

Vasomotor Symptoms in Menopausal Women

Current Developments and Future Opportunities

Vasomotor Symptoms: Disease and Market Overview

The global menopausal hot flashes market is expected to post a CAGR of 4.5% during the next five years (2022–2027), driven by a rise in the incidence of vasomotor symptoms and increasing R&D studies looking for effective therapies

Vasomotor symptoms (VMS), such as hot flashes or night sweats, are considered the cardinal symptoms of menopause. These are characterized by sudden episodes of rise in blood flow, often to the face, head, neck, chest, and upper back. These episodes cause sensations of extreme heat and profuse sweating



North America is the largest VMS market globally



Among the EU5 countries, the UK and Germany have the highest VMS prevalence



About 80% of women experience hot flashes during menopause transition



Only 20–30% of women in the US seek medical attention for VMS



The hot flashes market is fragmented, with several key players present in the market

Epidemiology

- In 2018, the VMS-prevalent population in the US was ~**19 million**
- A survey conducted in 2019–2020 revealed that
 - The prevalence of **moderate-to-severe VMS was higher in the EU (40%) than in the US (34%)**
 - **About 73%** of US women in the 40–65 age group **are currently not treating** their menopausal symptoms
 - Among the women under treatment, **65% would not opt for hormonal replacement therapy**

Market Size

CAGR 4.5%



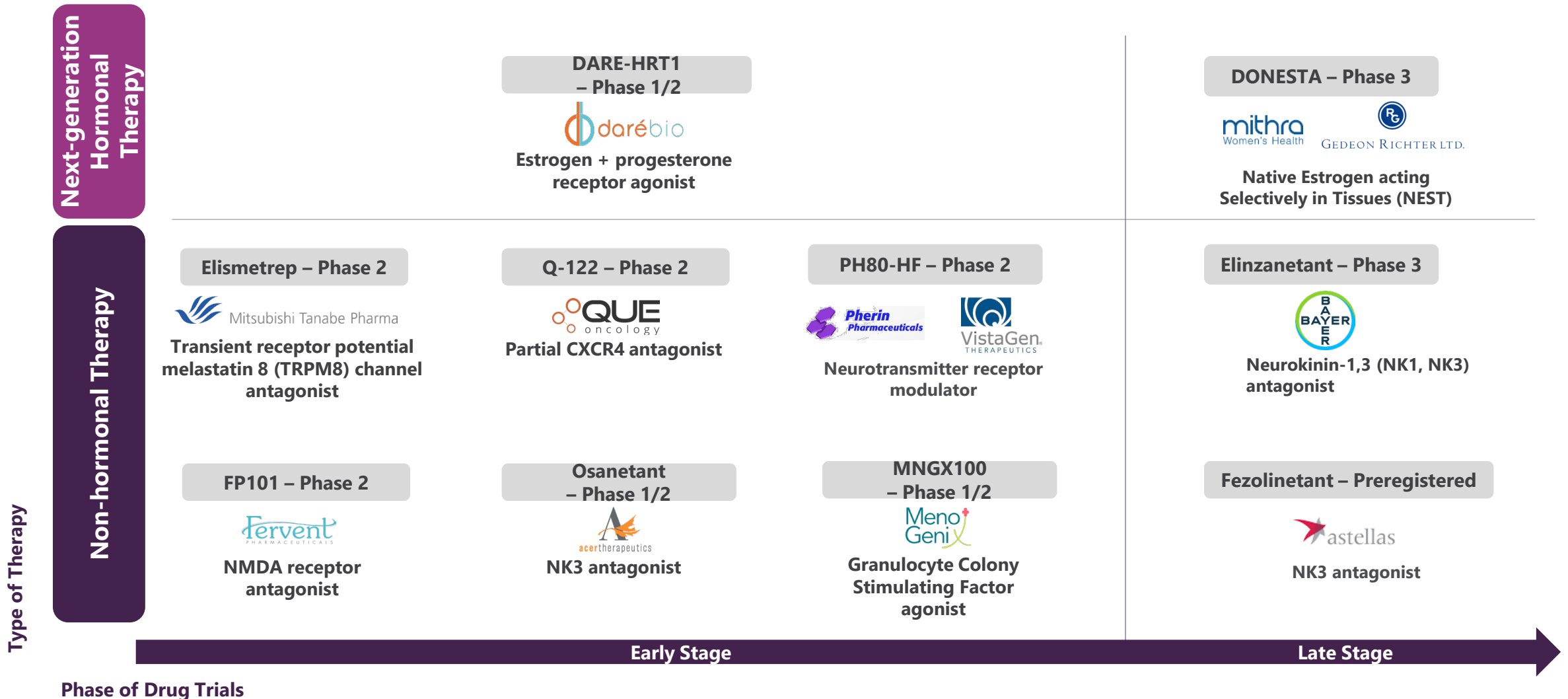
- The global menopausal hot flashes market was valued at ~**USD 16.34 billion in 2022**
- It is **expected to reach USD 20.36 billion by 2027, posting a 4.5% CAGR during 2022–2027**
- By **2025, over 1 billion women** (~12% of the global population) are expected to **experience menopause**, implying lucrative opportunities in the market

Growth Drivers

- **Increasing geriatric population and rising incidence** of menopausal vasomotor symptoms
- Increasing **awareness**
- Changes in **lifestyle** (e.g., smoking, alcohol consumption, and obesity)
- **Technological advancements** and increasing **focus on R&D** of new drugs for treatment, other than hormone replacement therapies
- Demand for **effective drugs** to relieve psychological issues like mood swings and brain fog

Market Map for VMS Pipeline Therapies

Bayer's entry could have a positive impact on growing the VMS therapeutics market (expected to reach ~USD 20.4 billion by 2027) and unlocking significant market opportunities for NK3 antagonists



VMS Hormonal Therapy: Market Landscape

The hormonal VMS market, although declining, may continue to lead among available therapies, given its advantages in treating bone loss and vaginal atrophy along with VMS. Innovative hormonal VMS therapies such as Donesta and DARE-HRT1 may further boost its growth



Key Products



- Well positioned with its stellar products such as **Prempro, Premphase, Premarin, and Duavee**
- Strong patient assistance programs and patient-centered outcome assessment
- Knowledge exchange programs



- Brands such as **Femoston** and **Zumenon** that contribute to its key position in the VMS HT* space
- Inorganic portfolio expansion
- First-mover advantage (launched first generic of Allergan's Estrace in US)



- **Offers Donesta**** (estetrol), a next-generation hormonal therapy
- Safer alternative to low-dose estrogens with positive clinical profile
- **Late-stage Phase 3 E4Comfort studies ongoing**; potential approval in 2024



- **Offers DARE-HRT1**, potentially the first monthly therapy for both VMS and vaginal symptoms of menopause
- Offers an intravaginal ring
- **Positive results in Phase 1/2**; potential approval in early 2026

Highlights from a 2021 IQVIA survey

- Among 500 surveyed women, **46% reported that they seek medical attention** for menopausal symptoms, while 54% said they do not

According to physicians, the **usage of HT treatments** is split as under:

- FDA-approved hormones (37%)
- Other approved hormones (24%)
- Compounded hormones (11%)
- OTC (11%)
- No treatment (17%)

- Donesta has **significant opportunity** to capture market share from the currently treated and untreated women across the US and the EU

Physician opinion on Donesta

- Positive perception as a safe estrogen
- Reduced risk of breast cancer and thrombotic disease
- No drug-drug interactions
- Treats multiple menopausal symptoms

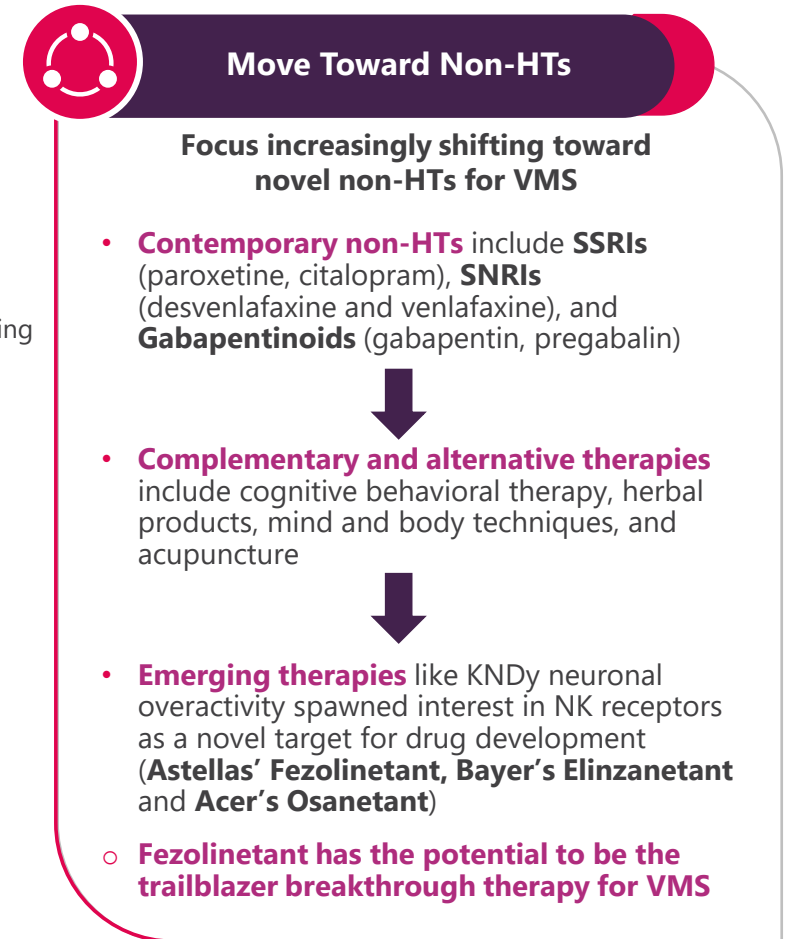
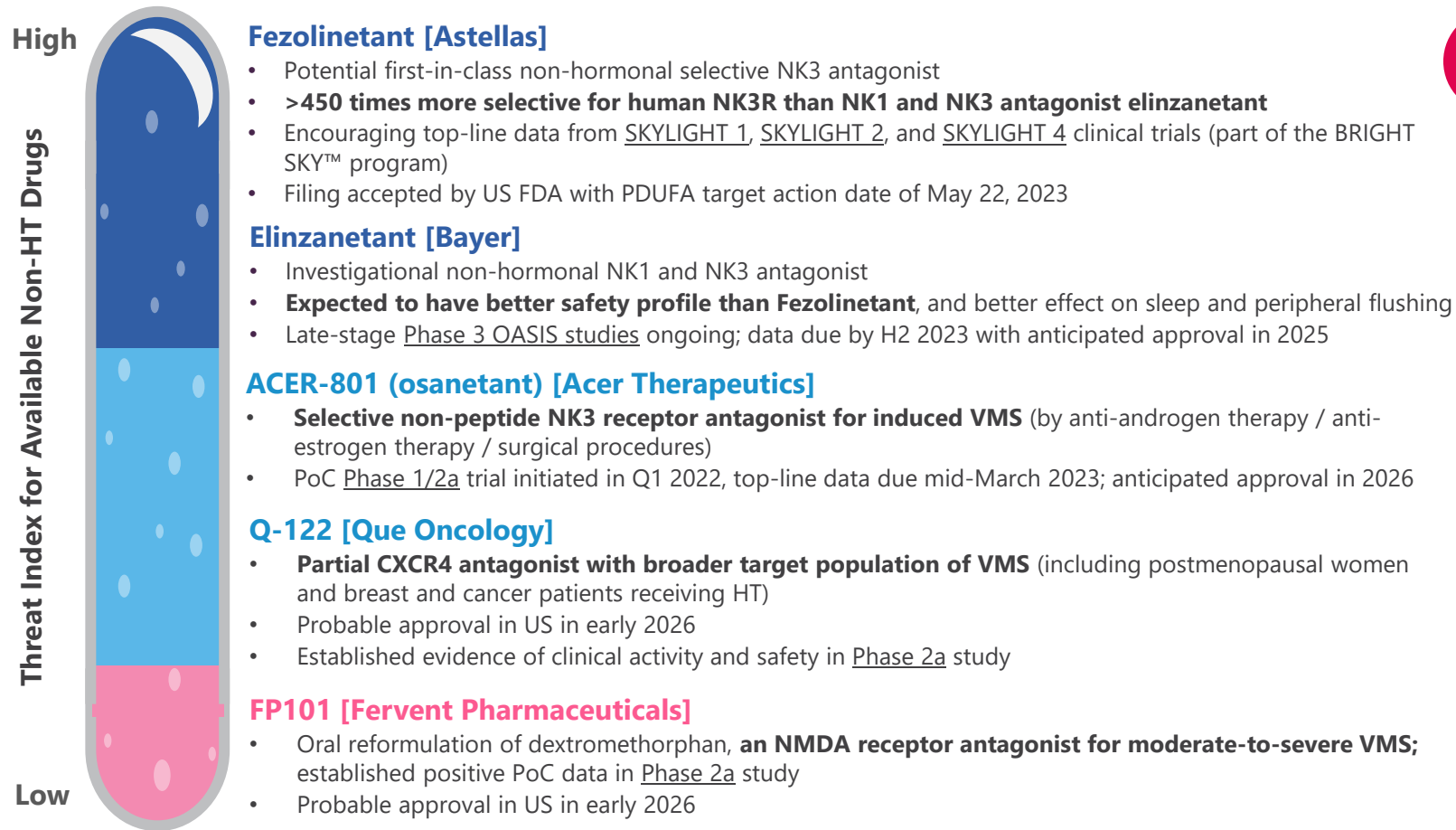
Patient opinion on Donesta

- Considered for treatment by a significant number of women
- Safe profile
- Natural
- Potential to treat many menopausal symptoms

HTs have dominated the market for a long time. However, their market has been consistently shrinking after safety issues (risk of stroke, breast cancer, and CAD) were observed in the early 2000s. Significant unmet need exists for safe and effective non-hormonal therapies.

VMS Non-hormonal Therapy

Non-HT is suitable for women with mild-to-moderate hot flashes, who are against using HTs or prefer not to, have contraindications to HT (e.g., estrogen-responsive cancer, liver disease), or are looking for short-term treatments



Level of threat determined on the basis of clinical activity and current development stage

Sources: 1. Evalueserve analysis; 2. Cortellis; 3. Company websites

NK3 Antagonists: Market Overview

A potentially safer alternative to conventional hormonal and other therapies, NK3 antagonists could soon change the treatment landscape of menopausal VMS

The stimulation of NKB-neurokinin 3 receptor (NK3R) signalling can induce hot flashes, leading to **antagonism of NK3R garnering much interest** among researchers as a **novel therapeutic target** to help ameliorate hot flash symptoms. These drugs work by blocking NKB binding on the kisspeptin / neurokinin / dynorphin (KNDy) neuron to regulate neuronal activity in the thermoregulatory center of the brain (hypothalamus)



NK3 is a more specific treatment than hormone therapies, and it can improve women's QoL



This can be an option for women with prior estrogen-sensitive cancers, blood clots, or age above 60 years



NK3 antagonists are more effective and safer than other alternatives like SSRIs or SNRIs



NK3 antagonists could shake up the VMS treatment landscape, long dominated by traditional HTs



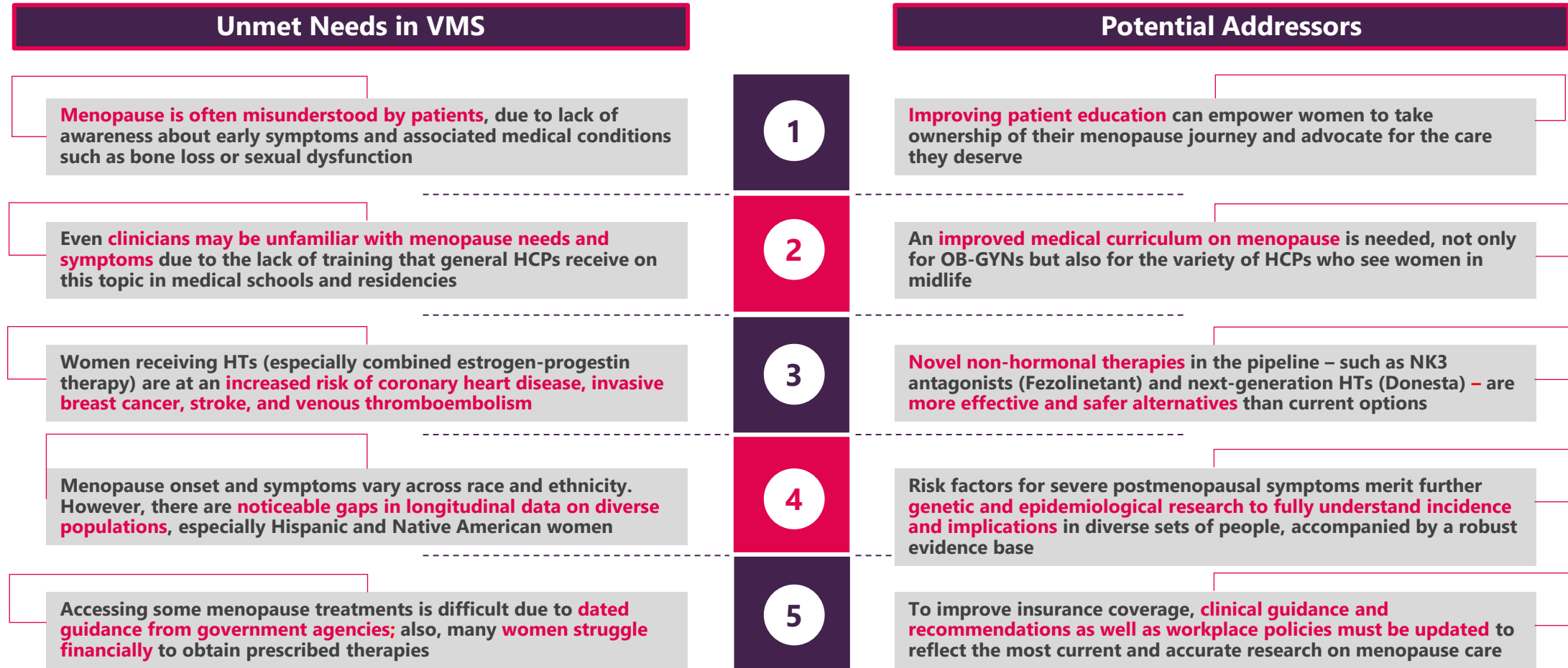
NK3 antagonists will, however, not address other menopausal issues like bone loss and vaginal dryness

NK3 Antagonists Under Development for VMS

	fezolinetant	elinzanetant	osanetant (ACER-801)
Company			
Mechanism of action	First-in-class, non-hormonal, selective, NK3 antagonist	Non-hormonal, NK1 and NK3 antagonist	Novel, selective, non-peptide, NK3 receptor antagonist
Current Status	Pre-registered (in the US)	Phase 3	Phase 1/2a
Approval	PDUFA target action date of May 22, 2023	2025 (reported by company)	2026 (anticipated)
Patient Population Targeted	Moderate to severe VMS associated with menopause	Moderate to severe hot flashes; VMS caused by adjuvant endocrine therapy in women with HR+ breast cancer	Induced VMS (by anti-androgen therapy / anti-estrogen therapy / surgical procedures)
Advantage Over Others	>450 times more selective for human NK3R	Better safety profile and better effect on sleep and peripheral flushing	Broader VMS target population
Other Indications (LCM)	NA	Endometriosis, uterine fibroids	PTSD, prostate cancer

Unmet Needs and Potential Addressors

Menopause is still understudied in research, often misunderstood by providers and patients, unaddressed in many areas of healthcare policy, and in need of more effective and safer therapies that avoid the risks related to HTs



Whitespace Analysis

How can companies maximize their share in the USD20.4 billion (anticipated) VMS market in 2027?



Market Size and Potential



Go-to-market Strategy and Customer Outreach



Competitive Intelligence and BD&L*



Market Access

VMS HT – Mature Market

- Identifying current market pool and its evolution with time
- Observing **sentiments and drivers of patients** currently on HT
- Forecasting market size, including best- and worst-case scenarios**
- Understanding potential **drivers** that companies can leverage

- Lessons that **companies can learn from existing customer-centric journeys**
- Analyzing how a **company is positioned against market leaders** in terms of promotional messaging and customer outreach strategies
- Discussions on how to enhance the marketing and promotional angles

- Identifying **upcoming novel and innovative therapies and monitoring competitor activities in hormonal VMS**
- Analyzing how a company can fence its **market share**
- Identifying **promising licensing and partnering opportunities**

- Identifying the **geographies to focus** on to maximize current market share
- Analyzing how market leaders are competing in those geographies
- Identifying the **niche market spaces / target pools** that can be looked at as potential expansion goals for non-HTs

VMS Non-HT – Emerging Market

- Identifying short- and long-term **drivers / barriers** for patients to move to non-HTs
- Loyalty of customers** to brands and companies during switching
- Proportion of new patient pool** that can be expected to switch to non-HT
- Expected evolution of **treatment landscape** with the entry of Fezolinetant

- Finalizing the appropriate **patient outreach strategies** (i.e., patient support programs, financial assistance, partnerships with patient advocacy groups / non-profit organizations, etc.)
- Evolution of **patient journey** form HT to non-HT
- Analyzing **promotional messaging based on patient and HCP sentiment / perception** and changing dynamics (switching behavior from HT to non-HT)

- Identifying **emerging competition and potential threats**
- Analyzing emerging **clinical trial data** in terms of efficacy and safety
- Estimating **launch timelines** and finalizing **pricing strategy, promotional strategy, product messaging, positioning, and targeting**

- Identifying and analyzing **country-specific pricing and reimbursement scenarios** and the **HTA* assessment** (clinical and cost benefit evaluation)

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Thank you!