

Rheumatology

Unmet need is driving more R&D and treatment options for rheumatoid arthritis, including Pfizer's oral drug poised to land on the market later this year. As **Noah Pines** finds, it won't be easy for any newcomer to challenge the nine RA biologics that rule the space

There are nine biologic medicines approved for rheumatoid arthritis (RA). While they have proven very effective in about half of patients, “they leave another 50% not so well-treated,” explains Joan Bathon, MD, director of the rheumatology division at Columbia University College of Physicians and Surgeons.

About a third of RA patients don't attain an ACR20 score (20% improvement; the level considered minimally clinically important), adds Steven Weinstein, MD, PhD, who is VP of inflammation for Regeneron Pharmaceuticals. “That clearly indicates an unmet need for many patients and is probably what's driving the R&D for new options.”

The most promising near-term agents are the kinase inhibitors, both JAK and SYK. At press time, Pfizer's JAK3 inhibitor tofacitinib was reviewed by an FDA advisory

panel, which voted 8-2 that benefits outweighed potential risks. Analysts expect the pill to be approved in August, bringing an oral—and likely cheaper—option to a market that since the late 1990s has been dominated by injectable and infusion medicines, like Abbott's top-selling Humira and J&J's Remicade, respectively.

Bernstein Research has forecasted tofa' worldwide sales of \$1.4 billion by 2015. “The uncertainty is not whether it gets approved, but what labeling that gets approved,” notes Bernstein's Tim Anderson, MD,

Pfizer, which stopped selling Enbrel in the US in April, bringing a long-running US co-promotion deal with Amgen to a close a year early, stands to pocket any and all tofa' revenues.

KOLs have said that the small-molecule drug is at least as good as Humira in efficacy. The safety profile is manageable, although the advisory panel in May flagged malignancy concerns over time and a higher infection rate with long-term exposure of the 10mg dose.

If it does reach market, analysts expect slow uptake—a function both of the long-term safety data among the well-entrenched TNF inhibitors and anticipated tofa' labeling. Anderson foresees a third-, possibly a second-line label, and for the drug to be used initially in TNF-alpha failures.

Not that the new entrant wouldn't be potent—its launch could dampen uptake of Genentech's Actemra and Bristol-Myers Squibb's Ocrencia, and could make an even bigger splash overseas: “There are a lot of places in the world where TNF inhibitors are not used because they are hard to distribute,” adds Ben Weintraub, PhD, director of research for Wolters Kluwer's *inThought* unit.

But the RA market is more crowded than ever. Going forward, Enbrel and Humira are expected to remain dominant players not only as a result of the data but also their considerable DTC advertising. Additional orals and biologics could come down the pike, too. Weinstein counts 60 Phase II or III trials for RA drugs in ongoing or recruiting trials on ClinicalTrials.gov, including about a dozen new agents.

Analysts also expect cut-rate versions of the anti-TNF drugs to be introduced, although regulatory experts don't expect biosimilar policies to be in place for some time.

Once biosimilars arrive, they could lead to sales erosion among the innovator compounds, as payers mandate usage of the discounted forms. John Taenzler, PhD, a principal at Evolution Marketing Research, predicts that Remicade is likely to be the first to take a hit but that the drug will be buoyed by its potency as well as the different payer structure for an infusion med. “There will always be a role for it. It is the Sherman tank of TNFs.” ■



TOP 40 RHEUMATOLOGY PRODUCTS, 2011

Category leaders, ranked by US sales, and their media spend

Rank	Product	Manufacturer	US sales \$ (millions)*	Vs. prior 12 mos.	TRx (000s)	Vs. prior 12 mos.	US DTC media \$ (000s)**	Vs. prior 12 mos.	US journal media \$ (000s)**	Vs. prior 12 mos.
1	Humira	Abbott	\$3,531.1 ^{††}	26.0%	1,488.8	16.0%	\$94,143.4	187.9%	\$2,285.0	1,486.9%
2	Remicade	J&J	\$3,474.2 ^{††}	12.0%	67.5	41.0%	\$2.0	-99.8%	\$1,010.2	59.9%
3	Enbrel	Amgen/Pfizer	\$3,458.0 [†]	5.0%	1,453.9	2.0%	\$118,773.1	89.7%	\$1,100.9	-7.6%
4	Copaxone	Teva	\$2,955.6 ^{††}	29.0%	581.4	8.0%	\$0.0	N/A	\$247.7	14.7%
5	Rituxan	Roche/Biogen	\$2,924.5 ^{††}	6.0%	10.8	38.0%	\$471.9	-42.8%	\$52.5	-97.7%
6	Meloxicam	Generic	\$2,252.9	11.0%	19,928.8	13.0%	\$0.0	N/A	\$0.0	N/A
7	Celebrex	Pfizer	\$2,167.9	5.0%	9,648.8	-5.0%	\$115,227.2	218.2%	\$0.0	N/A
8	Avonex	Biogen Idec	\$1,628.3 [†]	9.0%	302.8	-4.0%	\$126.6	132.4%	\$532.2	2.2%
9	Rebif	Pfizer/Merck KGaA	\$878.9	8.0%	273.4	0.0%	\$1.8	-99.5%	\$301.6	-32.4%
10	Betaseron	Bayer	\$725.3 ^{††}	-12.0%	194.4	11.0%	\$0.0	N/A	\$131.3	-51.6%
11	Asacol	Warner Chilcott	\$665.1	-5.0%	1,232.6	-14.0%	\$0.0	N/A	\$0.0	N/A
12	Orencia	Bristol-Myers Squibb	\$615.0 [†]	12.0%	28.8	70.0%	\$45,768.2	19.5%	\$828.4	262.5%
13	Colcrys	URL Pharma	\$590.4	959.0%	2,468.9	1468.0%	\$657.3	228.6%	\$1,634.1	72.5%
14	Stelara	J&J	\$433.6 [†]	124.0%	48.6	107.0%	\$44,776.7	25.2%	\$730.9	-48.1%
15	Synvisc-One	Genzyme	\$426.8	40.0%	47.7	46.0%	\$0.0	N/A	\$291.6	67.4%
16	Lialda	Shire	\$408.9	21.0%	653.7	7.0%	\$77.1	85.6%	\$401.7	-43.7%
17	Diclofenac sodium	Generic	\$338.1	26.0%	7,383.5	4.0%	\$0.0	N/A	\$0.0	N/A
18	Tysabri	Biogen/Elan	\$326.5 [†]	29.0%	12.1	0.0%	\$444.1	419.8%	\$856.4	8.9%
19	Naproxen	Generic	\$321.5	-8.0%	16,118.5	4.0%	\$0.0	N/A	\$0.0	N/A
20	Pentasa	Shire	\$298.9	7.0%	461.5	-3.0%	\$0.0	N/A	\$160.7	9.0%
21	Cimzia	UCB Pharma	\$298.3 ^{†c}	21.0%	158.8	48.0%	\$34,116.9	71.8%	\$0.0	-100.0%
22	Entocort EC	Prometheus	\$294.6	-21.0%	224.5	-40.0%	\$0.0	N/A	\$0.0	N/A
23	Methotrexate	Generic	\$268.4	7.0%	5,543.6	3.0%	\$0.0	N/A	\$0.0	N/A
24	Simponi	J&J	\$235.0 [†]	22.0%	108.6	32.0%	\$11,450.8	-81.5%	\$539.9	-75.7%
25	Allopurinol	Generic	\$226.4	2.0%	15,052.2	7.0%	\$0.0	N/A	\$0.0	N/A
26	Nabumetone	Generic	\$217.5	-9.0%	3,244.6	-8.0%	\$0.0	N/A	\$0.0	N/A
27	Clobex	Galderma	\$210.4	9.0%	512.6	0.0%	\$0.0	N/A	\$369.9	22.7%
28	Asacol HD	Warner Chilcott	\$191.6	86.0%	341.8	69.0%	\$0.0	N/A	\$0.0	-100.0%
29	Uloric	Takeda	\$179.1	81.0%	833.6	58.0%	\$94,585.1	133.3%	\$987.1	-39.8%
30	Euflexxa	Ferring	\$173.8	47.0%	37.4	35.0%	\$0.0	N/A	\$70.8	-78.4%
31	Clobetasol propionate	Generic	\$167.9	9.0%	4,803.6	9.0%	\$0.0	N/A	\$0.0	N/A
32	Actemra	Genentech	\$157.9	213.0%	12.4	307.0%	\$174.7	75.2%	\$1,050.6	-26.8%
33	Synvisc	Genzyme	\$155.8	5.0%	34.6	17.0%	\$2,821.1	-48.7%	\$0.0	-100.0%
34	Desoximetasone	Generic	\$150.3	4.0%	1,192.5	-8.0%	\$0.0	N/A	\$0.0	N/A
35	Canasa	Axcan Pharma	\$135.5	20.0%	240.5	2.0%	\$0.0	N/A	\$0.0	N/A
36	Kenalog-40	Bristol-Myers Squibb	\$123.5	10.0%	37.8	-1.0%	\$0.0	N/A	\$0.0	N/A
37	Hydroxychloroquine sulfate	Generic	\$108.7	14.0%	4,338.0	7.0%	\$0.0	N/A	\$0.0	N/A
38	Etodolac	Generic	\$78.8	-3.0%	2,462.2	-5.0%	\$0.0	N/A	\$0.0	N/A
39	Benlysta	GSK/HGSI	\$54.0	N/A	2.1	N/A	\$1.5	N/A	\$370.0	N/A
40	Leflunomide	Generic	\$36.0	-26.0%	705.8	-2.0%	\$0.0	N/A	\$0.0	N/A

*Manufacturer benchmark sales (MBS), unless noted

Note: TRx count includes retail only. List includes products FDA indicates as approved for treating rheumatoid arthritis, psoriasis, lupus, Crohn's disease, ulcerative colitis, gout, ankylosing spondylitis and multiple sclerosis.

Sources: Sales/TRx, Wolters Kluwer Pharma Solutions, company reports; DTC media spend, Nielsen; journals, IMS Health.

† Company reported sales. †† IMS Health ‡ >90% of sales from oncology settings c Includes Canada