocturnal hemoglobinuria	Paroxysmal nocturnal hemoglobinuria	Disease or Syndrome
3	Treatment of chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)	Chronic Lymphocytic Leukemia	Neoplastic Process
3	Treatment of chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)	Small Lymphocytic Lymphoma	Neoplastic Process
3	Treatment of chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)	SLL	Gene or Genome
4	As a diagnostic for clinical management of soft tissue sarcoma, including rhabdomyosarcoma.	Rhabdomyosarcoma	Neoplastic Process
4	As a diagnostic for clinical management of soft tissue sarcoma, including rhabdomyosarcoma.	Soft tissue sarcoma	Neoplastic Process
4	As a diagnostic for clinical management of soft tissue sarcoma, including rhabdomyosarcoma.	Diagnostic	Diagnostic Procedure
5	Treatment of beta-thalassemia	BETA-THALASSEMIA	Disease or Syndrome

- Group 2 (3.4%; 199 records): Not directly related to disease or did not find any match

2247 For promotion of cutaneous wound healing in extreme burn treatment protocols.

2321 Prevention of graft rejection following solid organ transplantation

2611 Mobilization of hematopoietic stem cells to the peripheral blood for collection and subsequent transplant

3006 Prevention of graft rejection following solid organ transplantation

3090 For the promotion of early engraftment in bone marrow transplantation.

For promotion of cutaneous wound healing in extreme burn treatment protocols.

Prevention of graft rejection following solid organ transplantation

Mobilization of hematopoietic stem cells to the peripheral blood for collection and subsequent transplant

Prevention of graft rejection following solid organ transplantation

For the promotion of early engraftment in bone marrow transplantation.

Result

- Since some generic names do not have IDs in PubChem and MyChem.info, so we only included 3,149 records ($3149/5849=53.8\%$) in the final data set.

Discussion

- Data Presentation on FDA's website:

Search Orphan Drug Designations and Approvals

[FDA Home](#) [Developing Products for Rare Diseases & Conditions](#)

Generic Name:	(2S,3S,4E,6S,7R,10R)-7,10-Dihydroxy-3,7-dimethyl-12-oxo-2-[(2E,4E,6R)-6-(pyridin-2-yl)hepta-2,4-dien-2-yl]oxacyclododec-4-en-6-yl 4-methylpiperazine-1-carboxylate
Date Designated:	06/22/2017
Orphan Designation:	Treatment of chronic myelomonocytic leukemia (CMML)
Orphan Designation Status:	Designated
FDA Orphan Approval Status:	Not FDA Approved for Orphan Indication
Sponsor:	H3 Biomedicine Inc. (US Research Subsidiary of Eisai Co., Ltd.) 300 Technology Square Floor 5 Cambridge, Massachusetts 02139 United States

The sponsor address listed is the last reported by the sponsor to OOPD.

Discussion

- JSON Examples:

```
{  
    "_id": "PIBARDGJJAGJAJ-NQIIRXRSSA-N",  
    "fda_orphan_drug": [  
        {  
            "pubchem_cid": 118323590,  
            "pubchem_sid": "381128152, 439581800",  
            "inchikey": "PIBARDGJJAGJAJ-NQIIRXRSSA-N",  
            "generic_name": "(2S,4R)-1-(2-(3-acetyl-5-(2-methylpyrimidin-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridin-2-yl)-4-fluoropyrrolidine-2-carboxamide",  
            "designated_date": "2017-11-02",  
            "designation_status": "Designated",  
            "approval_status": "Not FDA Approved for Orphan Indication",  
            "sponsor": "Alexion Pharmaceuticals, Inc|300 George Street|New Haven|Connecticut|6511|United States",  
            "orphan_designation": {  
                "original_text": "Treatment of paroxysmal nocturnal hemoglobinuria",  
                "umls": "C0024790",  
                "parsed_text": "Paroxysmal nocturnal hemoglobinuria"  
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            "pubchem_cid": 118323590,  
            "pubchem_sid": "381128152, 439581800",  
            "inchikey": "PIBARDGJJAGJAJ-NQIIRXRSSA-N",  
            "generic_name": "(2S,4R)-1-(2-(3-acetyl-5-(2-methylpyrimidin-5-yl)-1H-indazol-1-yl)acetyl)-N-(6-bromopyridin-2-yl)-4-fluoropyrrolidine-2-carboxamide",  
            "designated_date": "2017-12-14",  
            "designation_status": "Designated",  
            "approval_status": "Not FDA Approved for Orphan Indication",  
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            "orphan_designation": {  
                "original_text": "Treatment of C3 glomerulopathy (C3G)",  
                "umls": "C4521256",  
                "parsed_text": "Glomerulopathy"  
            }  
        }  
    ]  
},
```



Thank you