

Market Overview and Upcoming Players in Graft vs. Host Disease

Perspective on the Changing Treatment Landscape

Market Overview

The global Graft vs. Host Disease (GvHD) market is expected to record a CAGR of more than 28.5% during 2021–2028. The market is moderately competitive, with a few key players, and it continues to be dominated by corticosteroids

Market Size and Growth



28.5%
(2021-2028)

- The global GvHD market stood at approximately USD626 million in 2022 and is expected to reach USD1.7 billion by 2028
- The major contributors towards the market growth are
 - **Rising prevalence of cancer in patients**
 - **Growth of the geriatric population**
 - **Increasing incidence** of bone marrow and allogenic transplants globally
 - **Increasing incidence of cGvHD** [the next stage of aGvHD for >50% of GvHD patients]
 - **Refractory nature of GvHD** (i.e., high likelihood of recurrence after initial treatment)

Key Market Players



JAKAFI



IMBRUVICA



REZUROCK



ORENCIA

These four players make up the key branded products pool for more targeted treatments, though they have not been able to challenge the dominance (in volume terms) of corticosteroids in the GvHD market

Epidemiology

The US market has the largest incidence of GvHD and is forecasted to record a CAGR of >15%



Europe has high incidence of GvHD, with Germany reporting the highest incidence within Europe

Asia is expected to show the fastest growth in incidence of GvHD, due to its high occurrence in Japan

- **aGvHD can occur in ~50% of patients** receiving HSCT from an HLA-matched sibling
- **The global incidence of chronic GvHD ranges from 6–80%**
- In 2020, **aGvHD accounted for 11,638 GvHD cases, while cGvHD accounted for 7,854 GvHD cases globally**

Current Market Revenue Share



2022



2031
forecast

- **Corticosteroids** accounted for **~28.97% of market revenues** in 2022 due to wide recommendation in frontline settings
- **Immunosuppressants** dominated the market with **32.91% of revenues** in 2022 due to their ready availability as over-the-counter drugs

The market is forecasted to shift away from corticosteroid use in the coming years. By 2031, **immunosuppressants are expected to contribute 40–45%** of market revenues, with **15–20%** coming from **corticosteroids**

Commercialization Strategies of GvHD Players

Strategies include establishing effective marketing and distribution models, collaborating with big pharma, and designing patient support programs

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Marketing and Distribution

- As GvHD is a niche indication with a limited patient pool, companies deploy **specialty sales forces for marketing** and engage with **specialty pharmacies** and **distributors** for distribution to offices, clinics, and hospitals
- In addition to treatment centers, **JAKAFI** is delivered through **direct mail** and **direct delivery** to the patient's pharmacy
- Companies engage with **patients and HCPs** through awards, web apps, and educational video guides
- Other approaches and tools include **social media advertisements, television, online posts and videos, KOL seminars, and DTC campaigns**

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Acquisitions and Partnerships

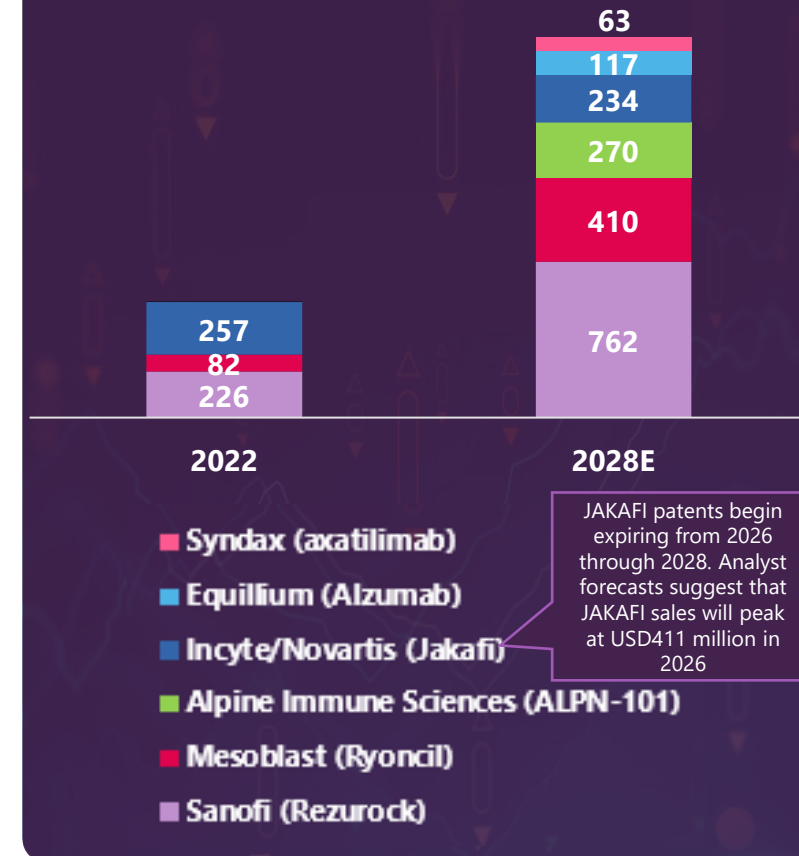
- Recent examples
 - Pharmacyclics** (a subsidiary of AbbVie) **partnered with Janssen** for IMBRUVICA
 - Incyte** **partnered with Novartis** for JAKAVI outside the US
 - Sanofi** **acquired Kadmon Holdings** to add REZUROCK to its transplant portfolio
- Commercial partners focus on marketing **in a particular geography** that generates more revenue
- Distribution partnerships**, a type of commercial partnership, are with **specialty pharmacies and distributors**

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Patient Support Programs (PSPs)

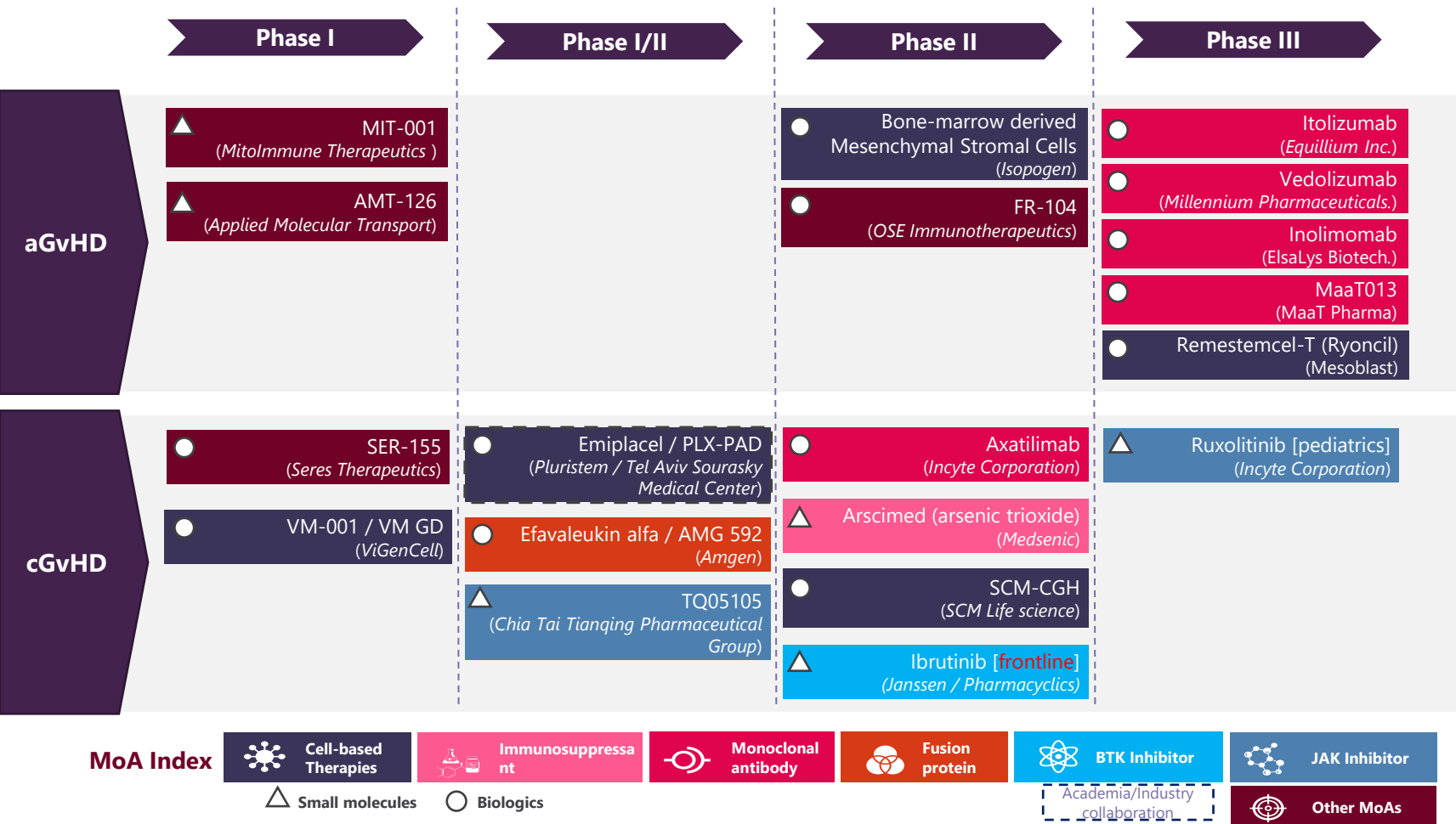
- Companies set up PSPs** to help with education about and access to treatment, insurance, out-of-pocket costs, and patient support
 - Janssen / IMBRUVICA:** By Your Side
 - Incyte / JAKAFI:** IncyteCARES
 - BMS / ORENCIA:** On Call
 - Sanofi / REZUROCK:** Kadmon ASSIST
- Cost-saving options** such as reimbursements and discounts can help eligible patients get temporary coverage or pay only USD0–10 / month with co-pay arrangements
- The programs also provide **support options** like 24*7 on-call support, nurse educators, connection to advocacy groups, and other benefits

Top Market Players by Annual Sales (USD million)



Key Pipeline Therapies

Historically, GvHD treatment has primarily been pharmaceutical. However, the present clinical pipeline is likely to herald a paradigm shift, as it contains several biologics that offer more specific and targeted treatment options



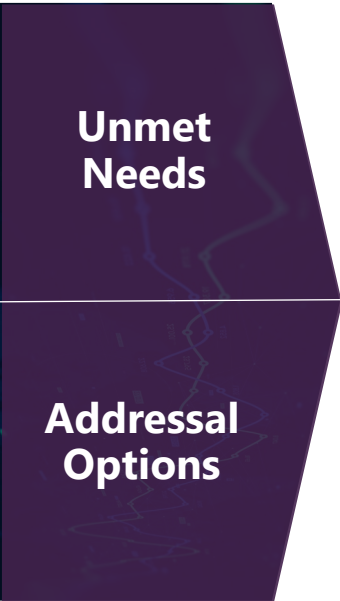
Market Insights

- Acute and chronic GvHD pipelines are **dominated by biologics** as compared to small molecules
 - The **late-stage pipeline for acute GvHD** consists mainly of **monoclonal antibodies (mAbs)**
 - mAbs are targeted therapies with low risk of toxicity and **better response rates / ORR (60–75%)** and **overall survival / OS (40–55%)** than conventional therapies such as steroids or CNIs with response rates as low as under 50%
- Cell therapies** are also being evaluated for both acute and chronic cases
 - In January 2023, a **BLA seeking approval of remestemcel-L** for pediatric patients with SR aGvHD **was resubmitted** to the US FDA
 - If approved. It would be the first allogeneic off-the-shelf cell therapy in the US for this population
- The cGvHD pipeline is more diverse**, with novel mechanisms and types of therapies, while the aGvHD pipeline is focused more on mAbs and stem cell therapies
- Manufacturers of drugs like **JAKAFI** and **IMBRUVICA** are considering **label expansions into pediatrics** and **frontline settings**

Note: This is an indicative list of key pipeline assets in acute and chronic GvHD. This is not the comprehensive clinical pipeline.

Unmet Needs and Options to Address Them

The outlook for steroids-based treatment is not promising, with 95% mortality and 53% five-year survival. To limit the use of steroids, some game-changing therapies are expected to be approved soon, which could address current unmet market needs in the following areas



Diagnosis

1. Identification of **biomarkers for early detection and treatment**
2. **Better understanding of disease biology** and identification of **specific treatment targets**
3. Identification and definition of **low-risk patient subset** for non-steroid treatment
4. **Accurate diagnosis and scoring** of acute and chronic GvHD
5. **Lack of non-invasive validated diagnostic tools** to diagnose intestinal GvHD, evaluate treatment response, and guide duration of immunosuppression

- Advances in understanding the underlying biology of GvHD have led to the investigation of novel therapies, such as **immunomodulatory and targeted therapies**
- An electronic tool, **the eGVHD App**, has been designed to **improve and harmonize GvHD assessment**. It allows the diagnosis of classic and late acute as well as classic and overlap cGvHD, using the most current guidelines of EBMT and NIH
- **Standard ultrasound and power Doppler are non-invasive tests** that can be used to confirm intestinal-GvHD diagnosis and follow-up in pediatric patients

Treatment

1. **Lack of consensus and standard guidelines** on the optimal treatment approach beyond 1L of treatment
2. **Better initial therapies** or **better prevention**
3. **Frontline therapy for moderate to severe GvHD** (except steroids)
4. **Replacement for corticosteroids**
5. More **effective therapies with better response and improved quality of life**
6. More **FDA-approved products for later lines of therapy**

- Treatments (If approved) that can change the treatment paradigm of 1L from steroids
cGvHD: **IMBRUVICA** (Janssen), **Arcimced** (Medsenic), **Obinutuzumab** (Roche)
aGvHD: **itolizumab / Alzumab** (Equillium)
- **Axatilimab** (Incyte), once approved in 3L, can be an important option for later lines of therapy
- **Remestemcel-L** (Mesoblast) will be the first cell therapy to be approved for pediatrics and adults with severe aGvHD
- As per REACH-5 results, **JAKAFI (Incyte)** could get **pediatric approval** for 2L cGvHD and aGvHD

Commercial

1. **Access to drugs in regions outside the US and EU**
2. **Increased biotech and transplant center collaboration** to improve the implementation of novel therapies
3. **Better reimbursement options** to reduce strain on the healthcare system

- New IRA law may **reduce reimbursement rates** or eliminate dual sources of payment, which could **reduce prices of JAKAFI, REZUROCK, IMBRUVICA, and other products**
- **Companies are implementing new PSPs** to facilitate **better access to their drugs for eligible patients** and to **provide monetary support**

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