Few markets are attracting as much attention from pharma as the autoimmune (AI) disease space. The best-known AI products – anti-TNFs such as Humira and Enbrel or interferon-betas such as Rebiš and Avonex – are blockbusters that significantly changed how diseases were managed, improved patient lives, and gained the confidence of physicians. These products are true blockbusters with revenues well in excess of $5 billion and pricing that ranges from $20,000 to $40,000 per patient per year. The space offers significant opportunity in the form of a large number of diseases with significant numbers of patients and unaddressed clinical need, and it has attracted tens of billions of dollars in R&D and clinical investment. More than 100 unique AI assets are currently in Phase I-III development, making AI one of the leading areas of pharmaceutical R&D. Nine companies have significant revenues (more than $2 billion) in AI. Another 10 of the top 30 companies are investing heavily to grow an AI business.
But though an attractive market, AI is not an easy one. The companies with traction in autoimmune had to do far more than develop molecules that met their endpoints and won regulatory approval. They also took bold steps to orient their business models toward critical success factors unique to AI, including a high-touch, patient-centric commercial model very different from pharma’s traditional approach. New entrants – and there are many – will have to play catch-up.

This study aims to answer four fundamental strategic and operational questions for biopharmas considering entry or who are in the early stages of development of an AI franchise:

1. Where should we participate?
2. How do we approach development?
3. How do we reorient our commercial model to serve patients and build loyalty?
4. How do we contend with a more demanding access environment in developed markets?

We will begin with an overview of key markets, pipeline intensity, and the options for growth in the space. Then we will describe the unique role of AI commercial models in driving success. We will conclude with a discussion of how payers will view AI disease spaces and what will drive access even with the prospect of biosimilars in the not too distant future.

**AUTOIMMUNE DISEASE AREAS**

The term **autoimmune disorder** refers to a constantly growing list of diseases (currently 80-100) in which the immune system attacks healthy body tissue. AI diseases display a broad range of symptoms. They may progress steadily or flare up intermittently, but they always contribute to the destruction of one or several target organs.

The American Autoimmune Disease Association (AADA) estimates that autoimmune diseases affect 50 million Americans. They are the second leading cause of chronic illness in the United States and one of the 10 leading causes of morbidity in women under the age of 65. According to AADA, the top seven diseases in the category (Crohn's disease, ulcerative colitis, systemic lupus erythematosus, multiple sclerosis, rheumatoid arthritis, psoriasis, and scleroderma) generate an estimated $51.8 billion to $70.6 billion in direct and indirect costs annually. (Direct costs are the cost of treatment. Indirect costs include factors such as lost wages and the cost of hiring help for housework and other tasks that the patient is unable to perform because of the disease.) The incidence of AI diseases is rising rapidly nationally and worldwide. As a result, drugs in the area have significant sales and growth potential. Exhibit 1 shows the size and growth rate of the drug markets in the larger AI disease markets. The overall growth rate of 7.9 percent is significantly higher than the projected growth rate of the industry as a whole.

Current treatment options vary in efficacy, but they are almost exclusively supportive: They relieve symptoms, control flare-ups, and in some cases slow or stall disease progression, but they rarely reverse the disease itself. AI disorders are exceptionally challenging to treat. It is
known that multiple autoimmune diseases share genetic links, which suggests a common pathogenesis, and multiple correlations have been discovered between AI diseases and environmental factors and infections, which may serve as disease triggers. As we learn more about these factors we will likely see new options for disease-modifying therapeutics.

Pharma companies thinking of entering the AI space face difficult choices. Each autoimmune disease offers multiple targets, multiple delivery mechanisms, different device options, significant patient diversity, and a broad range of symptom presentations. From a commercial perspective, each disease has its own dynamic, driven by some key questions: How effective are current therapies? How many underserved patients are there? What sales/promotion targeting tactics can be used across different types of physicians? How closely are payers scrutinizing the cost of drug therapy? Treatment regimens and drug administration tend to be complex in the space, and AI drugs are often required to have a risk evaluation and mitigation strategy (REMS). Together, these factors mean that pharma companies need to provide significantly more physician, patient, and stakeholder education and higher-touch interaction than in other clinical areas.

AI assets typically have multiple potential applications, not just in additional autoimmune conditions but in other therapeutic areas such as oncology. Companies need to decide how to allocate scientific effort and how to structure and size clinical trials. When evaluating a clinical trial focused on one disease, they need to consider how the results might apply across the full range of relevant diseases. Finally, key decisions on formulations and devices must be coordinated with clinical trial schedules to ensure the drug is developed in a form most useful for patients.
PARTICIPATION OPTIONS

Exhibit 2 maps the current AI pipeline, plotting the number of candidates in Phases II and III against the prevalence of the specific disorder. There are clusters of interest in several areas based on the prevalence of the disease and ability to address unmet need through pharmaceutical intervention.

Exhibit 3 attempts to characterize where the largest pharma players stand in the AI market. By our count, 19 aim to grow their AI franchises:

- Abbott, Roche, J&J, Amgen, and Pfizer are major players with strong multi-billion-dollar sales and large pipelines. These companies have a strong track record in the space and have invested to continue participating in the future
- Another four companies – Biogen Idec, Merck, Teva, and Merck KGaA – are targeted players. They tend to be strong in one area such as multiple sclerosis, with one or two major drugs. These companies may also have extended their presence in other indications such as RA or UC, although the initial lead indication continues to form the mainstay for sales
- The remaining companies we think of as pipeline players. They currently have relatively small AI sales but significant pipeline investments. If these companies succeed with their development programs, they can expect to participate strongly in the space. But in order to succeed, they will have to invest not just in drug candidates but in developing an AI commercial model

EXHIBIT 2: PIPELINE ACTIVITY VS. PREVALENCE – AI DISEASE MARKETS

† Pipeline activity based on data from Pharma Projects Pipeline
†† Prevalence sources: AARDa.org, NIH, Cooper 2003 Autoimmunity reviews, Medscape.com, PDSA.org, Emedicine.com, Moss and Adam’s heart disease in infants, children, and adolescents
### Exhibit 3: Big Pharma Presence in the Autoimmune Space

<table>
<thead>
<tr>
<th>COMPANY</th>
<th>2011 AI Sales ($BN)</th>
<th>Advanced Pipeline††</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Major AI Players</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abbott Labs</td>
<td>7.9</td>
<td>4</td>
<td>• Humira sales strong</td>
</tr>
<tr>
<td>Roche</td>
<td>7.3</td>
<td>10</td>
<td>• Rituxan sales strong</td>
</tr>
<tr>
<td>J&amp;J/Centocor</td>
<td>4.8</td>
<td>7</td>
<td>• Actemra sales increasing</td>
</tr>
<tr>
<td>Amgen</td>
<td>3.7</td>
<td>4</td>
<td>• Remicade sales strong</td>
</tr>
<tr>
<td>Pfizer</td>
<td>3.7</td>
<td>7</td>
<td>• Simponi and Stelara sales expected to increase</td>
</tr>
<tr>
<td><strong>Targeted AI Companies</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biogen Idec</td>
<td>3.5</td>
<td>7</td>
<td>• MS success with Tysabri and Avonex</td>
</tr>
<tr>
<td>Teva</td>
<td>3.0</td>
<td>5</td>
<td>• MS success with Copaxone</td>
</tr>
<tr>
<td>Merck &amp; Co</td>
<td>2.9</td>
<td>4</td>
<td>• Remicade and Simponi sales strong†††</td>
</tr>
<tr>
<td>Merck KGaA</td>
<td>2.4</td>
<td>7</td>
<td>• Rebif sales in MS, RA, UC, and Crohn’s</td>
</tr>
<tr>
<td><strong>Pipeline Companies</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMS</td>
<td>0.9</td>
<td>8</td>
<td>• Ocrenica sales expected to increase</td>
</tr>
<tr>
<td>Takeda</td>
<td>0.6</td>
<td>4</td>
<td>• Enbrel! and Rheumatrex sales</td>
</tr>
<tr>
<td>UCB</td>
<td>0.4</td>
<td>4</td>
<td>• Cimzia sales expected to increase</td>
</tr>
<tr>
<td>Novartis</td>
<td>0.7</td>
<td>14</td>
<td>• Gilenya sales expected to increase in MS</td>
</tr>
<tr>
<td>Sanofi</td>
<td>0.1</td>
<td>7</td>
<td>• Multiple product launches expected across AI indications</td>
</tr>
<tr>
<td>GSK</td>
<td>0.1</td>
<td>12</td>
<td>• Arzerra and Benlysta sales expected to increase</td>
</tr>
<tr>
<td>Astellas</td>
<td>0.01</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>0</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Eli Lilly</td>
<td>0</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Asahi Kasei</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>Current Products Only</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bayer</td>
<td>1.6</td>
<td>0</td>
<td>• Betaferon sales in MS decreasing</td>
</tr>
</tbody>
</table>

† Approximate 2011 sales for all AI indications. Source: EvaluatePharma
†† Advanced pipeline is defined as the number of products in Phase II or further as of 11/1/2011. Source: PharmaProjects Pipeline
††† Marketing rights in certain geographies
Whether companies are new to AI or established players, they have three options for how they participate. As illustrated in Exhibit 4, each option provides a unique risk-reward trade-off. They are probably mutually exclusive, given the resources required to commercialize AI drugs and the challenges associated with each option. Companies need to choose among them based on factors such as the pipeline status, risk assessment, commercial opportunity, and broader strategic fit:

**EXHIBIT 4: THREE OPTIONS FOR PARTICIPATING IN THE AUTOIMMUNE SPACE**

<table>
<thead>
<tr>
<th>ENTER WITH IMPROVED DRUGS IN ESTABLISHED CATEGORIES</th>
<th>ADDRESS DISEASE SUBTYPES WITH FEW OR NO CURRENT THERAPY OPTIONS</th>
<th>ADDRESS DISEASES WITH FEW OR NO DRUG THERAPY OPTIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Requires a significant improvement over current therapies</td>
<td>• Requires the ability to define patient subtypes</td>
<td>• Requires ability to define the disease, set diagnosis and treatment standard, and develop treatment algorithms</td>
</tr>
<tr>
<td>• Provides increased reach across the treatment algorithm or patient flow</td>
<td>• Differential effectiveness in patient subtypes</td>
<td>• Treatment needs to significantly improve on current drug and non-drug interventions</td>
</tr>
<tr>
<td>• Examples: Rheumatoid arthritis, psoriasis, Crohn's disease</td>
<td>• Examples: MS (non-relapsing, remitting), SLE (lupus)</td>
<td>• Examples: Sjögren's syndrome, systemic scleroderma</td>
</tr>
</tbody>
</table>

**Bring improved drugs to established categories.** Some categories – including rheumatoid arthritis (RA), psoriasis, and Crohn’s disease – already have established therapies that delay disease progression, reduce flare-ups, and alleviate symptoms with acceptable safety and tolerability. To succeed in one of these conditions, a drug must do one of two things. It can significantly improve on current therapy – for example an RA drug that causes remission or significantly lowers ACR/EULAR scores. Or, given the fact that no single therapy serves all patients, it can expand the company’s presence across the treatment algorithm. In relapsing-remitting multiple sclerosis (RRMS) this might mean a safer, more effective drug for post-first-line use; in RA, a drug for patients who do not tolerate existing treatments well.

For an example of how to pursue both options simultaneously, consider Biogen Idec, which has created a dominant position for itself in RRMS. (See Exhibit 5.) The company entered the space in 1996 with its interferon beta 1a Avonex as a first-line therapy. Today it is extending the value of this flagship drug with innovations including a pegylated interferon (in development) and a pen-injector Avonex (launched in the EU and Canada). But it is also awaiting approval of BG-12, a new oral monotherapy intended for first-line use. Tsyabri, reintroduced in 2006 fills an important niche in the second line, and the company has reduced its risk profile with a testing kit that identifies patients susceptible to a rare but potentially fatal infection that led to the drug’s temporary withdrawal in 2005. Additionally, Biogen is in partnership with Abbott Laboratories to develop a more balanced benefit-risk profile drug with Daclizumab. And it has obtained the non-US marketing rights for Famprya to help MS patients improve walking distance.
The key to this approach is to build a portfolio that lets you manage more patient types (for instance patients who don’t respond to particular therapies) and manage individual patients as they move through the disease life cycle. With this sort of portfolio, you can offer physicians a simpler, more risk-managed way of treating a spectrum of patients at every stage of the disease.

**Address disease subtypes with few or no current therapy options.** In developing drugs for disease subtypes, the strategy is to gain improved pricing and access to offset a necessarily smaller patient population. For example, there are many drugs for MS – but not for every type of MS. About half of the MS population has the non-RRMS variety, for which there are no effective treatments.

To address an underserved population you have to be able to identify it either clinically or through a companion diagnostic, perhaps supported by additional phenotyping strategies. This can be a complex process. The disease subtype will likely be less well understood, making it difficult to develop drugs or diagnostics. If clinical criteria are going to be used for differential diagnosis, the company will have to work with academic centers, disease advocacy groups, government health bodies, and others to establish those criteria as part of clinical practice. If a diagnostic is required, it will face its own regulatory requirements and will require its own research and clinical trial strategy, which must be coordinated with the drug development program.

---

**EXHIBIT 5: COMPETING IN AN ESTABLISHED CATEGORY – HOW BIOGEN BECAME A TREATMENT ALGORITHM LEADER IN RRMS**

**LINE OF THERAPY**

<table>
<thead>
<tr>
<th>1st</th>
<th>2nd</th>
<th>3rd</th>
<th>4th (last)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABCRs</td>
<td>IL RECEPTOR</td>
<td>T-CELL/B-CELL</td>
<td>OTHER</td>
</tr>
<tr>
<td>Avonex</td>
<td>BG-12</td>
<td>Tredia/Rituxan/Ocrelizumab</td>
<td>Campath/Novantrone</td>
</tr>
<tr>
<td>Daclizumab</td>
<td>ORALS</td>
<td>Infused options, side effects challenging</td>
<td></td>
</tr>
<tr>
<td>Current standard of care</td>
<td>Will compete for 1st line based on dosage form, efficacy</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Companies:**
- Biogen Idec
- Bayer
- MerckSerono
- Novartis
- Sanofi
- Teva
- Other
DEVELOPING NEW TREATMENTS FOR SCLERODERMA

Historically scleroderma has been poorly understood, and the situation is only now starting to improve, thanks in part to patient registries. One notable effort is the German Network for Systemic Scleroderma (D NSS), founded in 2003 with a grant from the German Federal Ministry of Education and Research (BMBF). Among its achievements has been a proposed reclassification of Scleroderma patients to capture them more fully.

Scleroderma is typically diagnosed and treated by rheumatologists or dermatologists, though there is some evidence that patients with musculoskeletal issues are more likely to be first diagnosed by a rheumatologist. But scleroderma (especially the limited cutaneous, diffuse cutaneous, and overlap types) is linked to many comorbidities, and as the disease progresses, treatment requires a broader team of physicians.

In order to increase the understanding of this disease, a host of research projects are under way. On the academic side, funding has been provided by a variety of sources, including the Scleroderma Research Foundation, which provided grants of more than $1 million in 2011-12 alone. On the commercial side, 10 companies, ranging from large companies such as Novartis and Sanofi to small biotechs such as United Therapeutics and Active Biotech are engaged in related projects.

REFINED/NEW CLASSIFICATION-BASED ON GERMAN NETWORK FOR SYSTEMIC SCLERODERMA PATIENT REGISTRY

<table>
<thead>
<tr>
<th>Condition</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Limited cutaneous</td>
<td>674</td>
</tr>
<tr>
<td>Diffuse cutaneous</td>
<td>484</td>
</tr>
<tr>
<td>Overlap syndrome</td>
<td>162</td>
</tr>
<tr>
<td>Undifferentiated</td>
<td>130</td>
</tr>
<tr>
<td>Sclerosis sine scleroderma</td>
<td>22</td>
</tr>
</tbody>
</table>


Address diseases with few or no therapy options. Diseases in this category – including Sjögren’s disease and scleroderma – often create a tremendous disease burden. Severe cases have a relatively poor prognosis. As a result, effective drugs in these areas will likely enjoy tremendous commercial success, but they can be challenging to develop. As the example of scleroderma illustrates (see side page), companies have the best chance of success when they collaborate with a wide range of stakeholders:

- Governmental bodies and associated registries to better understand patient populations and segments and to establish the disease as a significant health issue at a policy level
- Advocacy groups to assist with funding, finding clinical subjects, and lending legitimacy to a pharma company’s efforts
- Research bodies and clinical research sites to evaluate patients, conduct fundamental research, explore potential treatments, and conduct trials
- Academia to broaden the fundamental understanding of disease physiology and explore the full set of avenues that no one company could do on its own
- Physicians of a wide variety to understand not only the disease in its numerous presentations but also address the full set of needs as comorbidities occur
- Other pharmaceutical and biotechnology companies to share the research burden and pool expertise

This third option requires methodical, sustained, and risk-tolerant effort on the scientific, clinical, and business fronts. Its demands are great, but so, potentially, are its rewards.
**AUTOIMMUNE ASSET DEVELOPMENT AND PORTFOLIO IMPLICATIONS**

Drugs for one autoimmune indication are often effective in other autoimmune indications as well. And some may also find use in other categories – especially oncology. Exhibit 7 shows the indications covered by leading AI therapies.

This fact complicates AI portfolio management. Companies can’t analyze a drug asset simply in terms of a single application. Instead, they need to consider all potential uses over the full life cycle, then set development priorities and choose what indications to pursue with how much effort and speed. Clinical trial design, pricing, post-marketing surveillance, and overall management are all affected.

Some especially difficult decisions relate to how indications are sequenced, which has major implications for commercialization and pricing. Is it best to pursue the largest indication first with a drug that is only so-so, or would it be better to go for a smaller indication where the drug can dominate? What is the tradeoff between dollars of revenue and the opportunity to have KOLs and physicians view your company as a leader? How does speed to market change the equation? What about the probability of regulatory success?

In our experience, and that of senior executives we interviewed, the highest-impact indication is usually the one to pursue first. This is the indication that will position the company as a leader and build share of mind with key opinion leaders, physicians, and patients, which is the best way to build a long-term position in a disease space and overall AI. That said, it is common to see a large pharma “swing for the fences” by going after the indication with the greatest number of potential (though not likely) dollars.

At smaller companies, the pressure to “show revenue” can force leaders to select the fastest route to market or the route most assured of regulatory success, even at the cost of being seen as a less valuable product. Almost universally, when we talk with senior managers of these companies, they say this approach caused them to leave money on the table. Their also-ran status in the “easy” indication forced them to charge a low price – and left them underpriced when they came to market with later, more relevant indications.

While decisions like these are intricate and challenging, the organizational issues that accompany them are just as daunting. As the number of possible indications increases, the company must start to wrestle with questions like these:

- From a budget and resource standpoint, can we afford to pursue the full range of feasible indications or only those with a higher probability of success?
- What partnership alternatives would let us take maximum opportunity of multiple applications?
- How do we coordinate research, development, and commercial decisions across multiple disease teams and alliances?
**EXHIBIT 7: LEADING AUTOIMMUNE THERAPIES AND DISEASE COVERAGE**

**KEY COMMERCIAL AND PHASE II/III DRUGS IN MAJOR AUTOIMMUNE DISEASES**

<table>
<thead>
<tr>
<th>TOP FIVE IMMUNO DRUGS†</th>
<th>MECHANISM</th>
<th>COMPANY</th>
<th>AI INDICATIONS††</th>
<th>ONCOLOGY†††</th>
</tr>
</thead>
<tbody>
<tr>
<td>Humira (adalimumab)</td>
<td>TNF Antagonist</td>
<td>Abbott</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enbrel (etanercept)</td>
<td>TNF Antagonist</td>
<td>Amgen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rituxan (rituximab)</td>
<td>CD20 Antagonist</td>
<td>Roche</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Remicade (infliximab)</td>
<td>TNF Antagonist</td>
<td>J&amp;J</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Copaxone (glatiramer acetate)</td>
<td>Unknown</td>
<td>Teva</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**KEY PIPELINE DRUGS**

| Masitinib | Kinase inhibitor | AB Science |                |            |
| Secukinumab | IL-17 Antagonist | Novartis  |                |            |
| Alemtuzumab | CD52 Antagonist | Sanofi    |                |            |
| Ofatumumab | CD20 Antagonist | GSK       |                |            |
| Lenalidomide | TNF Antagonist | Genesis Pharma |                |            |
| Veltuzumab | CD20 Antagonist | Takeda    |                |            |
| Epratuzumab | CD22 Antagonist | TakedaUCB |                |            |

* Top drugs defined by 2010 total sales for AI indications. Source: EvaluatePharma
*†† MS = Multiple Sclerosis, all forms; RA = Rheumatoid Arthritis; PsA = Psoriatic Arthritis; Ps = Psoriasis; Chr = Chrone's Disease; UC = Ulcerative colitis; SLE = Lupus, all forms; AS = Ankylosing spondylitis; T1D = Type 1 Diabetes; Oth. AI = all other AI diseases
*††† C.lym = Cancer, lymphoma; C. leuk = Cancer, leukemia; C. mye = Cancer, Myeloma; C. oth = Cancer, other
• What is our strategy when the drug has high potential in one indication, but will likely be an also-ran in another? What are the implications for internal and external stakeholders?
• What is the appropriate planning horizon? Should we emphasize speed to market in an “easy” indication or wait to commercialize in an indication for which the asset can become a market leader?

As these asset-related issues are being addressed, the company must simultaneously answer important questions of broader organizational scope. How, for example, does the company plan to use biosimilars and bio-betters to occupy more positions in the treatment algorithm, offer the physician additional treatment options, and win against the competition? Can it develop biosimilars internally, or does it need partnerships or acquisitions. What are the management, scientific, and market implications of the choices it makes? This is an area of significant activity at the moment: Biogen’s pegylated interferon, which we mentioned above, is essentially a bio-better supplement to Avonex. Similarly Femta Pharmaceuticals is introducing an “improved Actemra” that blocks IL-6 instead of inhibiting it like Actemra, and Pfizer is working with Trubion to improve on Rituxan and Enbrel. It is worth noting that these companies are not waiting for the creation of a biosimilar regulatory pathway, but simply seeking approval for their drugs as novel biologics. The strategic decisions over biosimilars will become all the more important if a biosimilar pathway is defined, allowing cheaper products to come to market.

There are no stock answers to organizational and strategic questions like these. But there are disciplined ways to approach them. A company needs to base its decisions on its current market/disease area position, size, capacities, and attitude toward risk and rewards. It needs to address the full range of strategic issues, even if that has to happen in phases. Most important, it needs to set a deliberate strategy rather than respond to events after the fact. By taking this approach, a company will ensure that asset value is maximized. (See Exhibit 8.)

EXHIBIT 8: A PROCESS FOR DEVELOPING AN AUTOIMMUNE STRATEGY
SALES/CUSTOMER SERVICE MODEL – A DIRECT-TO-PATIENT MINDSET

Many drugs in the immunology drug space are high-cost biologics. Many require a Risk Evaluation and Mitigation Strategy (REMS). Factors like these mean that AI players need relatively direct, intimate interaction with patients, physicians, and payers in several major areas. Multiple members of the pharma team need to take on new or refined roles:

- Sales representatives need to act as mini-account managers for physicians, providing detailed, clinically oriented data and access to resources such as customer service and medical science liaisons
- The case management team ensures that patients understand their treatment and support options and that they start on therapy, are trained on drug use, and are appropriately monitored
- Reimbursement support provides materials to help physicians make reimbursement representations and ensures that patients are represented with payers if necessary
- Medical science liaisons provide physicians a rich, unbiased understanding of treatment options and evolving treatment paradigms, particularly for hard-to-treat cases
- Field training ensures that patients and providers know how to administer the drug and provider back-offices understand reimbursement processes

The goal is to deliver a comprehensive set of wraparound services. (See Exhibit 9.) To accomplish it, companies need to invest significant time and resources into their own sales force and customer service organization and ensure that they have the capabilities in place to coordinate with outside organizations such as distributors, specialty pharmacies, and nurse trainers.

EXHIBIT 9: AN AUTOIMMUNE WRAPAROUND SERVICE NETWORK

Wraparound service stakeholders

<table>
<thead>
<tr>
<th>Pharmaceutical company</th>
<th>Medical science liaisons</th>
<th>Case management call center</th>
<th>Reimbursement call center</th>
<th>Distr./3PL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sales</td>
<td>Health and disease management</td>
<td>Reimbursement support</td>
<td>Nurse/visits/training</td>
<td>Provider training</td>
</tr>
<tr>
<td>Health and disease management</td>
<td>Reimbursement support</td>
<td>Nurse/visits/training</td>
<td>Provider training</td>
<td>Spec. Pharma</td>
</tr>
</tbody>
</table>

Physician/small groups | Large hospitals/networks | Patients
A good starting point is the company’s own sales representatives. AI sales reps typically handle a single drug or a very small portfolio. They are rigorously trained and have a deep scientific understanding of the disease pathology and the state of current research, which allows them to comfortably engage specialist physicians on their questions. They provide a range of services, including:

- Detailed drug information, training, and education
- Support in managing REMS requirements
- Connecting key opinion leaders, other physicians, and the company’s medical science liaisons
- Supporting physicians in setting up reimbursement and payer-interfacing systems

Because many autoimmune therapies are expensive, payers have created detailed reimbursement requirements for them, including coding and pre-authorization requirements and step edits. Sales organizations can provide support in these areas through one-on-one sessions in the office, regional training sessions, and visiting “SWAT teams” that help resolve particularly difficult individual cases.

Manufacturers of high-priced, clinically sensitive biologics also typically provide a range of services directly to patients, often with the help of a specialized group focused on a particular disease. Many of these services focus on case management, including:

- Patient education and training on drug administration
- At-home nurse visits
- Navigation to alternatives to infusion centers, physicians who offer therapy, supportive care providers, advocacy groups, etc.
- Follow-up on drug effectiveness and compliance related services

In addition, patients receive reimbursement assistance. Reimbursement specialists gather detailed health insurance information from the patient, understand the recommended treatment regimen, and determine the patient’s ability to pay. Using that information, they coordinate with the physician’s office, patient, the drug company’s patient financial assistance program, and the payer to ensure appropriate reimbursement.

All of these wraparound services are delivered through a complex set of insourced teams and outsourced providers as shown in Exhibit 9.

To deploy these high-touch services successfully, a company needs an independent, disease specific customer and reimbursement services group with a high level of empowerment, decision-making authority, and resource/budgetary independence from the brand team. Together with the commercial, clinical, and compliance teams, this group must decide the extent to which services will be outsourced or managed in-house (with the understanding that the reimbursement team must retain significant in-house capability across all services to ensure that they are well executed). There is substantial evidence that when provided well and
in a way that stakeholders view as appropriate and reliable, patient services like these provide a tremendous benefit to patients, providers, and the company. They can result in faster drug uptake at launch, a greater rate of first prescription fills (one company said its “never start” rate dropped from 20% to 5%), improved compliance, and lower levels of switching.

Patient and provider wraparound services take time to set up: In our experience, it takes about 15 to 18 months to get from initial planning, through piloting, to launch. After launch, additional effort is required to fine-tune the program, determine how to optimize economics by deploying it across other similar drugs in the space, and promote organizational learning of the patient sub-types and their flow across drugs. The investment required is substantial: In the initial stages of introduction, a single $500 million to $1 million drug for a disease such as MS or RA requires a case management staff of 50 full-time equivalents or more, plus technology infrastructure and management oversight. And there needs to be a long-term commitment if the program is to be credible with stakeholders.

Do wraparound services offer a favorable return on investment? At the moment, that is an almost impossible question to answer. But given the benefits the services provide and the need to maintain competitive parity, the more successful among Oliver Wyman’s clients have generally taken a leap of faith. We think they have chosen well.

PAYER LANDSCAPE

For the moment, access and pricing in most areas of AI follow a similar pattern. In these areas, we would expect payers to respond to new drugs roughly as they have responded to Gilenya, a novel therapeutic for RRMS, which launched in September 2010. The drug has raised some safety concerns, which may limit future growth, but it has a differentiated mechanism of action and an oral formulation. It represents an improvement on the standard of care, and payers have been willing to grant it pricing of approximately $48,000 per year – roughly 35 percent above in-market therapies. (See Exhibit 10).

A notable exception to this pattern can be seen in RA, where the dynamics are quite interesting. First, drugs in the leading class of therapy, the anti-TNFs, have been very successful at managing the disease – so much so that the American College of Rheumatology has started to consider clinical standards for remission of the disease. There are multiple anti-TNFs on the market at an average cost of about $20,000 a year. Furthermore, biosimilars for RA products may hit the market in some parts of the world in 2015-16.

This is the context in which new oral agents such as Pfizer’s JAK 3 inhibitor, Tofacitinib, are coming to market. Tofacitinib, currently in the registration phase with FDA and expected to commercialize soon, will be introduced based on a comprehensive set of trials showing some patient improvement at both ACR 20 and ACR 50 and non-inferiority to the currently leading biologic (Abbott’s Humira). As Pfizer considers its access strategy, it will have to weigh the benefits that Tofacitinib offers (convenience of administration, novel mechanism
of action, results comparable to anti-TNFs, potentially reduced need to cycle therapies, etc.); compare them with the drug’s side-effects (higher potential for infection than Humira, cardiovascular risks, etc.); and assess the challenge of getting physicians and patients to adopt a new mechanism. In the face of strong competition from anti-TNFs, the prospect of biosimilars, and Pfizer’s desire to drive uptake among rheumatologists – typically a conservative group – the pricing analysis will have to include a broad spectrum of factors. Given the pushes and pulls, and the degree of competition that the drug will face, a premium price strategy is unlikely. But the company will have to give careful consideration to how it structures pricing, how big a discount it offers, and whether it wants to explore the possibility of a performance-based arrangement.

Beyond RA, we see no immediate access and pricing challenges in AI. That said, we believe that in the long term, as the larger indication spaces become more competitive and biosimilars become available, the space will come to look more like oncology in Europe – with more treatment guidelines, risk-sharing agreements, and capitated payments. Drugs in this category will have to perform well to gain preferential access treatment. A candidate going into Phase III today will almost certainly launch in a market with an access environment significantly different from today’s. A pharmaceutical company putting a molecule into development today needs to focus on cost of care and patient outcomes if it intends to satisfy the future expectations of payers.

EXHIBIT 10: COMPARATIVE ANNUAL DRUG COSTS FOR MS

ANNUAL COST $US

New product

<table>
<thead>
<tr>
<th>Drug</th>
<th>Immuno-modulator</th>
<th>Monoclonal antibody</th>
<th>Immuno-modulator</th>
<th>Interferon Beta</th>
<th>Interferon Beta</th>
<th>Interferon Beta</th>
<th>Interferon Beta</th>
<th>Anti-CD 20</th>
<th>Immuno-suppressant</th>
</tr>
</thead>
</table>
SUMMARY

We believe there will be losers as well as winners in AI, and companies should take steps to reduce their risk of loss. Here are four of the most important:

• When you are choosing which disease markets to participate in, make decisions that fit your portfolio and resource profile and afford you the best chance of success. Sometimes the best choice will be one of the smaller markets.

• Think carefully about the development plan for each molecule. A crucial step: When you select which indications to pursue and in what order, base your decisions on the competitive and internal factors governing commercial success.

• Develop “direct-to-patient” commercial abilities to assist patients with enrollment, start up, and reimbursement for new agents – especially biologics.

• Lastly, do not lose sight of the future. Affordability issues, competition, and the availability of biosimilars will reshape AI over the next few years. Development decisions today must consider the access and commercial market of tomorrow.

The autoimmune space is becoming more and more crowded as pharma companies double down their bets in areas that offer the greatest potential. That is a reasonable response: There is an attractive level of unmet need in autoimmune diseases and successful drugs receive favorable pricing treatment. But it is a space with many challenges: The pathologies are not well understood and drug development is inherently riskier. And, we cannot overemphasize, AI has its own commercial model rooted in close engagement with patients. Success in the space will require years of commitment and effort by many in the organization. But for those who understand the path forward and are up to its challenges, we believe that autoimmune is and will remain one of the industry’s most attractive classes of drugs.
ABOUT OLIVER WYMAN

Oliver Wyman is a global leader in management consulting. With offices in 50+ cities across 25 countries, Oliver Wyman combines deep industry knowledge with specialized expertise in strategy, operations, risk management, and organization transformation. The firm's 3,000 professionals help clients optimize their business, improve their operations and risk profile, and accelerate their organizational performance to seize the most attractive opportunities. Oliver Wyman is a wholly owned subsidiary of Marsh & McLennan Companies [NYSE: MMC], a global team of professional services companies offering clients advice and solutions in the areas of risk, strategy, and human capital. With 52,000 employees worldwide and annual revenue exceeding $10 billion, Marsh & McLennan Companies is also the parent company of Marsh, a global leader in insurance broking and risk management; Guy Carpenter, a global leader in risk and reinsurance intermediary services; and Mercer, a global leader in human resource consulting and related services.

Oliver Wyman’s Health & Life Sciences practice serves clients in the pharmaceutical, biotechnology, medical devices, provider, and payer sectors with strategic, operational, and organizational advice. Deep healthcare knowledge and capabilities allow the practice to deliver fact-based solutions.

For more information, visit www.oliverwyman.com.

Follow Oliver Wyman on Twitter @OliverWyman.

ABOUT THE AUTHORS

Mark Mozeson is a Partner in the Health & Life Sciences practice at Oliver Wyman. He has extensive expertise in the Pharmaceutical, Biotech, and Medical Device sectors and leads our practice focus in Managed Markets and Pricing, Reimbursement, and Access. He can be reached at mark.mozeson@oliverwyman.com.

Elizabeth Shakhnovich is an Associate in the Health & Life Sciences practice at Oliver Wyman. She can be reached at elizabeth.shakhnovich@oliverwyman.com.