

How to translate initiatives into realities - orphan drugs products

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Expertise Orphan Products & Rare Diseases

Rare Diseases - Orphan Drugs

- Rare Diseases affect about 350 million people world wide
 - 30 Million in the US
 - Mainly children
- A rare disease is one that affects a apecific portion of the population
 - Population is defined by each nation state
 - 80% are genetic in nature
 - 90% are serious/life-threatening
- Only 5% of rare diseases have approved treatments
 - The number only continues to grow as new diseases (7,000+) are discovered
- Rare diseases do not recognize borders or socioeconomic status

Orphan Drug Landscape

- Orphan Drugs are “IN”
- Estimated worth of the global market - \$50 Billion
- Percentage of orphan drugs with annual sales > 1 billion \$ - 29%
- Percentage of orphan drugs with additional rare disease indications – 15%
- 452 Orphan products under FDA review in U.S. (2013)
- A record 260 orphan drug designations were granted in the US in 2013
- Same standards for review and approval as non-orphans “except” for FDA flexibility

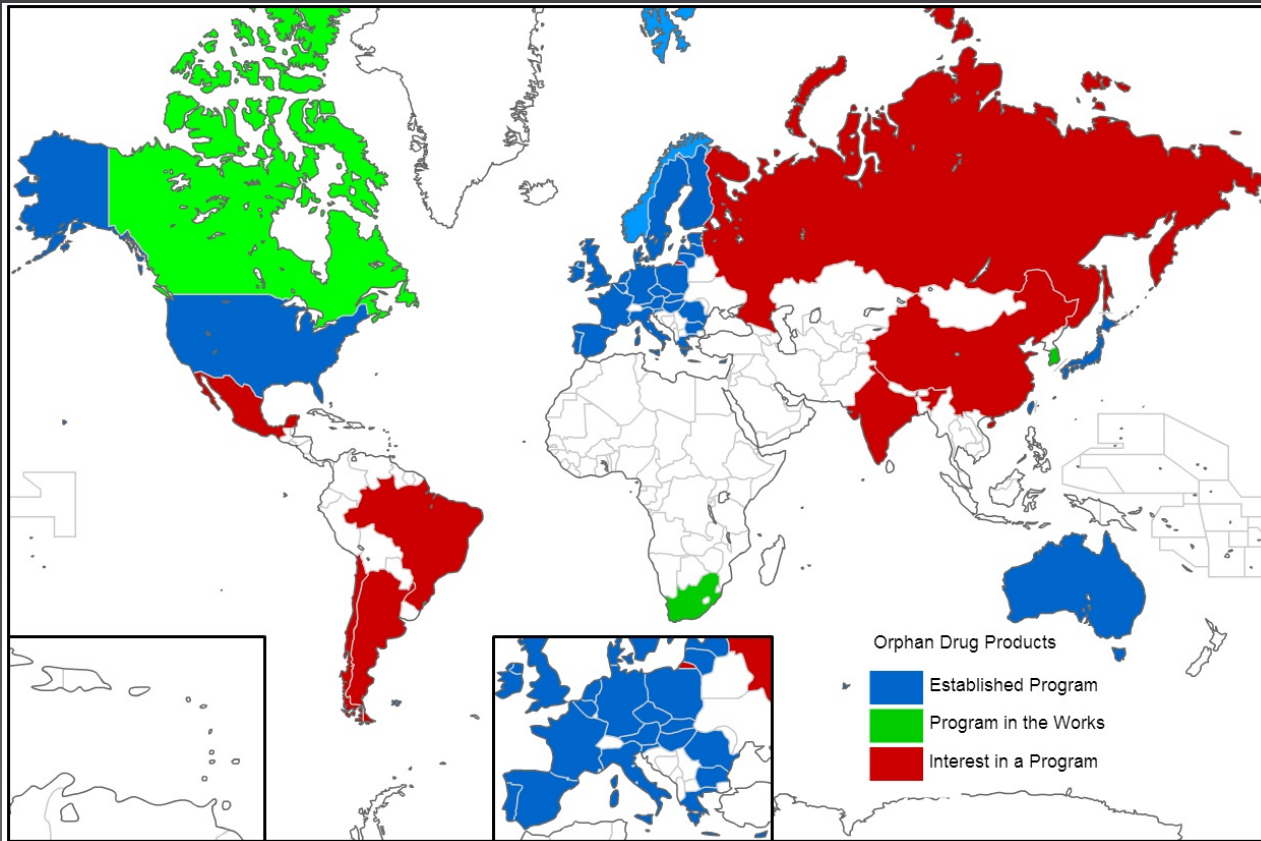
Orphan Drug Act - US

- Orphan Drug Act (1983)
- Rare disease = prevalence < 200,000
- 7 Year Market Exclusivity
- FDA Filing Fee Wavier
- Tax Credits for clinical trials
- Orphan Product Grants
- ~494 drugs approved; >3400 designated (FDA, 2014)
- Use of accelerated approval/fast track

EU Regulation

- Orphan Drug Regulation 141/2000 (1999)
- Rare disease = prevalence < 5 per 10,000
- 10 Year Market Exclusivity (6 + 4 years)
- Must be Serious or Life threatening disease
- Tax credits by member state
- Grants via 8th Framework
- COMP designates – 38 members
- chair, 1 from each MS, 3 patient organization members, 3 from CHMP, 1 each Norway, Lichtenstein, Iceland, 1 from EC
- 864 designated; 68 approved orphan drugs (2014)
- approved 15 treatments for rare diseases in 2014 (37% of all drugs approved)

Global Initiative



Challenges in developing orphan products

- Defining a rare diseases / Selecting a rare disease
 - Diagnosis
 - Natural History
- Appropriate Mechanism of the drug for the disease
- Clinical Trials
 - Finding a significant number of patients qualifying for the clinical trial
- Prescribing practices
- Pricing
- Cultural Differences

Benefits outweigh any risk (to industry)...

- Companies continue to invest
- Drugs are being approved
 - 41 New orphan drugs in US in 2014 (previous yearly avg 9-10)
- Repurposing drugs
- Patients are getting treatments
 - Post-marketing trials / studies
- Gene Therapy
 - Glybera
 - None yet in the US but many on the horizon

Top 10 Selling Orphan Drugs in 2014 by Sales in US

Rank	Product	Generic Name	Company	USA Sales (\$m) 2014	Revenues per Patient 2014*	No. of Patients 2014
1	Rituxan	rituximab	Roche	3,707	52,454	70,679
2	Revlimid	lenalidomide	Celgene	2,865	164,859	17,380
3	Copaxone	glatiramer acetate	Teva Pharmaceutical Industries	2,700	59,862	61,533
4	Gleevec	imatinib mesylate	Novartis	2,023	101,442	65,240
5	Avonex	interferon beta-1a	Biogen Idec	1,908	57,124	33,406
6	Alimta	pemetrexed disodium	Eli Lilly	1,251	47,300	26,453
7	Rebif	interferon beta-1a	Merck KGaA	1,238	60,571	20,442
8	Velcade	bortezomib	Takeda	983	61,053	16,093
9	NovoSeven/ NovoSeven RT	eptacog alfa	Novo Nordisk	829	12,686	65,348
10	Advate	factor VIII (procoagulant)	Baxter International	816	448,653	1,820

Source: EvaluatePharma® (27 OCT 2014)

Worldwide Top 20 Selling Orphan Drugs in 2020

Rank	Product	Generic Name	Company	Phase (Current)	Pharmacological Class	WW Product Sales (\$m)		
						2013	2020	CAGR
1	Revlimid	lenalidomide	Celgene	Marketed	Immunomodulator	4,280	8,012	+9%
2	Opdivo	nivolumab	Bristol-Myers Squibb	Marketed	Anti-programmed death-1 (PD-1) MAb	-	6,033	n/a
3	Rituxan	rituximab	Roche	Marketed	Anti-CD20 MAb	7,503	5,689	-4%
4	Soliris	eculizumab	Alexion Pharmaceuticals	Marketed	Anti-complement factor C5 MAb	1,551	5,510	+20%
5	VX-809 + ivacaftor	ivacaftor; lumacaftor	Vertex Pharmaceuticals	Phase III	Cystic fibrosis transmembrane conductance regulator (CFTR) corrector	-	4,227	n/a
6	Keytruda	pembrolizumab	Merck & Co	Approved	Anti-programmed death-1 (PD-1) MAb	-	3,879	n/a
7	Imbruvica	ibrutinib	Pharmacyclics	Marketed	Bruton's tyrosine kinase (BTK) inhibitor	14	3,602	+122%
8	Gazyva	obinutuzumab	Roche	Marketed	Anti-CD20 MAb	3	2,528	+159%
9	Obeticholic acid	obeticholic acid	Intercept Pharmaceuticals	Phase III	Farnesoid X receptor (FXR) agonist	-	2,522	n/a
10	Elelyso*	taliglucerase alfa	Pfizer	Marketed	Glucocerebrosidase	49	2,480	+75%
11	Tasigna	nilotinib hydrochloride monohydrate	Novartis	Marketed	BCR-ABL tyrosine kinase inhibitor	1,266	2,468	+10%
12	Yervoy	ipilimumab	Bristol-Myers Squibb	Marketed	Anti-CTLA4 Mab	960	2,377	+14%
13	Pomalyst	pomalidomide	Celgene	Marketed	Immunomodulator	305	2,097	+32%
14	Alimta	pemetrexed disodium	Eli Lilly	Marketed	Thymidylate synthase inhibitor	2,703	2,057	-4%
15	DCVax-L*	-	Northwest Biotherapeutics	Phase III	Cancer vaccine	-	2,046	n/a
16	Kyprolis	carfilzomib	Amgen	Marketed	Proteasome inhibitor	73	1,943	+60%
17	Avonex	interferon beta-1a	Biogen Idec	Marketed	Interferon beta	3,005	1,885	-6%
18	Sprycel	dasatinib	Bristol-Myers Squibb	Marketed	Tyrosine kinase inhibitor	1,280	1,815	+5%
19	NovoSeven/ NovoSeven RT	eptacog alfa	Novo Nordisk	Marketed	Factor VII	1,649	1,810	+1%
20	Imbruvica	ibrutinib	Johnson & Johnson	Marketed	Bruton's tyrosine kinase (BTK) inhibitor	-	1,741	n/a
Other						65,437	111,256	+7%
Total						90,079	175,977	+11%

Source: EvaluatePharma® (27 OCT 2014)

Summary

- The Orphan Drug Act in the US and beyond works to treat serious and life threatening diseases
- More than 19 million people in the US have benefitted directly from the ODA. But if the greater family is included – number is far greater
- Orphan diseases while, individually rare, in aggregate are a significant public health issue
- Many South American countries are exploring orphan drug legislation – time to do more than explore, enact needed legislation
- And, from a business perspective, there is money to be made
- Patients need therapies for their diseases

Muchas Gracias ¿Preguntas?

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