VENTURE VALUATION

# PRODUCT VALUATION REPORT

## GT-002 IN SCHIZOPHRENIA BY GABATHER AB

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# EXECUTIVE SUMMARY

## INTRODUCTION

This valuation was commissioned by Gabather AB (Gabather) to help establish a fair and equitable value of GT-002, Gabather's lead product, in the treatment of schizophrenia. Venture Valuation has calculated the rNPV (risk-adjusted net present value) of GT-002 at the point of CTA approval in Q4 2017 and considering two patent protection scenarios:

- Scenario 1, based on current patent protection, which covers Europe and Canada with expiration date of 2029 and the US with expiration date of 2031, as well as China and India (not included in the analysis); and
- Scenario 2, based on patents currently being prepared for submission, covering the above geographies, and including Japan, and with an expected priority date in 2017.

## PRODUCT

GT-002 is a small molecule GABAA receptor modulator and is initially being developed for schizophrenia. GT-002 is in preclinical development, with CTA-enabling studies ongoing. A CTA approval is targeted for Q4 of 2017. Clinical Phase I, single and multiple dose ascending studies in healthy volunteers, are projected to start in early 2018. GT-002 is positioned as an innovative therapy initially indicated in the treatment of schizophrenia, with a novel mechanism of action and the potential for a highly favorable safety profile.

## INDICATION

### Disease Overview

Schizophrenia is a complex, multifactorial and polygenic mental disorder, characterized by the heterogeneous presence of cognitive symptoms affecting perception, thought, attention, memory and emotion. It is among the most disabling and economically catastrophic medical disorders, ranked by the World Health Organization as one of the top ten illnesses contributing to the global burden of disease.

Symptoms of schizophrenia include positive, negative, cognitive and mood symptoms. Although there is no cure for schizophrenia, numerous drugs are available for initial and maintenance therapy, with the goal of controlling symptoms. Second-generation, atypical antipsychotics are the agents of choice for first line treatment of schizophrenia.

### Epidemiology

In 2011, schizophrenia was diagnosed in 21 million people worldwide. According to the WHO, schizophrenia is responsible for 1.1% of total disability adjusted life years, and absorbs 1.5%-3.0% of all healthcare expenditure in developed countries. In Europe, it is estimated that there are about 5 million persons with schizophrenia, with a prevalence of 0.6%-0.8%. The disease affects 1.2% Americans. In 98% of cases disease onset occurs before the age of 40 years with a slight male predominance.

### Target Patient Population

| | prevalence | number of patients 2023E |
|---|---|---|
| Europe | 0.70% | 3.7m |
| US & Canada | 1.20% | 4.6m |
| Japan* | 0.54% | 676'000 |

*Japan patients are considered in Scenario 2 only

MARKET

Competitive Landscape

Existing competitors: A multitude of antipsychotic products are currently available for the pharmacological management of schizophrenia, many of which are already available as inexpensive generics. None of the currently available therapies is curative. There is a large remaining medical need for novel therapies with enhanced safety profiles, as well as for therapies effectively addressing negative symptoms.

Upcoming competitors: There are 360 products in the pipeline for conditions associated with schizophrenia, 60 of which are "first in class", equating to more than 20% of products with a disclosed molecular target. Recent market analysis from Globaldata forecasted that serotonin receptor 5-HT2A antagonists contribute to 36.2% of total revenues in 2025. Most of the upcoming pipeline clinical compounds are phosphodiesterase inhibitors.

There is an increasing body of evidence from genetic and post-mortem studies implicating an altered GABA transmission as a significant component of schizophrenia pathophysiology. Recent research shows that low CSF GABA levels are associated with the severity of illness, psychotic symptoms and attention deficits.(11)

Pricing

We have based the potential cost of treatment with GT-002 on the average of the annual costs of treatment with the antipsychotics Latuda, Invega, Invega Sustenna, Cariprazine, Risperdal Consta, Seroquel & XR, Zyprexa and Abilify.

| In SEK | annual treatment price |
|---|---|
| Europe | 54'620 |
| US & Canada | 68'000 |
| Japan* | 68'428 |

*Japan patients are considered in Scenario 2 only

Sales Forecast

The sales forecast of GT-002 in the treatment of schizophrenia assumes:

- Scenario 1: a market launch in 2023 in Europe, in the US and in Canada.
- Scenario 2: market launch in 2023 in Europe, US and Canada, followed by launch in 2024 in Japan.

**Sales forecast GT-002 worldwide (SEKm)**

| | 2023 | 2024 | 2025 | 2026 | 2027 | 2028 | 2029 | 2030 | 2031 | 2032 |
|---|---|---|---|---|---|---|---|---|---|---|
| Scenario 1 | 965.9 | 3,495.2 | 7,026.0 | 8,826.1 | 12,810.6 | 17,623.9 | 19,402.7 | 17,471.4 | 15,845.0 | 11,529.5 |
| Scenario 2 | 965.9 | 3,581.7 | 7,336.0 | 9,443.6 | 13,579.4 | 18,729.5 | 21,400.9 | 21,669.6 | 21,750.0 | 21,828.7 |

RISK PROFILE

Included in the probability of success:

- Product Development Risk – rated **high;**
- Manufacturing Risk – rated **low to medium;**
- Regulatory/Approval Risk – rated **medium to high;**

Included in the discount rate:

- IP Risk – rated **medium;**
- Partnering Risk – rated **medium;**

- Financing Risk – rated **medium;**
- Competitive Risk – rated **low to medium;**
- Pricing and Reimbursement Risk – rated **medium;**
- Market Uptake Risk – rated **low.**

See body of the report for details.

KEY ASSUMPTIONS

| Variable | VV assumptions | VV Comments |
|---|---|---|
| Patient population | Schizophrenia patients eligible for antipsychotic treatment | Includes patients from first-break onward. |
| Markets | Scenario 1: Europe, US and Canada<br><br>Scenario 2: Europe, US, Canada and Japan | Includes countries covered by patent protection, excluding China and India. |
| Launch year | Scenarios 1 and 2: 2023 in Europe, US and Canada<br><br>Scenario 2: 2024 in Japan | Assuming 7 years of development for Europe and the USA and Canada starting in 2017 (Scenarios 1 and 2), and 4 years of parallel development in Japan starting in 2020, after Europe/US Phase IIb (Scenario 2). |
| Market share | 10% | Upside potential will be realized provided that the safety profile is clearly superior to current generic treatments, and provided there is efficacy in the treatment of negative symptoms. |
| Peak sales | Scenario 1:<br>Europe: SEK 7.6bn (2029)<br>US & Canada: SEK 12.4bn (2030)<br><br>Scenario 2:<br>Europe: SEK 7.6bn (2029)<br>US & Canada: SEK 13.1bn (2038)<br>Japan: SEK 1.7bn (2030) | Scenario 1: Peak sales will be reached at the patent expiration date of 2029 in Europe, and in 2030 in US and Canada where patent life expires in 2031 and 2029 respectively.<br><br>Scenario 2: Peak sales will be reached at the point of population peak in 2029 in Europe and 2030 in Japan, and at the point of patent expiration in 2038 in US and Canada. |
| Cumulative probability of success (6) | 7% | As determined for preclinical stage products in development for the treatment of diseases in the Neurology/Psychiatry field. |
| Cost of development | Scenario 1:<br>SEK 792m<br><br>Scenario 2:<br>SEK 1.16bn | Includes cost of development in Europe, USA and Canada (Scenarios 1 and 2) and Japan (Scenario 2). |
| Discount rate (%) | 20% | Typical for early-stage products. |

## VALUATION

### GT-002 in the treatment of Schizophrenia

Value Range

The value range for GT-002 was determined using the rNPV (risk adjusted Net Present Value) method.

**We note that**, the product value will only then be retained in full by Gabather if they market the product themselves in all geographies included in the current valuation. In the event of a licensing agreement, the product value will be shared between the licensor and the licensee, at a ratio what will be determined by the licensing negotiations.

This results in a present value for GT-002 of SEK 226m in Scenario 1 and SEK 335m in Scenario 2.

| **Product Valuation** | Discount rate | | | | |
|---|---|---|---|---|---|
| in SEKm | 22% | 21% | 20% | 19% | 18% |
| Scenario 1 | 169.5 | 196.0 | 225.9 | 259.5 | 297.3 |
| Scenario 2 | 253.2 | 291.7 | 335.3 | 384.6 | 440.6 |

# INTRODUCTION

Professional background

This report was prepared by Venture Valuation VV AG (Venture Valuation), a company that specializes in the independent assessment and valuation of Life Sciences (biotech, pharma, and medtech) companies and products. Additional information on the company is available at the back of this report.

Assignment

Venture Valuation was asked by Gabather AB (Gabather) to provide an independent, third party valuation of GT-002, the company's lead product. We calculated the value of GT-002 at the point of CTA approval in Q4 2017 and considering two patent protection scenarios:

- Scenario 1, based on current patent protection, which covers Europe and Canada with expiration date of 2029 and the US with expiration date of 2031, as well as China and India (not included in the analysis); and
- Scenario 2, based on patents currently being prepared for submission, covering the above geographies, and including Japan, and with expected priority date of 2017.

Assumptions

All of the assumptions that were made are set out in the body of this report. If any of these assumptions change, the valuation represented herein may change.

Information

In certain instances, we have relied on information provided by Gabather AB, and have not been able to verify or audit the information received. Wherever possible, we have tried to base the opinion set out in the report on our own research and independent sources.

Statement of Independence

This report is based on an independent opinion of Venture Valuation. Our fee in this case is not dependent on the outcome of the value.

# PRODUCT – GT-002 IN SCHIZOPHRENIA

## INDICATION OVERVIEW

Schizophrenia is a complex, multifactorial and polygenic mental disorder, characterized by the heterogeneous presence of cognitive symptoms affecting perception, thought, attention, memory and emotion. It is among the most disabling and economically catastrophic medical disorders, ranked by the World Health Organization as one of the top ten illnesses contributing to the global burden of disease (12). Several complex factors including environmental, social and genetic background are thought to contribute to the development of schizophrenia.

Symptoms of schizophrenia include positive, negative, cognitive and mood symptoms. Positive symptoms consist of hallucinations, delusions, and thought disorders while negative symptoms include apathy, lack of emotions, poverty of speech and poor social life. Cognitive symptoms comprise poor executive functions and disorganized thoughts. There is no known single cause underlying schizophrenia. Anatomic, neurotransmitter, and immune system abnormalities have been implicated in the pathophysiology of the disease.

Although there is no cure for schizophrenia, numerous drugs are available for initial and maintenance therapy, with the goal of controlling symptoms. According to the

American Psychiatric Association, second-generation (atypical) antipsychotics (with the exception of clozapine due to its risk for causing agranulocytosis or seizures) are the agents of choice for first-line treatment of schizophrenia, as they are associated with fewer extrapyramidal symptoms (3).

Since cognitive and negative symptoms rather than positive symptoms are more closely associated with psychosocial impairments in patients with schizophrenia, non-dopaminergic mechanisms including serotonin, glutamate, gamma-amino-butyric acid (GABA), acetylcholine, inflammation and oxidative stress have been proposed as potentially promising therapeutic targets. Long-acting injectable (LAI) antipsychotic medications offer a viable option for patients who are non-compliant with an oral medication (10).

## EPIDEMIOLOGY

In 2011, schizophrenia was diagnosed in 21 million people worldwide (WHO factsheet) (15). According to the WHO, schizophrenia is responsible for 1.1% of total disability adjusted life years, and absorbs 1.5%-3.0% of all healthcare expenditure in developed countries. In Europe, it is estimated that there are about 5 million persons with schizophrenia, with a prevalence of 0.6%-0.8%. The disease affects 1.2% Americans. In 98% of cases disease onset occurs before the age of 40 years with a slight male predominance (2).

Studies have found that incidence of schizophrenia increases in the teen years and reaches a peak of vulnerability between the ages of 16 and 25 years. The pattern of susceptibility to symptoms differs in men and women. Males are more vulnerable to develop schizophrenia between the ages of 18 and 25 years where female vulnerability peaks twice: first between 25 and 30 years, and then again around 40 years of age (9),(12).

Most schizophrenia patients (approximately 80-90%) experience a relapse during the course of their illness. Approximately 10-30% of patients are treatment resistant. The largest unmet medical needs relate to therapies addressing: Cognitive dysfunction; negative symptoms (such as lethargy, apathy, and social withdrawal); refractory patients; adverse events; and lack of compliance (3).

## TARGET PATIENT POPULATION

The projected target patient population for GT-002 is outlined below.

| Country | prevalence | Population that receives a prescription | Compliance rate (1),(7), (8) | Market share | Initial pool of patients (14) |
|---|---|---|---|---|---|
| Europe | 0.70% | 75% | 50% | 10% | 139'000 |
| US and Canada | 1.20% | | | | 172'000 |
| Japan* | 0.54% | | | | 25'000 |

*Japan patients are considered in Scenario 2 only

## PRODUCT OVERVIEW

There is an increasing body of evidence from genetic and post-mortem studies implicating an altered GABA transmission as a significant component of schizophrenia pathophysiology (10). Recent research shows that low CSF GABA levels are associated with the severity of illness, psychotic symptoms and attention deficits (11).

The GABA receptors are a class of receptors that respond to the neurotransmitter gamma-aminobutyric acid, the main inhibitory neurotransmitter in the mature vertebrate central nervous system. GABA receptors influence learning, memory, sleep regulation, pain, anxiety, epilepsy, muscle tension, and various forms of dependence. GABAA receptors are the most common receptors for GABA and are ligand gated ion channels that can be found in various areas of the brain. Benzodiazepines, such as diazepam (Valium) and clonazepam (Rivotril), as well as barbiturates, are well known therapeutic molecules that target the GABAA receptor.

GT-002, a small molecule, is a positive allosteric modulator of the GABAA receptor. GT-002 *in-vitro* was demonstrated to be highly selective for GABAA, and when evaluated in animal models of psychosis and anxiety, did not have sedative or convulsive side effects, while showing promising therapeutic efficacy.

GT-002 is initially being developed in the treatment of schizophrenia; follow on indications could include bipolar disorder, depression, and others. For the purposes of this valuation, we have focused on schizophrenia as the lead indication.

| | |
|---|---|
| Product Development and Timeline | GT-002 is in preclinical development, with IND-enabling studies ongoing. A CTA approval is targeted for Q4 of 2017. Clinical Phase I, single and multiple dose ascending studies in healthy volunteers, are projected to start in early 2018.<br><br>GT-002 in the treatment of schizophrenia is expected to follow a traditional drug development path. |
| Product Positioning | GT-002 is positioned as an innovative therapy initially indicated in the treatment of schizophrenia, with a novel mechanism of action and the potential for a highly favorable safety profile. The molecule's potency will likely be comparable with the potency of diazepam, but with a clearly distinct mechanism of action. |
| Manufacturing | GT-002 will be available in both IV and oral formulations. Gabather is currently working on formulating GT-002 in tablet form, and is completing scale-up and cGMP grade manufacturing runs. |

## REGULATORY CONSIDERATIONS

Gabather will begin discussing the upcoming CTA submission and clinical development plans for GT-002 with the European authorities in June 2017.

## INTELLECTUAL PROPERTY

GT-002 is protected by a family of composition of matter "chemistry" patents that has been issued in the US, Canada, China, India and in Europe. Projected expiration dates are 2029 and 2031.

Gabather is also in the process of filing an additional patent to cover innovations in formulation related to GT-002, among others. The new patent will also be filed in Japan.

# COMPETITIVE LANDSCAPE

## Existing Competitors

A multitude of antipsychotic products are currently available for the pharmacological management of schizophrenia, many of which are already available as inexpensive generics. None of the currently available therapies is curative. There is a large remaining medical need for novel therapies with enhanced safety profiles, as well as for therapies effectively addressing negative symptoms.

The following table summarizes the top-5 drugs for schizophrenia based on their sales in 2016.

| Product | Company | Indications | Mechanism of action | Administration and Dosage | Sales 2016 (USD Million) |
|---|---|---|---|---|---|
| Invega Sustenna (Paliperidone palmitate) | Johnson & Johnson | Schizophrenia, Schizoaffective Disorder | 5-HT2A Receptor Antagonist, Dopamine D2 Receptor Antagonist | Intramuscular (Recommended monthly maintenance dose is 117 mg in adults) | 2,214 |
| Abilify (Aripiprazole) | Bristol-Myers Squibb, H. Lundbeck A/S, Otsuka Pharmaceutical Co Ltd | Schizophrenia, Tourette Syndrome, Autism; Bipolar I, Major Depressive Disorder | 5-HT Reuptake Inhibitor, 5-HT1A Receptor Partial Agonist, 5-HT2A Receptor Antagonist, Dopamine D2 Receptor Partial Agonist | Intramuscular, Oral (10-15mg/day in adolescents and adults) | 1,697 |
| Latuda (Lurasidone hydrochloride) | Sunovion Pharmaceuticals Inc | Schizophrenia, Bipolar I | 5-HT2A Receptor Antagonist, 5-HT7 Receptor Antagonist, Dopamine D2 Receptor Antagonist | Oral (40 to 160 mg /day in adolescents and adults) | 911 |
| Risperdal (Risperidone) | Johnson & Johnson | Schizophrenia, Autism, Bipolar disorders, Bipolar I, Psychiatric disorders | 5-HT2A Receptor Antagonist, Dopamine D2 Receptor Antagonist | Intramuscular, Oral (4-16 mg/day in adults; 1-6 mg/day in Adolescents) | 893 |
| Seroquel (Quetiapine fumarate) | Astellas Pharma Inc, AstraZeneca | Schizophrenia, Bipolar disorders, Bipolar I, Generalized Anxiety Disorder, Major Depressive Disorder | 5-HT2 Receptor Antagonist, Dopamine D2 Receptor Antagonist | Oral (10-750mg/day in adults; 400-800mg/day in Adolescents) | 810 |

## Upcoming Competitors

Late-stage pipeline compounds:

Growth in the schizophrenia market likely will be driven by the potential introduction of the promising late-stage pipeline products, which are directed towards significant unmet needs.

Promising example compounds include:

- ALKS-3831, a fixed-dose combination of samidorphan, a mu-opioid receptor antagonist, and the atypical antipsychotic drug olanzapine, is expected to be launched in the U.S. in the third quarter of 2019.
- AVN-211 has received attention as a potential adjunctive treatment for the cognitive impairments associated with schizophrenia.
- ITI-007 is expected to be launched in the U.S. in the first half of 2018 if it gains FDA approval for the treatment of patients with acute or residual schizophrenia.
- Lu AF35700 is expected to reduce the occurrence of adverse events associated with the use of several antipsychotics, including extrapyramidal symptoms, elevated prolactin levels, dysphoria/anhedonia, and depressed mood.
- RBP-7000, a monthly sustained-release formulation of risperidone, is expected to launch in the fourth quarter of 2017 for acute and maintenance treatment of patients with schizophrenia.
- BB0817, a non-biodegradable, drug-eluting implant, is designed to deliver risperidone for maintenance treatment of schizophrenia patients. NaBen, sodium benzoate, showed greater improvements in negative symptoms and cognitive deficits in a Phase II study and is currently being evaluated in Phase III by SyneuRx and National Institute of Health.

In the table below we outline compounds for the treatment of schizophrenia that are currently in Phase III development.

| Product name | Company name | Molecule type | Mechanism of action | Route of administration |
|---|---|---|---|---|
| ALKS3831 | Alkermes plc | Small | (5-HT2A) Receptor Antagonist, Dopamine D2 Receptor Antagonist, Opioid Receptor Antagonist | Oral |
| AVN211 | Avineuro Pharmaceuticals Inc | Small | 5-HT6 Receptor Antagonist | Oral |
| BB0817 | Endo International plc, Braeburn Pharmaceuticals | Small | 5-HT2A Receptor Antagonist, Dopamine D2 Receptor Antagonist | Subcutaneous |
| DSP5423P | Sumitomo Dainippon Pharma Co Ltd | N/A | Unknown | Percutaneous |
| HP3070 | Hisamitsu Pharmaceutical Co Inc, Noven Pharmaceuticals Inc | N/A | Unknown | Transdermal |
| ITI007 | Intra-Cellular Therapies Inc | Small | 5-HT2A Receptor Antagonist, Dopamine D2 Receptor Antagonist, Dopamine D2 Receptor Partial Agonist | Oral |
| LuAF35700 | H. Lundbeck A/S | N/A | 5-HT2A Receptor Antagonist, 5-HT6 Receptor Antagonist, Dopamine D1 Receptor Antagonist, Dopamine D2 Receptor Antagonist | Oral |
| LY03004 | Luye Pharma Group Ltd | Small | 5-HT2A Receptor Antagonist, Dopamine D2 Receptor Antagonist | Intramuscular |
| Naben | SYNEURX INTERNATIONAL CORP | Small | D-amino acid oxidase inhibitor | Oral |
| RBP7000 | Indivior PLC, Reckitt Benckiser plc | Small | 5-HT2A Receptor Antagonist, Dopamine D2 Receptor Antagonist | Subcutaneous |
| ALKS3831 | Alkermes plc | Small | 5-HT2A Receptor Antagonist, Dopamine D2 Receptor Antagonist, Opioid Receptor Antagonist | Oral |

## Upcoming Competitors Contd.

Pipeline segmentation:

There are 360 products in the pipeline for conditions associated with schizophrenia, 60 of which are "first in class", equating to more than 20% of products with a disclosed molecular target (13). Recent market analysis from Globaldata forecasted that serotonin receptor 5-HT2A antagonists will contribute to 36.2% of total revenues in 2025 (17). Most of the upcoming pipeline clinical compounds are phosphodiesterase inhibitors.

The following table segments the pipeline compounds based on their distinct mechanism of action in schizophrenia.

| Product name | Company name | Development Phase | Molecule type | Mechanism of action | Route of administration |
|---|---|---|---|---|---|
| ALKS3831 | Alkermes plc | Phase III | Small | 5-HT2A Receptor Antagonist | Oral |
| AVN211 | Avineuro Pharmaceuticals Inc | Phase III | Small | 5-HT6 Receptor Antagonist | Oral |
| ADX71149 | Addex Therapeutics | Phase II | Small | Glutamate Receptor, Metabotropic 2 (GRM2) Positive Allosteric Modulator | Oral |
| AQW051 | Novartis AG | Phase II | Small | Alpha7 Neuronal Nicotinic Receptor (NNR) Agonist | Oral |
| AVP786 | Rottapharm SpA | Phase II | Small | N-Methyl-D-Aspartate (NMDA) Receptor Antagonist | Oral |
| F17464 | Pierre Fabre SA | Phase II | Unknown | 5-HT1A Receptor Partial Agonist | Oral |
| GSK239512 | GlaxoSmithKline plc | Phase II | Small | Histamine H3 Receptor Antagonist | Oral |
| GWP42003 | GW Pharmaceuticals plc | Phase II | Small | Cannabinoid CB2 Receptor Agonist | Oral |
| Idazoxan | Pierre Fabre SA | Phase II | Small | Alpha-2 Adrenergic Receptor (ADRA2) Antagonist | Oral |
| MK0777 | Merck & Co Inc | Phase II | Unknown | Gamma-Aminobutyric Acid Type A (GABAA) Receptor Agonist | Oral |
| NE100 | Taisho Pharmaceutical Co Ltd | Phase II | Small | Sigma1 Receptor Antagonist | Unknown |
| NTx028 | Trillium Therapeutics Inc | Phase II | Large | Erythropoietin (EPO) Receptor Agonist | Unknown |
| NW3509 | Newron Pharmaceuticals SpA | Phase II | Small | Sodium Channel, Voltage-Gated, Type III, Alpha Subunit (SCN3A) Blocker | Oral |
| RG1662 | Roche | Phase II | Small | Gamma-Aminobutyric Acid A Receptor, Alpha 5 (GABRA5) Negative Allosteric Modulator | Oral |
| SB223412 | GlaxoSmithKline plc | Phase II | Small | Neurokinin NK3 Receptor Antagonist | Oral |
| SCH900435 | Merck & Co Inc | Phase II | Small | Glycine Transporter-1 (GLYT1) Inhibitor | Oral |

| | | | | | |
|---|---|---|---|---|---|
| TAK063 | Takeda Pharmaceutical Company Limited | Phase II | Small | Phosphodiesterase-10A (PDE-10A) Inhibitor | Oral |
| Arvisol | Echo Pharmaceuticals BV | Phase I | Small | Cannabinoid CB1 Receptor Antagonist | Unknown |
| BI409306 | Boehringer Ingelheim GmbH | Phase I | Unknown | Phosphodiesterase 9A (PDE9A) Inhibitor | Unknown |
| HTL9936 | Heptares Therapeutics | Phase I | Small | Muscarinic M1 Receptor Agonist | Oral |

## Upcoming Competitors Contd.

GABA Modulators in Schizophrenia and other CNS indications:

There is an increasing body of evidence from genetic and post-mortem studies implicating an altered GABA transmission as a significant component of schizophrenia pathophysiology. Recent research shows that low CSF GABA levels are associated with the severity of illness, psychotic symptoms and attentional deficits (11).

The below table summarizes the clinical status of various GABA modulators in Schizophrenia and associated CNS disorders.

| Product | Company | Indication | Development Phase | Mechanism of action | Molecule type | Administration |
|---|---|---|---|---|---|---|
| SAGE 547 | Sage Therapeutics | Depression, Status Epilepticus | Phase III | GABAA Receptor Positive Allosteric Modulator | Small | Intravenous |
| Lorediplon | Grupo Ferrer Internacional SA | Insomnia | Phase III | GABAA Receptor Modulator | Small | Oral |
| RG 1662 | Roche | Schizophrenia, Ischemic stroke | Phase II | GABAA Receptor, Alpha 5 (GABRA5) Negative Allosteric Modulator | Small | Oral |
| ASP 8062 | Astellas Pharma Inc | Fibromyalgia | Phase II | GABAB Receptor Positive Allosteric Modulator | NA | Oral |
| EVT 201 | Evotec AG | Insomnia | Phase II | GABAA Receptor Positive Allosteric Modulator | Small | Oral |
| Ganaxolone | Marinus Pharmaceuticals Inc | Epilepsy, Post-Traumatic Stress Disorder, West Syndrome | Phase II | GABAA Receptor Modulator | Small | Intravenous, Oral |
| PF 06372865 | Pfizer Inc | Epilepsy, Non Nociceptive Pain | Phase II | GABAA Receptor Modulator | NA | Oral |

| | | | | | | |
|---|---|---|---|---|---|---|
| SAGE 217 | Sage Therapeutics | Depression, Major Depressive Disorder, Parkinson's Disease | Phase II | GABAA Receptor Positive Allosteric Modulator | Small | Intravenous |
| CPP 115 | Catalyst Pharmaceuticals | Complex Partial Seizures, Post-Traumatic Stress Disorder, Tourette Syndrome, West Syndrome | Phase I | GABAA Receptor Modulator | Small | Oral |
| AP 325 | Algiax Pharmaceuticals GmbH | Neuropathic Pain, Spinal Cord Injuries | Phase I | GABAA Receptor Modulator | Small | Oral |

Market Share

Based on our analysis, there are currently over 50 new therapeutic products in different stages of development for schizophrenia, of which 11 are in Phase III clinical development. Thus we can safely assume an increasing competition in the future, with new products coming to the market. Based on the pipeline, we could see 5 to 6 new products on the market within 3 to 5 years. This risk has been taken into account in the market share.

## GT-002 SALES FORECAST

GT-002 PRICING

We have based our estimates on the average annual costs of treatment with the antipsychotics Latuda, Invega, Invega Sustenna, Cariprazine, Risperdal Consta, Seroquel & XR, Zyprexa and Abilify.

| In SEK | **Annual treatment price with GT-002** |
|---|---|
| Europe | 54,619 |
| USA & Canada | 68,000 |
| Japan* | 68'428 |

*Japan patients are considered in Scenario 2 only

GT-002 SALES FORECAST

Sales are projected assuming a market entry in 2023 for the US, Canada and Europe (Scenarios 1 and 2) and in 2024 in Japan (Scenario 2).

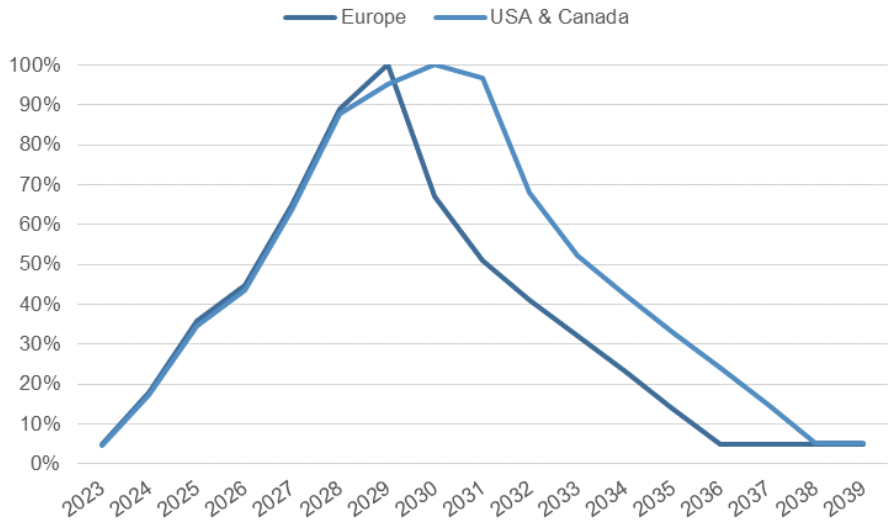
GT-002 SALES FORECAST – SCENARIO 1

| SEKm | 2023 | 2024 | 2025 | 2026 | 2027 | 2028 | 2029 | 2030 |
|---|---|---|---|---|---|---|---|---|
| Europe | 380.4 | 1,370.2 | 2,741.7 | 3,428.1 | 4,952.2 | 6,780.4 | 7,616.7 | 5,101.4 |
| USA & Canada | 585.5 | 2,125.0 | 4,284.2 | 5,398.0 | 7,858.4 | 10,843.5 | 11,786.0 | 12,370.0 |
| Total | 965.9 | 3,495.2 | 7,026.0 | 8,826.1 | 12,810.6 | 17,623.9 | 19,402.7 | 17,471.4 |

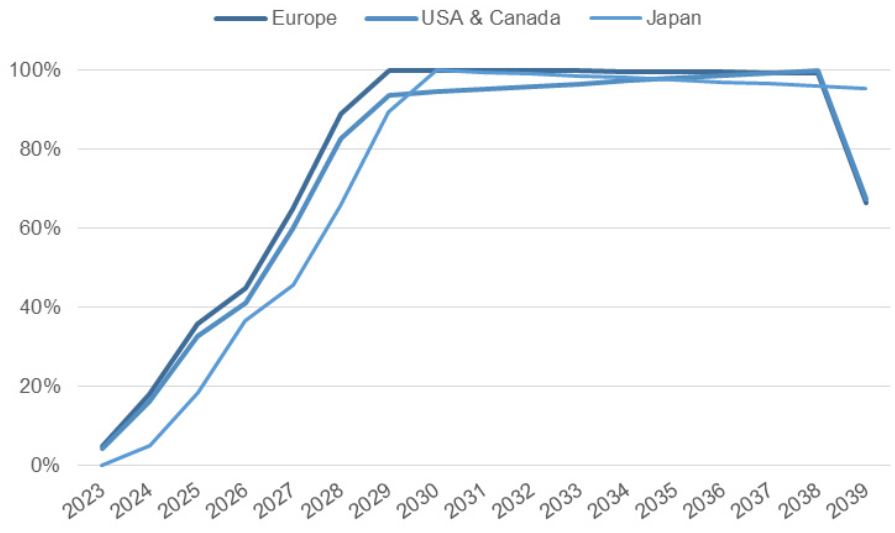
GT-002 SALES FORECAST – SCENARIO 2

| SEKm | 2023 | 2024 | 2025 | 2026 | 2027 | 2028 | 2029 | 2030 |
|---|---|---|---|---|---|---|---|---|
| Europe | 380.4 | 1,370.2 | 2,741.7 | 3,428.1 | 4,952.2 | 6,780.4 | 7,616.7 | 7,614.0 |
| USA & Canada | 585.5 | 2,125.0 | 4,284.2 | 5,398.0 | 7,858.4 | 10,843.5 | 12,277.1 | 12,370.0 |
| Japan | 0.0 | 86.4 | 310.0 | 617.6 | 768.8 | 1,105.7 | 1,507.1 | 1,685.6 |
| Total | 965.9 | 3,581.7 | 7,336.0 | 9,443.6 | 13,579.4 | 18,729.5 | 21,400.9 | 21,669.6 |

MARKET UPTAKE FOR GT-002 IN THE TREATMENT OF SCHIZOPHRENIA – SCENARIO 1




MARKET UPTAKE FOR GT-002 IN THE TREATMENT OF SCHIZOPHRENIA – SCENARIO 2



# RISK ANALYSIS

## RISK ASSESSMENT

### Risk Factors

Below we summarize the risk factors, as we see them associated with GT-002. Risks are presented as product development specific risks and non-product development specific risks.

**We note that**, product specific risks are reflected in a direct risk adjustment as part of the rNPV method, whereas non-product specific risks are reflected in the overall discount rate.

The risk ratings used are designated as low (lower than average as compared to similar products), medium (average), and high (higher than average).

### Product Development Specific Risks

We see the key product development specific risks as follows:

Product Development Risk:

- Risk Rating – **high**. Largely due to early development stage, but mitigated by promising proof of concept results in animal models.

Manufacturing Risk:

- Risk Rating – **low to medium**. Largely due to the fact that GT-002 is a small molecule and manufacturing is typically straight forward.

Regulatory/Approval Risk:

- Risk Rating – **medium to high**. Largely due to novel mechanism of action, risk will decrease to medium once positive clinical safety and efficacy become available.

### Non-Product Development Specific Risks

We see the key non-product development specific risks for GT-002 as follows:

Intellectual Property (IP) Risk:

- Risk Rating – **medium.** Due to limited limited patent life for issued patents. This is mitigated to medium to low, once additional patent filings progress in their path to approval.

Partnering Risk:

- Risk Rating – **medium.** Largely due to high interest from large Pharma companies to add innovative products to their antipsychotic products portfolio.

Financing Risk:

- Risk Rating – **medium.** Largely due to the fact that Gabather is a listed company with access to public capital markets.

Competitive Risk:

- Existing competitive risk: **low to medium.** Due to the limited market availability of effective and safe treatment options for schizophrenia.

- Upcoming competitive risk: **low to medium.** Due to novel mechanism of action, potential for superior safety, some promising late stage examples, and highly limited competitors based on GABA.

Pricing and Reimbursement Risk:

- Risk Rating – **medium.** Due to the fact that new effective and safe antipsychotic drugs are likely to receive reimbursement approval, provided the target price is backed by positive clinical trial results.

Market Uptake Risk:

- Risk Rating – **low** in the short term, driven by the unmet need for a therapeutic product in schizophrenia with superior safety and efficacy profile. In the long run, market uptake will be shaped by the safety/efficacy of earlier stage products currently in development.

# VALUATION

## OVERVIEW

**Methods used**

The risk-adjusted Net Present Value (rNPV) was used to provide an objective assessment of the value of GT-002 in the treatment of schizophrenia.

**rNPV/Risk-Adjusted NPV**

The most appropriate method to value pharmaceutical/biotechnology products is the risk-adjusted net present value (rNPV) method that factors in the success rate of therapeutic products in development. These success rates are then used to discount yearly free cash flows for the entire product lifetime. The full assumptions for the expected revenues from GT-002 in schizophrenia are described in the following sections.

**Deal Value Split**

In the event of a licensing agreement, the product value will be shared between the licensor and the licensee. The deal split in this case will be determined as part of the licensing negotiations (5).

**We note that** the product value will only then be retained in full by Gabather if they market the product themselves in all geographies included in the current valuation. For the purpose of this report, and, as requested by Gabather, we have only included the full value of the product.

## DISCOUNT RATE

**Product specific risks**

Taking into consideration the stage of development and the cumulative success rate of GT-002 in schizophrenia, the probability of a product launch has been determined to be 7%.

| | Success rate (6) | | | | |
|---|---|---|---|---|---|
| | Phase Ia | Ph Ib/IIa | Ph IIb | Ph III | Approval |
| Probability of Success | 60% | 71% | 32% | 63% | 82% |
| Cumulative POS | | 43% | 14% | 9% | 7% |

**Non-product specific risks at 20%**

The non-product specific risks take into account that for the rNPV, the attrition risk of each phase (including the post-marketing phase), has already been included in the risk adjustment. Thus the discount rate only includes risks that are not directly associated with the development of an individual product. We set this risk at 20%.

| Discount rate for rNPV | |
|---|---|
| Risk free rate of return (16) | 0.21 % |
| Systematic risk (4) | 3.60 % |
| Non product specific risks | 16.20 % |
| Discount rate | 20.00 % |

| | |
|---|---|
| Discount rate based on CAPM | Our calculation of the discount rate is based on the Capital Asset Pricing Model (CAPM). The CAPM provides a way to compute Cost of Capital, based on rates of return on debt and equity. Its uses the risk free rate of return as a basis and adds the systematic risk. We also add the non-product specific risk as described above. |

RISK-ADJUSTED NPV VALUATION (rNPV)

| | |
|---|---|
| Calculation based on development plan | The figures for the rNPV calculation were based on information researched by Venture Valuation or provided by Gabather, and adjusted by Venture Valuation. By determining the potential development costs and market revenues of GT-002 using the rNPV method the value of GT-002 in schizophrenia was calculated.<br><br>A median discount rate of 20%, and a range from 18% to 22% for sensitivity analysis were used. |

VALUATION OF GT-002 IN THE TREATMENT OF SCHIZOPHRENIA

Product valuation SEK 226m in Scenario 1 and SEK 335m in Scenario 2

In Scenario 1, the full value of GT-002 is between SEK 170m and SEK 297m. Using a discount rate of 20%, the average value is SEK 226m.

In Scenario 2, the full value of GT-002 is between SEK 253m and SEK 441m. Using a discount rate of 20%, the average value is SEK 335m.

| **Product Valuation** | **Discount rate** | | | | |
|---|---|---|---|---|---|
| In SEK 000's | 22% | 21% | 20% | 19% | 18% |
| rNPV Scenario 1 | 169.5 | 196.0 | 225.9 | 259.5 | 297.3 |
| rNPV Scenario 2 | 253.2 | 291.7 | 335.3 | 384.6 | 440.6 |

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# APPENDIX I: GT-002 VALUATION ASSUMPTIONS

| Criteria | Value | Reference |
|---|---|---|
| Patent expiration | Scenario 1:<br>Europe & Canada: 2029<br>U.S.: 2031<br><br>Scenario 2:<br>Europe, Canada, US, Japan: 2028 | Gabather/ VV assumption |
| Patient population | Schizophrenia patients eligible for antipsychotic treatment | Gabather/ VV assumption |
| Prevalence rate | Europe: 0.7%<br><br>US & Canada: 1.2%<br><br>Japan: 0.54% | WHO |
| Market share | 10% | VV assumption, driven by presence of generics and other competitors |
| Price annual treatment (SEK) | Europe: 54,619<br><br>US & Canada: 68,000<br><br>Japan: 68'428 | Based on the average of the annual costs of treatment with the antipsychotics Latuda, Invega, Invega Sustenna, Cariprazine, Risperdal Consta, Seroquel & XR, Zyprexa and Abilify |
| Peak sales | Scenario 1 (2029): SEK 19.4bn<br><br>Scenario 2 (2038): SEK 22.3bn | Model estimate |
| Total sales (2023-2040) | Scenario 1: SEK 145bn<br><br>Scenario 2: SEK 300bn | Model estimate |

**Key expenses for the product valuation**

| Expense | Value | Reference |
|---|---|---|
| Clinical & Manufacturing expenses (SEKm) | Scenarios 1 and 2:<br>Europe, US & Canada:<br>Phase I (9 months): 1.9<br>Phase Ia (3 months): 9.6<br>Phase Ib/IIa (12 months): 48 | Venture Valuation assumption |

| | | |
|---|---|---|
| | Phase IIb (12 months): 240<br>Phase III (24 months): 480<br>Approval (18 months): 14.4<br><br>Scenario 2:<br>Japan:<br>Phase IIb (12 months): 120<br>Phase III (24 months): 240<br>Approval (12 months): 9.6 | |
| Launch date | Europe, US & Canada: 2023 (Scenarios 1 and 2)<br><br>Japan: 2024 (Scenario 2) | Venture Valuation estimate |
| COGS (% of revenue) | 15% | Venture Valuation estimate |
| Sales & Marketing (% of revenue) | 25% | Venture Valuation estimate |
| Discounts, Returns and Allowances (% of revenue) | 5% | Venture Valuation estimate |
| G&A (% of revenue) | 5% | Venture Valuation estimate |
| Tax rate | 23.5% | OECD average |

# ABOUT VENTURE VALUATION

Mission statement

Venture Valuation specializes in independent assessment and valuation of technology-driven companies in the Life Sciences (biotech, pharma, medtech) and other high growth industries (ICT, high-tech, nanotech, renewable energy).

Besides valuation services, Venture Valuation offers high quality, focused information services based on the company's unique positioning in the industry. Through focus and unique position, Venture Valuation strives to fulfill and surpass customers' needs and add value in the partnership. Clients include investors, companies and development agencies.

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With access to scientific, product development, regulatory affairs, patenting and financial expertise, Venture Valuation is able to provide insightful valuation reports to customers. Company experts perform comprehensive analyses of financial and technical value while accounting for soft factors such as management experience and track record, assessment of scientific and technological quality, intellectual property and market developments and trends.

A valuation report from Venture Valuation helps to highlight critical success factors and strategic elements that will drive a company's value in the long-term. Venture Valuation also has developed a sophisticated system to follow a company's progress, and provides valuation updates based on balanced scorecard measurements. Using Venture Valuation's market expertise the company offers individual product valuations and tools for licensing deal negotiations.

Venture Valuation also provides information services, including Biotechgate (www.biotechgate.com), a global database containing over 35'000 life science companies. As a supplier of unique data, venture valuation is able to fully complement its valuation services with in-depth market and industry knowledge in a growing international market.

Track Record

Since 1999, Venture Valuation has worked with over 400 high growth companies and several prominent venture funds, including Novartis Venture Fund and the European Investment Bank, providing evaluations of companies and products.

The solidity of Venture Valuation's approach has been validated by a number of publications, including articles in high-profile journals such as Nature Biotechnology. Venture Valuation experts are invited on a regular basis to provide seminars and courses to top-ranking business schools such as IMD and EPFL and have contributed to several books on the valuation of high growth companies.

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