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INDEPENDENT EQUITY RESEARCH

Initiation of Coverage Report **12 June, 2018**

Kadimastem offers treatment of diabetes and neurological diseases such as ALS by cellular therapy; Company is pursuing clinical trial (ALS), and pre-clinical processes (diabetes); target price set at NIS 0.85

Primary Exchange: TASE

Ticker: TLV:KDST

Sector: Healthcare

Industry: Pharmaceuticals

Data as at 12 June, 2018
(Source: TASE)

Closing price: NIS 0.53

Market cap: NIS 32.3M

# of shares: 61.6M

Stock performance (12 mos.): -77%

Daily-trading-vol. (12 mos.): NIS 205k

Stock target price: NIS 0.85

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Company Overview

Kadimastem Ltd. (hereinafter "Kadimastem" or "the company") is a clinical stage biopharmaceutical company that specializes in developing different types of human body cells (known as differentiated cells) – such as neural cells (e.g. oligodendrocytes and astrocytes) and insulin secreting beta cells, derived from human embryonic stem cells. The company has its technological platform and two current stem cell based therapies in research phase – AstroRx (consists of astrocytes, a type of brain cell) and Encapsulin (insulin secreting beta cells) for treating amyotrophic lateral sclerosis (ALS) and diabetes respectively.

Highlights & Analysis

Kadimastem addresses the global ALS therapy market, which stood at $53M in 2016 and is expected to grow to between $468M and $840M million by 2021, as new therapies enter the market.

- According to the company, ALS also has a heavy economic burden with estimated healthcare expenditure at $6B p.a. in the US alone.
- The company expects to complete phase I/IIa clinical trials by August 2020. If it is able to demonstrate the efficacy and safety of AstroRx in treating ALS patients, it can further evaluate its AstroRx therapy for treating other neurological disorders.
- Research suggests that astrocytes can play a positive role in Alzheimer's disease, Parkinson's disease, multiple sclerosis and epilepsy – diseases with no cure and pressing unmet needs.

The market for insulin is expected to grow at a CAGR of 8.3% and reach $43.6 billion by 2021. [1] **Although the market is highly competitive, we assume there is room for innovative companies, to enter and grow.**

- The company is developing its diabetes program in collaboration with French based medical device manufacturer Defymed.
- The companies' plan to conduct a joint proof of concept pre-clinical test to combine the former's stem cell derived - islet-of-Langerhans-like cell clusters (insulin secreting beta cells) with the latter's medical device (MailPan) and evaluate the efficacy of the combination in treating diabetes.

We estimate the company's equity value at NIS 52.11M ($14.64M) corresponding to a target price ranging between NIS 0.77 and NIS 0.93; a mean of NIS 0.85.

- 2019 will be a crucial year for Kadimastem with the forecasted release of one early-stage clinical trial results and a POC trial, both which have the potential to impact the company's strategic position within the stem cells domain.
- We see both short and long term investment potential in Kadimastem stock.

Executive Summary

Investment Thesis

Kadimastem Ltd. (hereinafter “the Company" and/or " Kadimastem”) is an Israeli publicly-traded specialty biopharmaceutical company focused on the development of stem cell-based therapies.

Indication 1: In March 2018 it began its first clinical trial, a phase I/IIa study using astrocytes, for treating ALS, which is expected to be completed by August 2020. There are just two drugs currently approved by the FDA for treating ALS – Rilutek (riluzole), which was approved in 1995 and now has several generic alternatives, and Radicava (edaravone), which received FDA approval in May 2017. None of the drugs can reverse or even halt the progression of ALS. While riluzole is a glutamate antagonist that has been shown to extend the life of ALS patients by up to 3 months,[1] Edaravone is a free radical scavenger that delays progression of disability.

There is one stem cell-based therapy (consisting of mesenchymal stem cells), Neuronata-R, which is marketed by Corestem and has been approved in South Korea since 2014. Corestem is potentially looking to apply for US approval either in late 2018 or in early 2019.

Another stem cell-based therapy (again based on mesenchymal stem cells) is BrainStorm Cell Therapeutics’ (BrainStorm) NurOwn, which is currently undergoing phase III clinical trials. If the trial is successful, the company is expected to launch NurOwn by 2020. Both the therapies (Neuronata-R and NurOwn) require isolation of mesenchymal stem cells from a patient and developing them into the final product. The whole process takes several days (e.g. NurOwn needs about 28 days) and requires a laboratory for the isolating and processing of the cells. This limits Corestem’s and BrainStorm’s ability to provide therapy to ALS patients, which are spread across regions. Kadimastem’s AstroRx, as an off-the-shelf product, does not face such challenges.

The global ALS therapy market stood at $53M in 2016 and is expected to grow to between $468M and $840M million by 2021 (based on conservative and optimistic scenarios respectively), as more therapies are introduced to the market.[2]

Indication 2: For its diabetes program, the company has also signed a memorandum of understanding with Defymed, a France based manufacturer of medical devices, to jointly develop a device for the treatment of diabetes. The medical device will be targeted at diabetic patients who currently take insulin to manage their blood glucose levels. The market for insulin is expected to grow at a CAGR of 8.3% till 2021 when the market is projected to be valued at $43.6B.[3] Although the market is highly competitive, we assume it has room for companies with innovative mechanisms for addressing diabetic patient needs, to enter and grow.

2019 will be a significant year for Kadimastem with the forecasted release of one early stage clinical trial and one proof of concept, both of which have the potential to impact the company’s strategic position within the stem cells domain. We see investment in Kadimastem as an investment risky opportunity.

[1] Petrov, D., et al., *ALS Clinical Trials Review: 20 Years of Failure. Are We Any Closer to Registering a New Treatment?* Frontiers in Aging Neuroscience, 2017. 9: p. 68.
[2] Evaluate Pharma. In general, some data discuss total healthcare economic burden of $6B in the US (2012 data) for ALS. We refer to specific therapy ALS market.

[3] Zion Market Research

Pipeline Summary

Kadimastem has an ongoing phase I/IIa trial for its lead product, AstroRx (consists of astrocytes – a type of cells found in the brain). It is manufactured from human embryonic stem cells using a proprietary process.

The trial (NCT ID: NCT03482050) is an interventional, dose-escalating, four subject-groups clinical study. 21 Patients with ALS at the early disease stage will be administered AstroRx through spinal injection. AstroRx is expected to provide relief to patients by replacing the patient's malfunctioning astrocytes, which will protect the damaged motor neurons and help in significantly slowing down the progression of the disease.

The company enrolled its first patient on April 26, 2018. Patient recruitment is on-going at Department of Neurology of the Hadassah Ein-Kerem Medical Center, Israel. The study is expected to be completed by August 2020, when the company will likely announce details of AstroRx's efficacy and safety demonstrated in the clinical trial.

The company is also expected to launch a proof of concept pre-clinical study in collaboration with Defymed, a France based medical device manufacturer, for developing a medical device for treating diabetes. It will benefit diabetic patients who currently utilize insulin for managing their glucose levels in the blood (all type 1 diabetics and around 30% of type 2 diabetic patients administer insulin.)[4]

Upside scenarios	Downside scenarios
Should Kadimastem succeed in its phase 1/2a clinical trial (59% success rate, 2020), company's value will add to our current forecast approx. NIS 128M with other positive effects on its technological platform.	Should Kadimastem will not succeed in its phase 1/2a clinical trial, company's value will be affected.
There are just two drugs currently approved by the FDA for treating ALS, should Kadimastem show positive outcomes it can revolutionized treatment.	Kadimastem needs to raise additional capital **before** clinical results outcomes which can lead to share price decrease

[4] Diabetes Teaching Center at the University of California, San Francisco

Upcoming Potential Catalysts

Program	Event	Significance	Timeline
AstroRx trial with ID NCT03482050: A Phase I/IIa, Open-Label, Dose-escalating Clinical Study to Evaluate the Safety, Tolerability and Therapeutic Effects of Transplantation of Astrocytes Derived From Human Embryonic Stem Cells (hESC), in Patients With Amyotrophic Lateral Sclerosis (ALS)	Results on drug safety and efficacy will be declared. Information on measurable parameters such as improvement in muscle strength and quality of life due to the use of AstroRx will be reported.	High	**Mid 2019**
AstroRx pivotal clinical trial	Commencement of a pivotal clinical trial.	High	**Q1, 2020**
Encapsulin	Proof of concept pre-clinical test using Defymed's MailPan device and Kadimastem's islet-of-Langerhans-like cell clusters to evaluate the efficacy of the combination in treating diabetes.	High	**Mid 2019**

Valuation Methodology

R&D company valuations are challenging due to a non-cash valuation with a long time-to-market in most cases. Methods typically used for company valuations, such as asset valuation or multiplier methods, are incompatible with the valuation of R&D companies. In such companies, the current status of business cannot be analyzed by the capital in the balance sheet, and in most cases cannot be compared to similar companies due to their uniqueness, from both technological and financial aspects.

As part of a discounted cash flow (DCF), the accepted method used in financial valuations, there are several modifications to an R&D company's valuation. In general, there are three primary methods within the DCF method:

1. **Real Options** - valuation method designated for pre-clinical and early-stage clinical programs/companies where the assessment is binary during the initial phases, and based upon scientific-regulatory assessment only (binomial model with certain adjustments).

2. **Pipeline assessment** - valuation method used for programs/companies prior to market entrance. The company's value is the total discounted cash flow plus unallocated costs and assessment of future technological basis. The assessment of the future technological basis is established based on the company's ability to "produce" new clinical and pre-clinical projects and their feed rate potential.

3. **DCF valuation** - similar to companies not operating in the life sciences field, this method applies to companies with products that have a positive cash flow from operations.

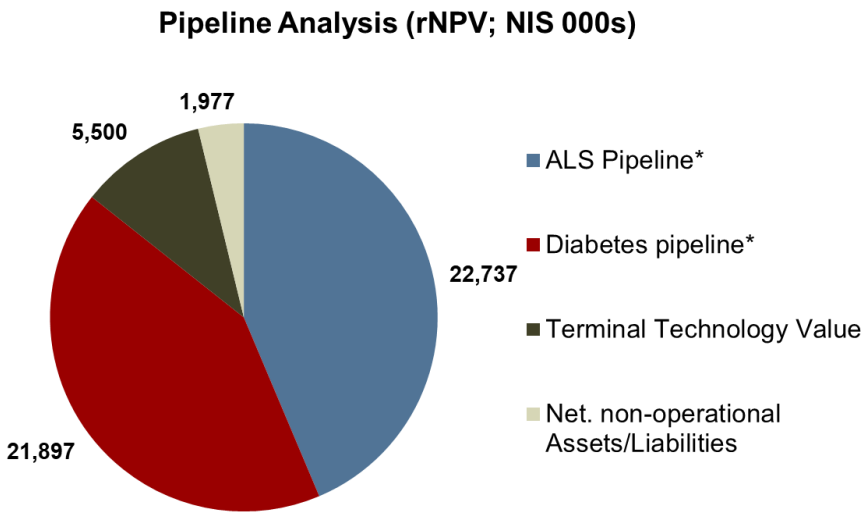
Kadimastem's valuation was conducted under the "Pipeline assessment" method, suitable for the development stages of the company's products. The company's valuation is calculated by examining the company as a holding company vis-à-vis existing projects, with Risk-adjusted Net Present Value (rNPV) capitalization to the net present value, including the weighing of several scenarios. These primarily include analysis of the company's income, evaluated in accordance with scientific/technological assessment, based on various sources and estimates relating to the market scope, the degree of projected market success, and regulatory risk.

The weighted average of company revenue in the pharmaceutical and medical equipment market is based on the following data:

- Total Market - market potential for the product/product line
- Market Share – the company's ability to penetrate the market during the forecast period
- Peak Sales - peak sales of the company/product during the forecast period
- Annual Cost of Treatment – estimated annual cost per patient, based on updated market studies
- Success Rate - chances for success of clinical trials and transition to the next phase in the examined sub-field.

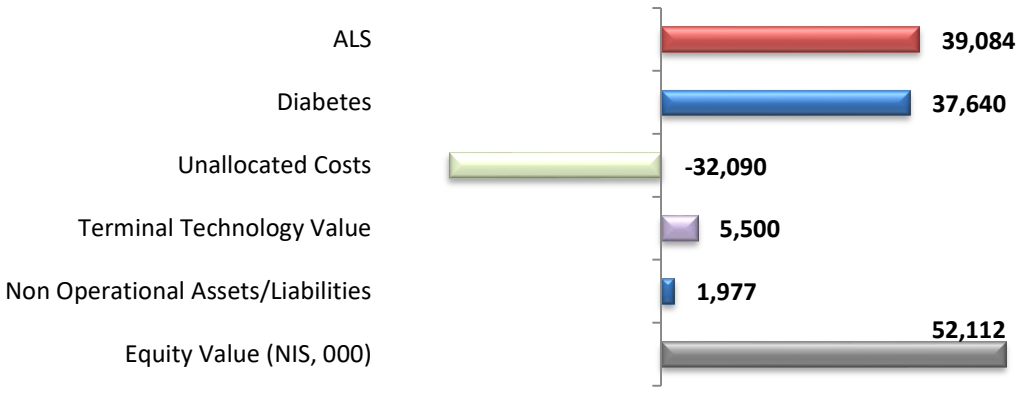
Valuation of Kadimastem's "technological basis" is, in fact, a valuation of the company's "residual value". This valuation was conducted using the Feed Rate methodology that is common in the field of Life Sciences, rather than using the conventional terminal value, normally used by non- Life-Science companies.

Valuation Summary



Source: Frost & Sullivan analysis

we evaluate the company as follows:



Based on the aforementioned parameters, we estimate Kadimastem's equity value at NIS 52.1M.

Sensitivity Analysis

The table below presents Kadimastem's target price relative to the capitalization rate. We set a range of 0.5% change from our CAPM model (see Appendix B). Kadimastem has 61.6M shares.

Sensitivity Analysis - Capitalization Rate vs. target price

Cap. Rate	
23.0%	0.70
22.0%	**0.77**
21.0%	**0.85**
20.0%	**0.93**
19.0%	1.01

We estimate the target price to range between NIS 0.77 and NIS 0.93; a mean of NIS 0.85.

12 months stock movement

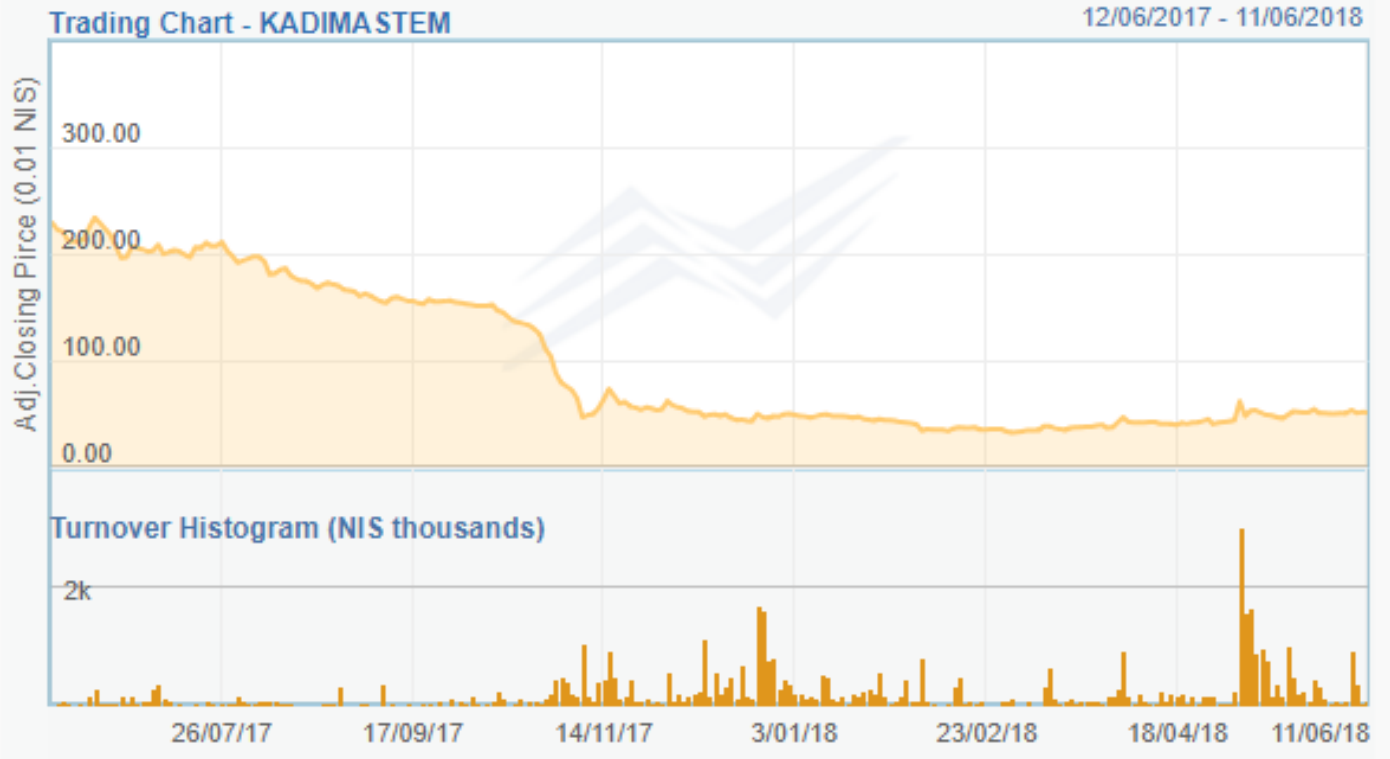


Table of Contents

Executive Summary 2
Investment Thesis 2
Pipeline Summary 3
Upcoming Potential Catalysts 4
Valuation Methodology 4
Valuation Summary 5
12 months stock movement 6
Background 9
Diagnosis 10
Epidemiology 11
Standard of care 12
ALS market and its future 13
Pricing analysis 17
AstroRx® 17
Clinical Programs: Incapsulin (stem cell therapy for the treatment of diabetes) 19
Background 19
Diagnosis 20
Epidemiology 20
Standard of care 21
Diabetes market and its future 21
Pricing analysis 24
Encapsulin - Kadimastem's Cell Therapy Solution for Diabetes 25
Financial Valuation & Projections 28
Financial Analysis – FY2017 28
Valuation 29
Price Forecast Risks 35
Company Contact Details & Management 36
Key Executives 36
Appendicies 37
Appendix A - Financial Reports 37
Appendix B - Capitalization Rate 38
Appendix C – Team Bios 39
Disclaimers, Disclosures and Insights for more responsible investment decisions 40
About Frost & Sullivan 41

Company Activity and Strategy

An enabling platform for regenerative medicine

Kadimastem has the expertise of generating different types of functional human cells from pluripotent stem cells (i.e. embryonic or induced pluripotent stem cells):

> Pluripotent stem cells are cells that can divide infinitely and differentiate into different target human cells. Kadimastem uses Human embryonic stem cells (hESC) as its starting material. hESC are derived from surplus fertilized eggs in a laboratory of an in vitro fertilization clinic (IVF) and that are donated for research and development purposes with donor's consent (instead of being destroyed). Once derived, the hESCs have the ability to divide and multiply infinitely. Kadimastem maintains hESCs in an in-house stem cell banks, giving it a stable supply of stem cells, without dependence on external sources.

Maintaining a stem cell bank in-house increases the cost of capital. However, in the field of stem cells, it is an important strategic investment. It shields the company from an uncertain supply of stem cells and pricing fluctuations which could arise from a high dependence on donors.

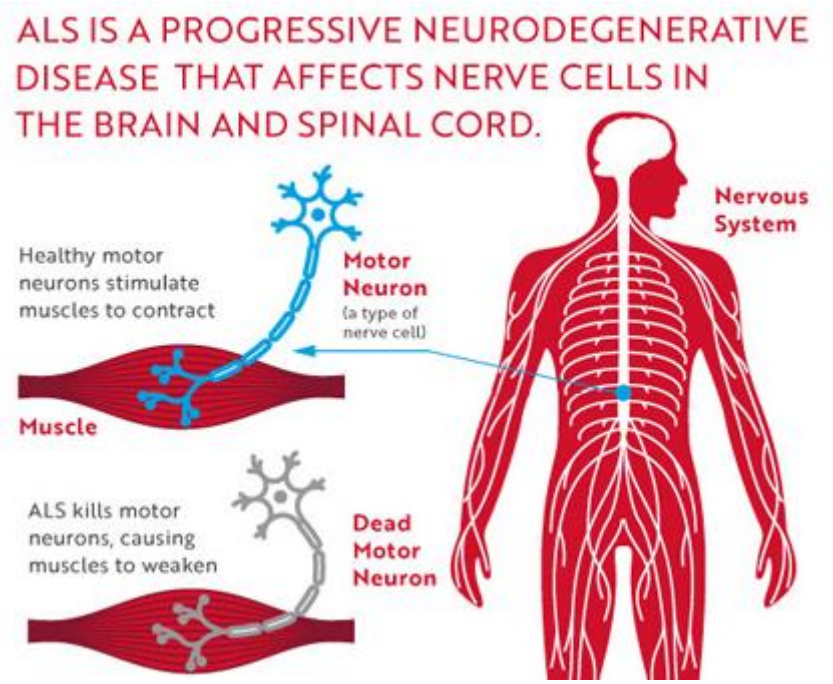
Kadimastem plans to generate long-term revenues from regenerative medicine for ALS and diabetes that are based on human cells derived from stem cells.

Clinical Programs: AstroRx® (astrocytes for the treatment of ALS)

Background

Amyotrophic Lateral Sclerosis (ALS, also known as Lou Gehrig's disease, or motor neuron disease) is a disease in which nerve cells in the brain and the spinal cord, specifically the upper and lower motor neurons, degenerate. In "healthy" individuals, the upper and lower motor neurons are responsible for controlling the voluntary movement of skeletal muscles, throughout the body. In ALS patients, degeneration of motor neurons leads to deterioration of skeletal muscles (Figure 1) resulting in gradual paralysis involving loss of ability to walk, muscle cramps, spasticity, muscle weakness, slurred and nasal speech, and difficulty in chewing or swallowing. It could eventually lead to respiratory failure, leading to death. The mortality rate in ALS is high – more than 75% don't survive beyond 5 years post-diagnosis.[5] ALS is a rare disease, which provides Kadimastem with an opportunity to apply for Orphan drug designation.

Figure 1: Illustration of the neurodegeneration in ALS



Source: ALS Association

More than 90% of the cases of ALS are sporadic in nature, i.e. it develops at random, with no known associated risks and genetic causes. 5% to 10% of the ALS cases are familial, which means that an individual inherits the genes for the disease.[6] Genes linked with ALS include Cu/Zn Superoxide dismutase (SOD1), TAR DNA binding protein-43 (TDP-43), Fused in sarcoma (FUS), and C9Orf72.[7]

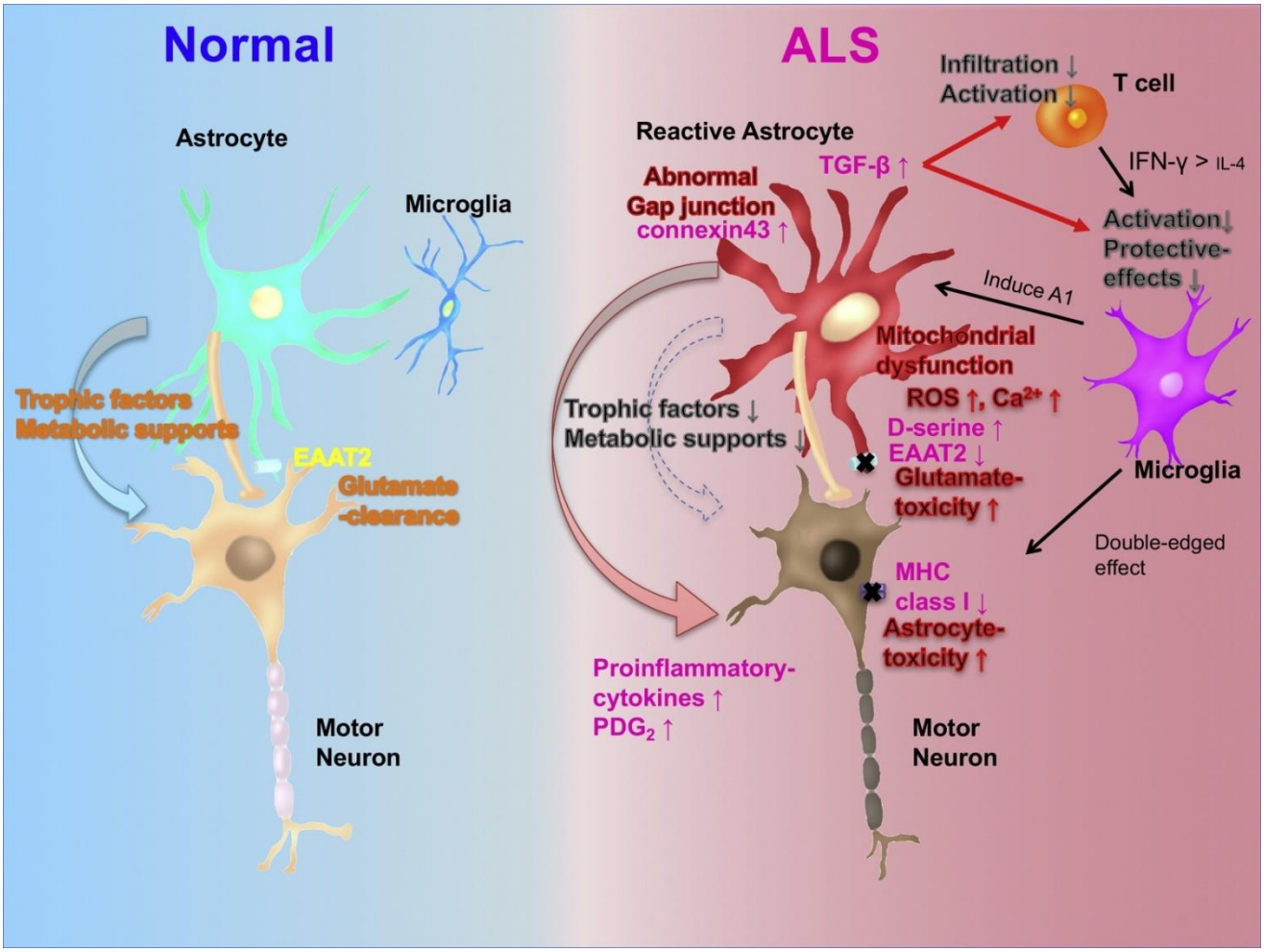
Multiple pathogenic pathways have been linked to ALS including oxidative stress, mitochondrial dysfunction, abnormalities in RNA metabolism and proteostasis and glial-mediated neuroinflammation.[8]

Astrocytes are specialized glial cells that contiguously tile the entire central nervous system (CNS), especially from the blood vessels towards the parenchyma and play multiple roles in nursing the neurons, regulating various brain functions including orchestrating synaptic formation, regulating the concentration of

[5] ALS Association
[6] ALS Association
[7] Yamanaka, K. and O. Komine, *The multi-dimensional roles of astrocytes in ALS.* Neuroscience Research, 2018. 126: p. 31-38.
[8] Gan, L. and J.A. Johnson, *Oxidative damage and the Nrf2-ARE pathway in neurodegenerative diseases.* Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease, 2014. 1842(8): p. 1208-1218.

neurotransmitters at synapses, and providing neurotrophic factors[9]. In neurodegenerative diseases, including ALS, the shape and molecular pattern of astrocytes changes, which disrupts the complex interaction between astrocytes and motor neurons leading to disease progression in ALS. Astrocytes lose their homeostatic function and release numerous toxic factors that affect motor neurons (Figure 2).[10]

Figure 2: Astrocytes in a normal situation and ALS



Source: Yamanaka, K. and O. Komine, *The multi-dimensional roles of astrocytes in ALS.* Neuroscience Research, 2018. 126: pp. 31-38.

Diagnosis

ALS usually strikes people aged 55 years and above.[11] It is more common in men than women.[12] Currently, there is no test that can provide a definitive diagnosis of ALS in the initial stages of the disease. Its diagnosis involves a detailed examination of the history of signs and symptoms. This could be followed by Electromyogram (EMG) and nerve conduction study (NSC). In EMG, electrical activity of various muscles is recorded during contraction and relaxation. In NSC, a physician measures the electrical activity of the nerves and muscles. A physician may also conduct a magnetic resonance imaging (MRI) test, of the brain and spinal cord. Any abnormalities in EMG, NSC, or MRI readings help physicians in diagnosing ALS or determining a different muscle or nerve condition that may be causing the symptoms.[13]

[9] Burda, J.E. and M.V. Sofroniew, *Reactive gliosis and the multicellular response to CNS damage and disease.* Neuron, 2014. 81(2): p. 229-48.
[10] Yamanaka, K. and O. Komine, *The multi-dimensional roles of astrocytes in ALS.* Neuroscience Research, 2018. 126: p. 31-38.
[11] Amyotrophic Lateral Sclerosis (ALS) Fact Sheet, National Institute of Health (NIH)
[12] McCombe, P.A. and R.D. Henderson, *Effects of gender in amyotrophic lateral sclerosis.* Gend Med, 2010. 7(6): p. 557-70.
[13] Mayo Clinic

In patients with familial ALS, generally more than one person in the family has ALS or a related condition called frontotemporal dementia (FTD), which is a progressive brain disorder that affects decision-making, behavioral control, emotion and language. People with ALS patients in the family could benefit from genetic testing if early signs of ALS appear (such as muscle twitching, cramping, stiffness, slurred speech, and difficulty chewing or swallowing). Genes which are commonly found mutated in familial ALS include C9orf72 gene (account for 30–40% of familial ALS in the US and Europe) and SOD1 gene (causes 15–20% of familial ALS worldwide). The other genes that have been associated with familial ALS each account for a small proportion of cases. [14]

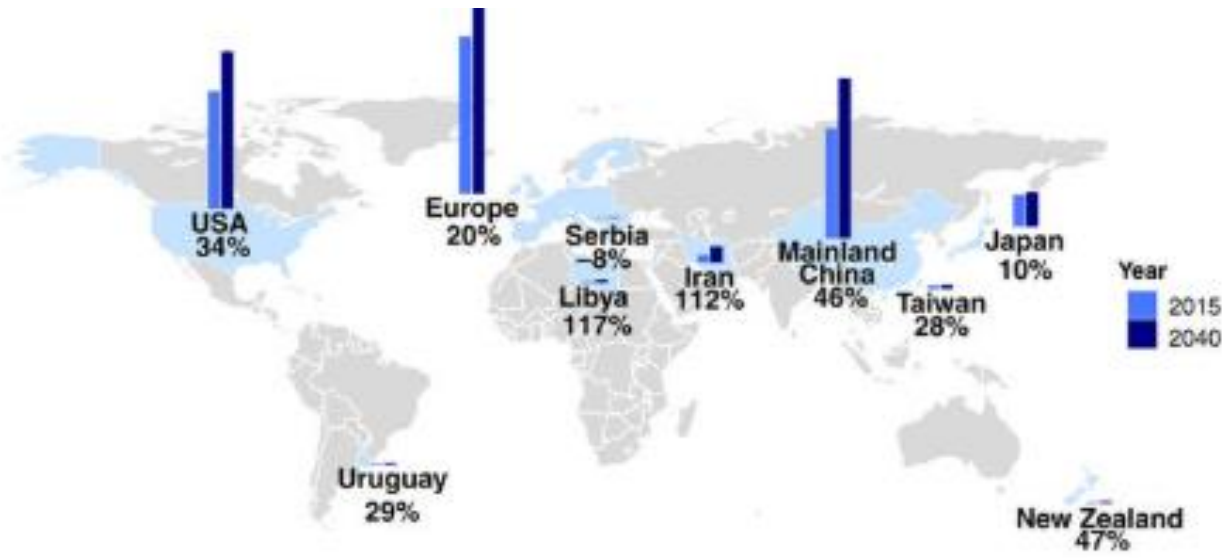
A physician can also conduct additional blood and urine tests to rule out other diseases (such as HIV AIDS, polio and multiple sclerosis) that can have similar symptoms. Diagnosing ALS can take several months, during which time the disease continues to progress.

Epidemiology

An estimated 222,801 people suffered from ALS globally in 2015.[15][16] By 2040, the number is expected to reach 376,674, mainly due to the ageing of the population, particularly among developing nations. Europe, US and China account for the largest number of ALS patients. Every year, about 1.9 patients are diagnosed with ALS per 100,000 people.[17] By 2040, developing countries like China are expected to register the maximum growth in the number of ALS patients.

Figure 3).[18]

Figure 3: Projected increase in the number of individuals with ALS from 2015 to 2040



Source: Arthur, K.C., et al., Projected increase in amyotrophic lateral sclerosis from 2015 to 2040. Nat Commun, 2016. 7: p.124-8.

[14] Genetics Home Reference, US National Library of Medicine
[15] Arthur, K.C., et al., *Projected increase in amyotrophic lateral sclerosis from 2015 to 2040.* Nat Commun, 2016. 7: p. 12408.
[16] Other data points on 450,000 patients (https://www.als.net/about-als-tdi/als-faq/#how-many-people-have-als)
[17] Chio, A., et al., *Global epidemiology of amyotrophic lateral sclerosis: a systematic review of the published literature.* Neuroepidemiology, 2013. 41(2): p. 118-30.
[18] Arthur, K.C., et al., *Projected increase in amyotrophic lateral sclerosis from 2015 to 2040.* Nat Commun, 2016. 7: p. 12408.

Standard of care

Currently, there is no drug that can halt or reverse ALS. There are two FDA approved drugs that slow progression of disability. The first ALS drug, Rilutek (riluzole), marketed by Sanofi, was approved in 1995. The second drug, Radicava (edaravone), developed by Mitsubishi Tanabe Pharma, received FDA approval in May 2017. Every year, between $256M and $433M is spent on providing care to ALS patients[19], which demonstrates the need for better treatments.

Riluzole is an anti-glutamate molecule and works on the observation that overactivation of the glutamatergic system may lead to damage of the motor neurons in ALS. However, its use has been reported to increase survival by a mere 2 to 3 months[20].

Radicava's approval, backed by a six-month Japanese trial that could only show a slower progression of disability, suggests that FDA is keen to promote drugs that are safe and could provide some relief to ALS patients. This could be a good indicator for Kadimastem which could apply for FDA approval if the clinical study for AstroRx® shows promising results.

Radicava is able to delay the deterioration of a patient's symptoms by acting as a free radical scavenger and preventing oxidative stress damage to motor neurons. In pre-clinical studies, Kadimastem showed that AstroRx® possesses the activities of functional healthy astrocytes, including glutamate re-uptake, increase of neuronal survival by releasing important pro-survival neurotrophic factors and protection of motor neurons from oxidative stress. A secretome analysis shows that these AstroRx® also secrete several inhibitors of metalloproteases as well as a variety of neuroprotective factors (e.g. TIMP-1&2, GDNF, VEGF, MIF and Midkine). This indicates multiple mechanism of action by which AstroRx® cells might compensate for the loss of function of ALS patients' astrocytes. Intrathecal injections of AstroRx® to transgenic $hSOD1^{G93A}$ mice and rats (animal model for ALS) significantly delayed disease onset and improved motor performance compared to sham-injected animals. The company's safety study in immunodeficient mice showed that intrathecal transplantation of AstroRx® is safe. Transplanted AstroRx® attached to the meninges along the neuroaxis and survived for the entire duration of the study without formation of tumors or teratomas. Once Kadimastem will prove these effects from transplanted astrocytes in ALS patients, it could revolutionize the ALS market.

Apart from the two FDA approved drugs, there's another treatment in the global market, Neuronata-R, which is a stem cell-based therapy (consists of autologous bone marrow mesenchymal stem cells (MSCs) grown in a lab for four weeks after being harvested from the ALS patient) approved in South Korea since 2014. It is marketed by Corestem, which is likely to apply for FDA authorization in late 2018 or early 2019. The cell therapy was reported to be safe and improved the quality of life for ALS patients in phase 2 clinical trial conducted on 72 ALS patients in South Korea.

The implication of Neuronata-R FDA approval for Kadimastem

If Neuronata-R gets FDA approval, it would be a good strategy for Kadimastem to include a small study in its trial, which directly compares the efficacy and safety profile of its drug with Neuronata-R. This will greatly enhance its chances of gaining approval and access in the US market.

Nonetheless, Neuronata-R therapy is based on extracting MSCs from a patient, processing them, and then injecting back to the patient. This requires a laboratory and limits the reach of a company to treat large population of ALS patients. Kadimastem faces no such obstacle as its product AstroRx® is being developed as potentially an off-the-shelf therapy.

[19] Giuseppe Fiorentino, Antonio M. Esquinas. (2018) Cost-effectiveness associated with amyotrophic lateral sclerosis: some questions and answers pending. *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration* 19:3-4, pages 315-316.
[20] Petrov, D., et al., *ALS Clinical Trials Review: 20 Years of Failure. Are We Any Closer to Registering a New Treatment?* Frontiers in Aging Neuroscience, 2017. 9: p. 68.

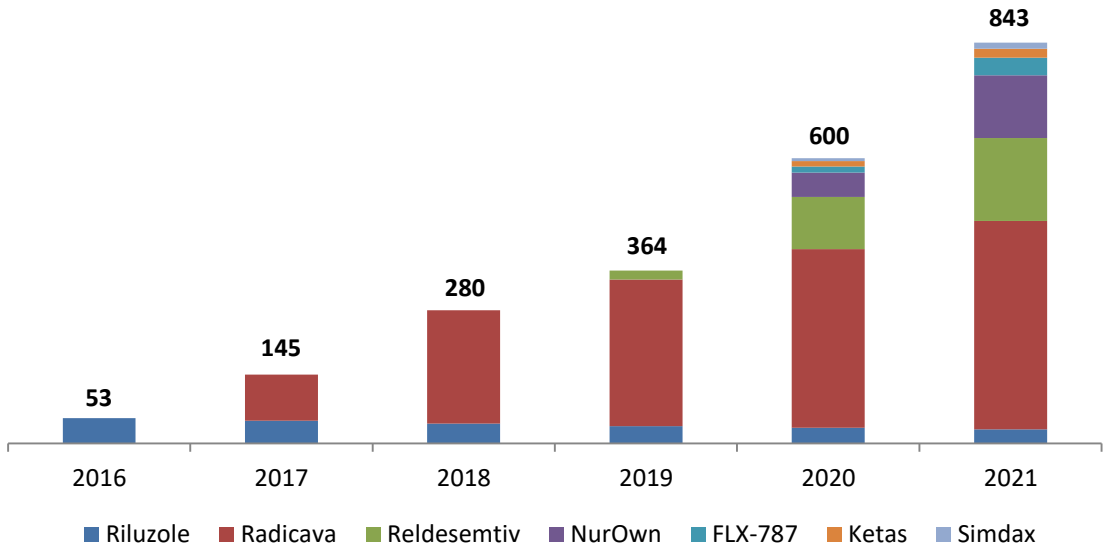
ALS market and its future

The global amyotrophic lateral sclerosis treatment market stood at $53 million in 2016 and is expected to reach $843 million by 2021, growing at a CAGR of 73.9% during the forecast period.

Figure 4). Key drivers for growth include rising adoption of Radicava among ALS patients and launch of new drugs, currently in clinical research. The market has been forecasted based on the assumption that the most promising drugs in pipeline included in the forecast (Reldesemtiv, NurOwn, FLX-787, Ketas, and Simdax) will meet their endpoints and receive approval.

Figure 4: Global ALS Market – Optimistic Scenario[21]

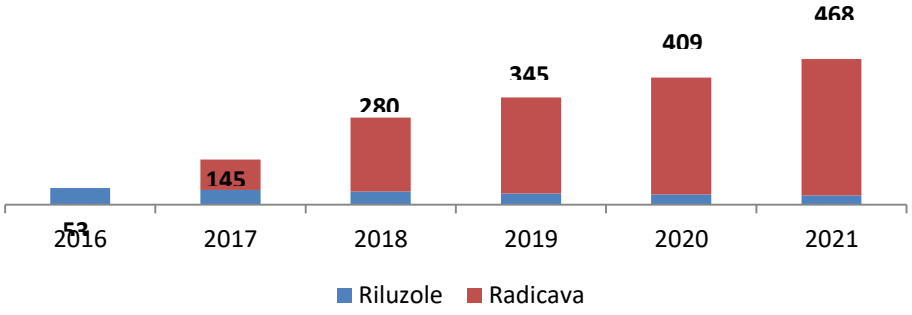
($ million, 2016-2021)



Source: Visiongain, EvaluatePharma

However, it could be a situation wherein none of the drugs considered in the forecast above succeed. Traditionally, the high attrition rate of pipeline drugs has been reported. For instance, between 1995 and July 2016, more than 60 molecules were investigated as a possible treatment for ALS, however, none got approved. [22] In such a conservative scenario, the ALS market will likely grow to $468 million, at a CAGR of 54.6% during 2016–2021 (Figure 5).

Figure 5: Global ALS Market – Conservative Scenario
($ million, 2016-2021)



Source: Visiongain, EvaluatePharma

[21] Revenue for Riluzole has been represented by expected revenue of its main branded drug, Rilutek, forecasted by Visiongain
[22] Petrov, D., et al., *ALS Clinical Trials Review: 20 Years of Failure. Are We Any Closer to Registering a New Treatment?* Frontiers in Aging Neuroscience, 2017. 9: p. 68.

Pipeline drug analysis

ALS has a robust pipeline of molecules, with around 36 molecules in different stages of research, as of 14 May 2018 (

Table 1).

Table 1: ALS molecules in clinical research - by phase (May 2018)

Phase	Number of molecules
Pre-registration	1
III	3
II	22
I	10

Source: EvaluatePharma

Table 2: Late stage and pre-registration molecules in ALS (May 2018)

Phase	Therapy	Company	Company Headquarters	Drug class
Pre-registration	Masitinib	AB Science	France	Platelet-derived growth factor receptor kinase inhibitor
III	NurOwn	BrainStorm Cell Therapeutics	Israel	Stem cell therapy
III	Riluzole	Aquestive Therapeutics	US	Glutamate antagonist
III	Mecobalamin	Eisai	Japan	Vitamin B12 agonist

Source: EvaluatePharma

Key late phase drug

The most promising candidate drug in late-stage clinical trials (Table 2) is BrainStorm Cell Therapeutics' (BrainStorm) stem cell therapy NurOwn. Similar to Corestem's Neuronata-R, it is based on mesenchymal stem cells (MSC) that are extracted from the bone marrow of a patient. The extracted MSCs are then induced to produce and release neurotrophic factors (NTFs), known to support the survival of neurons in the central nervous system. The company is expected to complete the phase 3 trial by July 2019.[23] NurOwn has been granted fast track designation by the US FDA. This suggests that if the company is able to demonstrate positive clinical performance in phase 3 clinical trial, it can expect to launch the cell therapy in the US by 2020.

The implication of NurOwn approval for Kadimastem

NurOwn needs around 28 days to isolate the MSCs from a patient and develop them into a final product that tries to mimick astrocytes' ability to release neurotrophic factors (BDNF, GDNF and VEGF).[24] Since the final product can be developed only in a laboratory, it is a big limitation in tapping the ALS patient

[23] ClinicalTrials.gov
[24] BrainStorm Investor Presentation, March 2018

population, which is spread across different regions. Kadimastem can leverage the difference in its product administration to counter competition from BrainStorm.

Other drugs in pre-registration and late phase clinical trial do not pose a significant threat to Kadimastem

Other drugs in pre-registration or late clinical phase are yet to register any significant development. In April 2018, Committee for Medicinal Products for Human Use (CHMP) of the European Medicine Agency (EMA) shared a negative opinion for the marketing authorization of masitinib in the treatment of ALS. As per CHMP, the clinical data was not robust enough to support regulatory approval. AB Science plans to file a re-examination plea, on which CHMP will likely respond by July 2018.

Aquestive Therapeutics' clinical program, if successful, will introduce another riluzole generic in the market, and is not expected to have much impact.

Eisai's mecobalamin is a vitamin B12 supplement, which is not expected to have any major impact on improving the condition of ALS patients. In March 2016, the company had withdrawn its new drug application after it observed in discussions with Japan's Pharmaceuticals and Medical Devices Agency (PMDA) that the data submitted for ultra-high dose mecobalamin as a treatment for ALS was not sufficient for approval.

Most promising drugs in phase II clinical trials which are expected to launch by 2020

There are around four drugs in phase II clinical trial that are expected to be launched by 2020 (Table 3).

Table 3: Phase II molecules expected to be launched by 2020 (as of 14 May 2018)

Phase	Molecule	Company	Company Headquarters	Drug class
II	Reldesemtiv	Cytokinetics (licensee is Astellas)	US	Troponin calcium combination agonist
II	FLX-787	Flex Pharma	US	Transient receptor potential ankyrin 1 (TRPA 1) agonist
II	Ketas	MediciNova	US	Phosphodiesterase 4 inhibitor
II	Simdax	Orion Pharma	Finland	Troponin calcium combination agonist

Source: EvaluatePharma

Reldesemtiv

Reldesemtiv (CK-2127107) is a fast skeletal muscle troponin activator (FSTA) being evaluated for its effect on skeletal muscle function and respiratory function in patients with ALS. It plans to enroll 445 patients and is estimated to complete by July 2018.[25]

FLX-787

FLX-787 works by activating transient receptor potential ion channels in primary sensory neurons producing a signal that suppresses hyperexcitability of alpha-motor neurons, thereby reducing muscle

[25] ClinicalTrials.gov (ID: NCT03160898)

cramps and spasms in ALS patients. The drug molecule has been granted fast track designation by the FDA.[26] It plans to assess the drug in 120 patients and complete the study by June 2018.[27]

Ketas

Ketas (MN-166 or ibudilast) is an anti-inflammatory drug already approved in Japan since 1989, for treatment of post-stroke complications and bronchial asthma.[28] The drug is a glial attenuator that suppresses pro-inflammatory cytokines including tumor necrosis factor-a (TNF-a) and interleukins (IL-1b and IL-6). It concluded a phase 2 study on December 2017 and presented data at the American Academy of Neurology (AAN) 70th Annual Meeting. The trial was a randomized, double-blind, placebo-controlled study which included a six-month treatment period followed by a six-month open-label extension. Subjects who completed six months or twelve months of treatment with Ketas showed improved survival in the 30 months post-treatment with Ketas. Buoyed by positive results, the company is currently discussing the next steps of its development plan with FDA.[29]

Simdax

Simdax (levosimendan, ODM-109) is an approved drug for the short-term treatment of acutely decompensated severe chronic heart failure (ADHF). It is an inodilator (calcium sensitizer and potassium channel opener), which is being evaluated for its ability to improve breathing in ALS by improving the performance of muscles in the diaphragm. The drug was evaluated in a randomized, double-blind, placebo-controlled phase 2 trial. Although the trial could not establish that Simdax improved respiratory function in ALS patients, the company plans to continue with its development program.[30]

Implications for Kadimastem

None of the drugs currently in phase 2 clinical research are based on stem cell therapy. They are all targeted at providing symptomatic relief to ALS patients. For instance, reldesemtiv and levosimendan are intended to improve muscle function and physical performance in ALS patients. FLX-787 is targeted at providing relief from muscle spasms or muscle cramps to ALS patients and Ketas is being developed to attenuate glial cells and delay progression of nerve damage in ALS patients. AstroRx® would not face significant competition from these drugs, if it is able to demonstrate clinical superiority in clinical trials.

[26] FlexPharma
[27] ClinicalTrials.gov (ID: NCT03196375)
[28] Medicinova
[29] *'MediciNova Announces Additional Data from Completed Clinical Trial of MN-166 (ibudilast) in ALS Presented at the American Academy of Neurology (AAN) 70th Annual Meeting',* GlobeNewswire (April 2018)
[30] Orion Investor Presentation (February 2018)

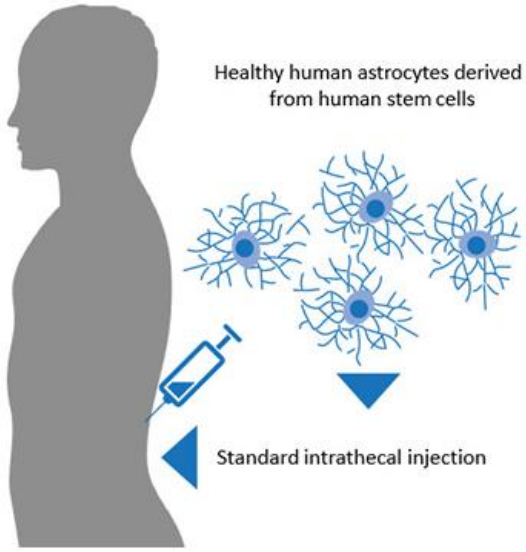
Pricing analysis

A year's treatment with Radicava costs around $145,000 (before discounts) in the US.[31] In South Korea, stem cell therapy with Neuronata-R costs around 60 million won (~$55,000)[32]. This suggests that AstroRx® could be launched in a similar price range (between $50,000 and $150,000).

AstroRx®

AstroRx® are astrocytes (a type of brain cells) developed from human embryonic stem cells (hESC). The company is developing the treatment as an off the shelf product, that can be injected into the cerebrospinal fluid (CSF) of patients (Figure 6). The treatment is expected to provide biological support to ALS patients' motor neurons in the brain and spinal cord by replacing the functions of malfunctioning ALS patients' astrocytes, thereby slowing the progression of the disease and improving the patients' quality and expectancy of life (Table 4).

Figure 6: Administration of AstroRx® into ALS patients



Source: Kadimastem

Table 4: Limitations in malfunctioning astrocytes in ALS patients

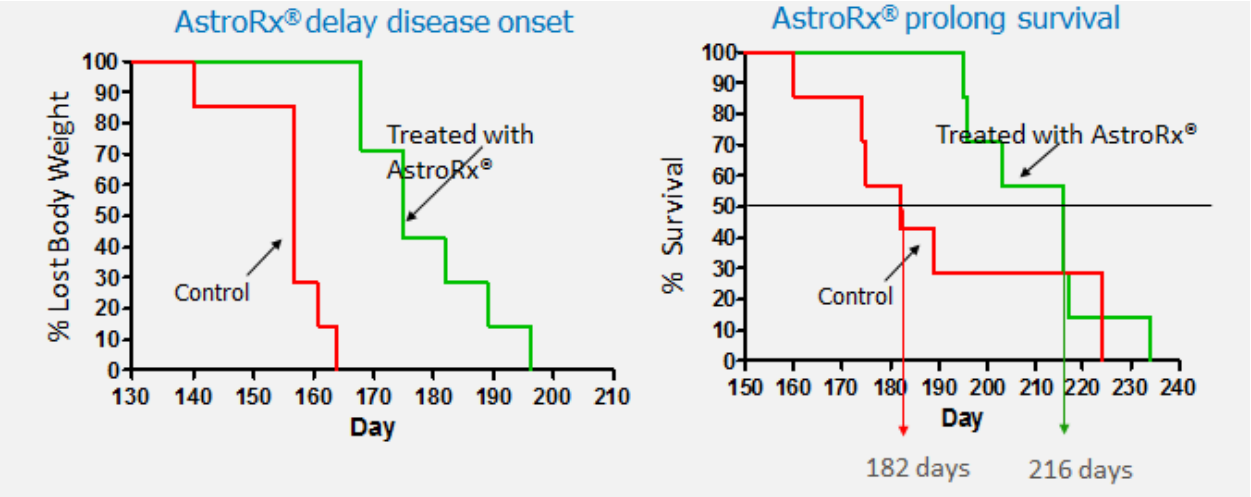
Parameter	Astrocytes in ALS Patients	AstroRx® (Kadimastem's Astrocytes)
Produce neuron supporting factors	↓	↑
Uptake of toxic glutamate	↓	↑
Protection from oxidative stress	↓	↑

Source: Kadimastem

In pre-clinical studies (Izrael et al., 2018, Stem Cell Research & Therapy (2018) 9:152), AstroRx® was reported to be safe, non-toxic, and non-tumorigenic. It was also observed that AstroRx® delays disease onset and prolongs survival and muscular activity of mice and rat models of ALS (Figure 7).

[31] '*The First ALS Drug In 22 Years is Approved - and It Costs 4 Times what it does in Japan*', Forbes (May 2017)
[32] '*Corestem's NeuroNata-R Marks Increase in Foreign Patients*', Korea Biomedical Review (December 2017)

Figure 7: AstroRx® results from pre-clinical studies



Source: Kadimastem

It is currently being evaluated in a dose-escalating study in which 21 ALS patients will be tested in four cohorts (100 x10^6 (n=5), 250 x10^6 (n=5), 2X250 (n=7) x10^6 and 500 million (n=4) AstroRx® cells). The primary outcome of the study is to assess the safety and tolerability of the therapy. Secondary outcomes include efficacy assessment to measure various factors that suggest a delay in disease progression, such as respiratory muscle strength, hand grip strength, muscle strength in limb muscles, ALS functional rating scale and quality of life metrics (ClinicalTrials.gov Identifier: NCT03482050).

Long-term view

Malfunctioning astrocytes have been linked to multiple neurodegenerative disorders, which currently lack any cure and have high unmet needs in treatment. In a recently published study, researchers found that astrocytes in patients with an Alzheimer's disease (AD) produced significantly more beta-amyloid (a toxic protein that accumulates in the brains of AD patients) and secreted more cytokines (causes inflammation) than astrocytes in normal people.[33] Similarly, evidence suggests that disruption of astrocytes is involved in dopaminergic neuron degeneration in Parkinson's disease (PD).[34] In multiple sclerosis (MS), malfunctioning astrocytes have been linked to lesion formation and providing peripheral immune cells access to the central nervous system.[35] Dysfunctional astrocytes have also been observed to play an important role in disease progression in epileptic patients.[36] Research also suggests that astrocytes could be explored as therapeutic targets in stroke[37] and spinal cord injury.[38]

Once Kadimastem demonstrates the safety of its AstroRx® therapy in ALS patients, it could evaluate the efficacy of the cells in treating other neurological disorders in future programs. In this case, the regulatory pathway for approving new clinical trials for additional indications will be fast. Kadimastem currently assumes that only a pivotal study will be needed (as safety of the treatment will be assured by that time), i.e., a phase IIb/III clinical trial.

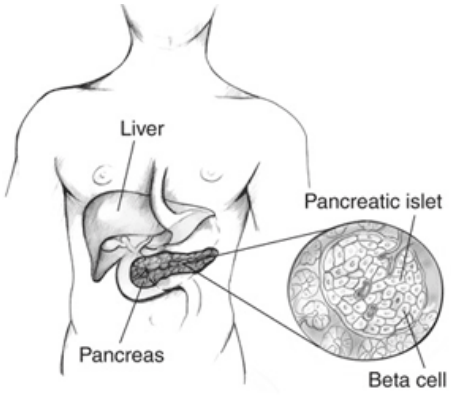
[33] Oksanen, M., et al., *Mutant iPSC-Derived Model Reveals Severe Astrocyte Pathology in Alzheimer's Disease.* Stem Cell Reports, 2017. 9(6): p. 1885-1897.
[34] Booth, H.D.E., W.D. Hirst, and R. Wade-Martins, *The Role of Astrocyte Dysfunction in Parkinson's Disease Pathogenesis.* Trends in Neurosciences, 2017. 40(6): p. 358-370.
[35] Ponath, G., C. Park, and D. Pitt, *The Role of Astrocytes in Multiple Sclerosis.* Frontiers in Immunology, 2018. 9: p. 217.
[36] Coulter, D.A. and C. Steinhäuser, *Role of Astrocytes in Epilepsy.* Cold Spring Harbor perspectives in medicine, 2015. 5(3): p. a022434-a022434.
[37] Becerra-Calixto, A. and G.P. Cardona-Gómez, *The Role of Astrocytes in Neuroprotection after Brain Stroke: Potential in Cell Therapy.* Frontiers in Molecular Neuroscience, 2017. 10: p. 88.
[38] Huang, X., et al., *[Astrocytes as therapeutic targets after spinal cord injury].* Sheng Li Xue Bao, 2017. 69(6): p. 794-804.

Clinical Programs: Incapsulin (stem cell therapy for the treatment of diabetes)

Background

Diabetes is a disease in which a body is not able to digest glucose in the blood. This happens due to a malfunctioning pancreas, an organ located behind the lower part of the stomach. It has tiny clusters of cells called pancreatic islets, or islet-of-Langerhans, which contain several types of cells, including beta cells that produce the hormone insulin (Figure 8). When the level of blood glucose rises after a meal, the pancreas responds by releasing insulin into the bloodstream, which helps in reducing blood glucose by accumulating glucose into muscle, fat and liver tisues.

Figure 8: Structure of Pancreas



Source: National Institute of Diabetes and Digestive and Kidney Diseases

Diabetes develops when the pancreas does not make enough insulin or the body does not use insulin effectively. It is of two types: type 1 and type 2. In type 1 diabetes, the pancreas produces little or no insulin. It usually appears during childhood or adolescence, when the body's immune system attacks and destroys the insulin-producing beta cells. There are no known specific causes of type 1 diabetes (though there are several theories). It could be caused due to genetic predisposition. The risk of developing type 1 diabetes is increased by certain variants of the HLA-DQA1, HLA-DQB1, and HLA-DRB1 genes, which seem to increase the risk of an inappropriate immune response to beta cells.[39] Other factors such as viral or bacterial infection or presence of chemical toxins within food could also trigger an autoimmune response against insulin-producing beta cells in the pancreas.

In type 2 diabetes, the body doesn't produce enough insulin, or the body's cells don't react to insulin. It could be caused due to a mutation in certain genes that regulate glucose levels, and lifestyle factors. Genes associated with type 2 diabetes include TCF7L2 (affects insulin secretion and glucose production), ABCC8 (helps regulate insulin), GLUT2 (helps move glucose into the pancreas), GCGR (controls glucagon hormone involved in glucose regulation).[40] Other factors that could lead to type 2 diabetes include obesity, sedentary lifestyle, rising age, and an unbalanced diet.

Symptoms of diabetes include increased thirst, frequent urination, extreme hunger, unexplained weight loss, fatigue, blurred vision, slow-healing sores, and frequent infections of gums and skin. Diabetes is a chronic disease which in the long term could result in several life-threatening complications, including cardiovascular diseases and kidney failure or irreversible end-stage kidney disease. It could also lead to gradual deterioration of nerves, especially in legs, leading to tingling, numbness, burning or pain. Blood

[39] Genetics Home Reference, US National Library of Medicine
[40] Healthline

vessels of the retina could also be damaged, potentially leading to blindness. In the eyes, it also increases the risk of other serious vision conditions, such as cataracts and glaucoma.[41]

Diagnosis

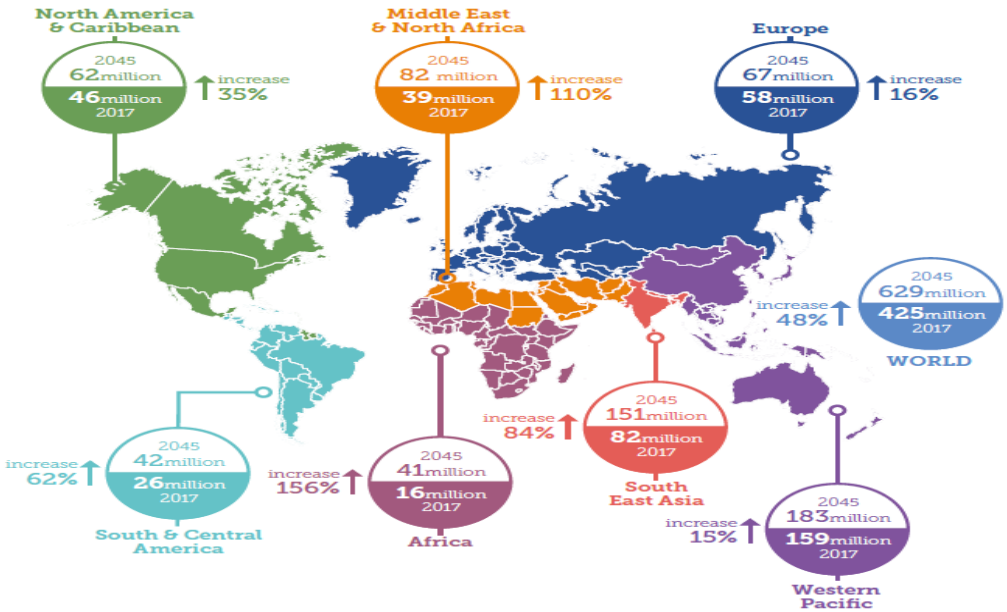
Fasting plasma glucose (FPG), random plasma glucose (RPG), and A1C are the commonly used tests for diagnosing diabetes. In FPG, blood glucose level is tested on a patient who has not consumed food or drink (except water) for at least eight hours before the blood draw. RPG test can be done anytime without fasting. It gives rapid results and is useful in cases where physicians might need a quick check on elevated glucose levels (e.g. in type 1 diabetes, where a delay in diagnosis could lead to complications). A1C test measures the percentage of hemoglobin (a protein in red blood cells that carries oxygen) that is coated with glucose. A higher A1C level suggests high blood glucose. Physicians sometimes (e.g. in gestational diabetes – generally a reversible situation in pregnant women where blood glucose levels elevate) also conduct glucose tolerance test to measure the absorption of glucose by body cells. It follows an FPG test. A patient is given 75g of glucose syrup to drink. Blood glucose level is then tested from a sample taken after 2 hours of syrup feed.[42] A simple blood glucose test can show if a person has diabetes or not.

Despite the good availability of standard diagnostic tests, underdiagnosis of disease remains a challenge – 1 in 2 individuals remain undiagnosed[43]. It usually occurs as people tend to ignore the early symptoms of diabetes such as frequent urination, increased hunger, numbness in fingers or toes, and slow healing wounds. Different organizations across the globe such as International Diabetes Federation and American Diabetes Association are actively promoting awareness about diabetes and its symptoms to encourage people for early screening and detection. Initiatives like 'World Diabetes Day' and 'National Diabetes Awareness Month' are being increasingly used to spread awareness about the importance of early diagnosis. These initiatives are expected to decrease the number of undiagnosed cases in future.

Epidemiology

In 2017, there were 424.9 million people who suffered from diabetes. By 2045, the number is expected to increase to 628.6 million (Figure 9).

Figure 9: Global epidemiology of diabetes (2017, 2045)



Source: IDF Diabetes Atlas, 2017

[41] Mayo Clinic
[42] Diabetes.co.uk
[43] International Diabetes Federation (IDF)

Standard of care

Type 1 diabetes is managed by regular administration of insulin. In type 2 diabetes, about 30% patients are managed through insulin.[44] Other drugs used in treating type 2 diabetes include the following:[45]

- Drugs that increase insulin output by the pancreas. E.g. chlorpropamide (Diabinese), glimepiride, (Amaryl), glipizide (Glucotrol), glyburide (Diabeta, Glynase), nateglinide (Starlix), and repaglinide (Prandin)
- Drugs that decrease the amount of glucose released from the liver. E.g. metformin (Glucophage)
- Drugs that decrease sugar absorption by the intestines E.g. acarbose (Precose) and miglitol (Glyset)
- Drugs that decrease reabsorption of glucose by the kidney and increase its excretions in urine. E.g. canagliflozin (Invokana), dapagliflozin (Farxiga), and empagliflozin (Jardiance)

Additionally, physicians might suggest transplant of pancreas or Pancreatic islets (islet-of-Langerhans) to treat diabetes. However, due to a severe shortage of donors and a life-long dependence on immunosuppressive drugs to prevent rejection of transplanted pancreas (or pancreatic islets), physicians generally suggest it only for non-controllable insulin-dependent diabetic patients who are critical and suffering from end-stage renal disease.[46]

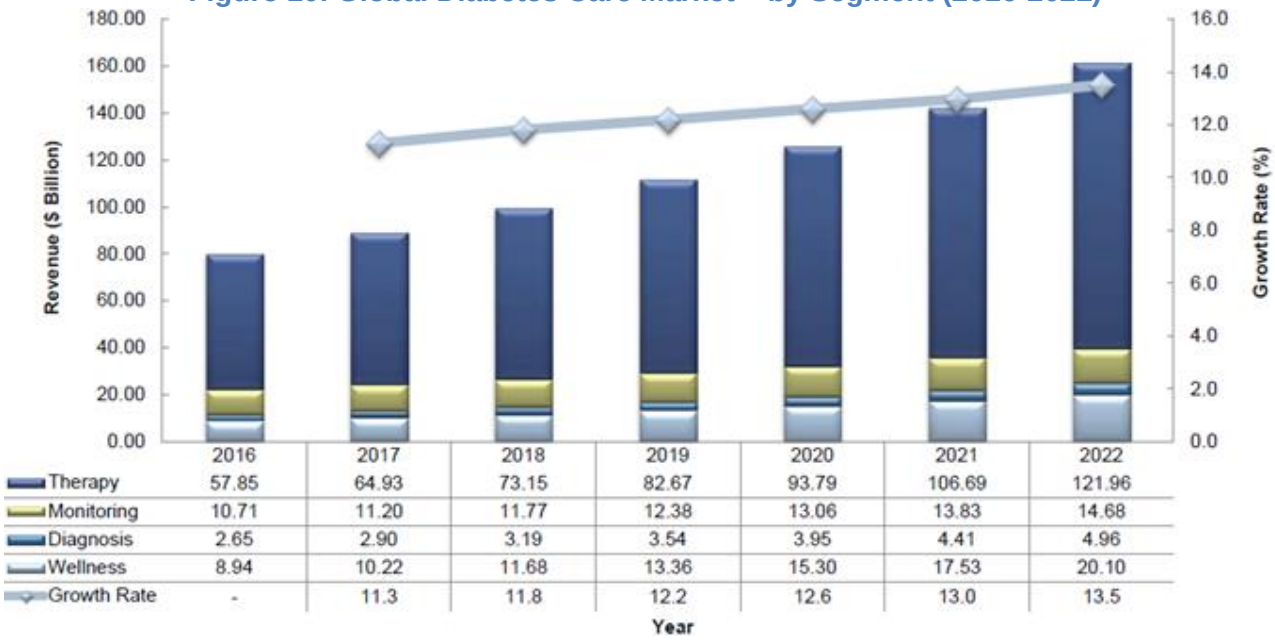
Diabetes market and its future

Overview

By 2022 the Diabetes Care market will be valued at $161.69 billion with a CAGR of 12.4% since 2016 (Figure 10).[47] The market can be segmented by the sequential stages of treatment; wellness (including interventions for pre-diabetics), diagnosis (Point-of-care testing and the like), continuous glucose monitoring (CGM), and therapies (such as insulin be it; injectable, oral, transdermal or inhalable). Kadimastem will be competing in the Therapy segment, which accounts for 72.2% of the entire care market as of 2016. By 2022, Frost & Sullivan estimates this figure to increase to 75.4%, corresponding to a therapy segment value of $121.96 billion, a CAGR of 13.2% since 2016.

[44] Diabetes Teaching Center at the University of California, San Francisco
[45] Understanding Diabetes - Diagnosis and Treatment, WebMD
[46] Gruessner, A.C. and R.W. Gruessner, *Pancreas Transplantation of US and Non-US Cases from 2005 to 2014 as Reported to the United Network for Organ Sharing (UNOS) and the International Pancreas Transplant Registry (IPTR).* Rev Diabet Stud, 2016. 13(1): p. 35-58.
[47] '*Future of Diabetes Care Paradigms, Forecast to 2022 – Innovations to Disrupt Diabetes Wellness, Diagnosis, Monitoring, and Therapy.*', Frost & Sullivan (March 2017)

Figure 10: Global Diabetes Care Market – by Segment (2016-2022)



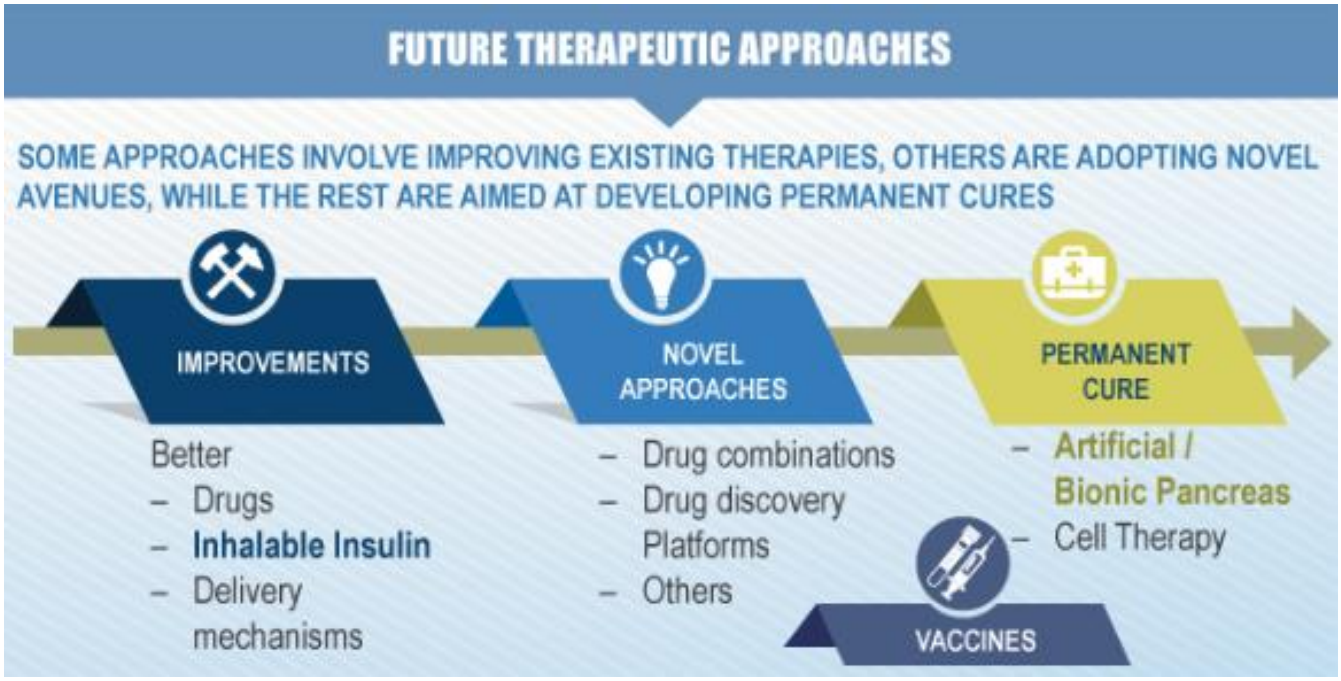
	2016	2017	2018	2019	2020	2021	2022
Therapy	57.85	64.93	73.15	82.67	93.79	106.69	121.96
Monitoring	10.71	11.20	11.77	12.38	13.06	13.83	14.68
Diagnosis	2.65	2.90	3.19	3.54	3.95	4.41	4.96
Wellness	8.94	10.22	11.68	13.36	15.30	17.53	20.10
Growth Rate	-	11.3	11.8	12.2	12.6	13.0	13.5

Source: Frost & Sullivan

Within the therapy market, insulin is expected to generate $43.6 billion by 2021, growing at a CAGR of 8.3% during 2016–2021. This will be the total addressable market for Kadimastem's diabetes program, however, due to reimbursement constraints for their premium product, it will likely be prescribed for selected patients population only.

The market is expected to grow backed by several factors including rising prevalence of diabetes, reduced number of underdiagnosed cases due to a higher awareness of the disease, and launch of new innovative solutions for treating diabetes such as stem cell-based therapies and bionic pancreas (Figure 11).

Figure 11: Future Therapeutic Approaches for Treating Diabetes



Source: Frost & Sullivan

However, low adherence to insulin regimen is a major barrier to market growth. Insulin is majorly administered through injections, which are generally perceived as painful, causing patients with poor glycemic control to postpone taking insulin shots for up to seven years. It has been reported that 73% of type 2 diabetes patients delay insulin injection therapy, and of those, approximately 25% refuse insulin despite their physician's recommendation.[48]

Another major barrier to growth is the high competition in the market. Due to a large number of approved insulin products, any new innovation is critically evaluated for its cost and benefits vs current products. If the benefit from a new therapy does not significantly outweigh currently approved drugs, it might not be approved or reimbursed at a price higher than those of marketed drugs.

The increasing importance of prevention and wellbeing is likely to motivate people towards adoption of healthier lifestyles, which could offset the number of diabetics in future – potentially acting as a barrier to market growth.

Innovations to tackle low adherence among patients resulting from frequent injections

Companies are innovating to explore other routes of insulin delivery (Figure 11), such as oral and inhalable, but without much success. In 2006, the world's first inhalable insulin, Pfizer's Exubera, was launched. But the company soon withdrew the drug from the market after it struggled to compete with injectable drugs, particularly due to a pricing pressure from payers.[49] It wasn't until February 2015, with the release of Sanofi's inhalable insulin (Afrezza), that the potential seemed to rise again. However, in January 2016, Sanofi too withdrew the drug from the market citing lack of reimbursement as a major reason.[50]

Novo Nordisk was another player actively trying to develop insulin that could be delivered through a non-injectable route. However, in October 2016, Novo Nordisk announced that it was putting its clinical development of oral insulin on hold. This was despite early-stage data exhibiting similar efficacy to the market gold-standard *Lantus* injection, developed by Sanofi.[51] The development was halted for both

[48] *'Analysis of the Global Diabetes Drug Delivery Market'*, Frost & Sullivan (2015).
[49] *'Novo Nordisk pressured into Dropping Needle-Free Oral Insulin'*, Fernandez (2016).
[50] *'Inhalable insulin: a losing battle',* Pharmaceutical Technology (April 2016)
[51] *'Oral insulin could still be a reality says Novo Nordisk'*, Pharmasource. (June 2017)

economic and scientific reasons. Scientifically, the tablet's low insulin bioavailability meant that patients would have to take several of them, at regular intervals, to sufficiently replace a single injection. The low bio-availability diminishes patient demand, as the higher dosages and frequencies imply higher costs. On the supply side, the level of investment required for an oral solution to compete with increasingly less invasive injections would necessitate a price point that is simply too high to achieve that precise objective. Already, in 2016, Pharmacy Benefit Managers (PBMs) forced pharma companies to lower diabetes drug prices. The price of injectable diabetes drugs had increased up to 1000% in 20 years,[52] and given that the nature of the disease usually requires at least once-daily injections, the burden on patients was simply intolerable. As an example, Eli Lilly's *Humalog* increased from $21 in 1996 to $255 in 2016.[53]

Use of pancreas transplant to manage diabetes

Pancreas transplant has been used to treat diabetes. It has been reported that recipients were able to control their high blood glucose levels without administration of external insulin.[54] Every year, more than 2,200 pancreases are transplanted globally, of which, more than 50% are in the US.[55] However, the clinical advantages offered by transplants are severely limited by the lack of organ donors. Another major challenge is a need for lifelong immunosuppressive therapy to prevent graft rejection. Due to these limitations, currently, a pancreas transplant is only recommended to insulin-dependent diabetic patients with the end-stage renal disease who require kidney co-transplant.[56]

Implications for Kadimastem

Cell Therapy for diabetes could be a game-changing approach to meet the needs of insulin dependent patients. A major cause of concern, especially in young kids and adolescents, is the correct dosing of insulin. While lesser dosage would lead to accumulation of glucose in the blood causing complications, the higher dosage could lead to a condition called hypoglycemia, which could be fatal, especially if it happens while a patient is asleep. If Kadimastem is able to address these concerns through its cell therapy product, it could expect strong adoption among diabetes patients. Also, it should be able to overcome the need for administering lifelong immunosuppressive therapy for preventing rejection, making it a pioneer in a competitive market.

It could potentially be adopted by all type 1 and around 30% of type 2 diabetics that are dependent on insulin (together representing around 157 million patients in 2017). By 2021, that could represent a market worth $43.6 billion.[57]

Competition from marketed and pipeline advanced insulin pumps and implications for Kadimastem

In September 2016 the US FDA approved Medtronic's MiniMed 670G System, marketed as the first 'artificial pancreases.[58] The device system is an advanced insulin pump, which continuously monitors blood glucose levels through implanted sensors, and administers insulin, as and when required. Similar devices are currently in development phase. For example, iLet, an advanced insulin pump from Beta Bionics, can deliver insulin as and when required, based on input from sensors that are implanted in patients. Additionally, to counter the problem of hypoglycemia, the device can also deliver glucagon, which inhibits the action of excess insulin.

[52] *'Novo Nordisk pressured into Dropping Needle-Free Oral Insulin'*, LabBioTech.(November 2016)
[53] *'HHS Nominee made Millions in Pharma'*, HealthExec, November 2017
[54] Lei, L. and Y. Mao, *New Advances in Stem Cell Therapy for Diabetes Mellitus*, in *Pancreas, Kidney and Skin Regeneration*, P.V. Pham, Editor. 2017, Springer International Publishing: Cham. p. 89-105.
[55] *'Pancreas Transplantation of US and Non-US Cases from 2005 to 2014 as Reported to the United Network for Organ Sharing (UNOS) and the International Pancreas Transplant Registry (IPTR)'*, The Review of Diabetic Studies (May 2016)
[56] Gruessner, A.C. and R.W. Gruessner, *Pancreas Transplantation of US and Non-US Cases from 2005 to 2014 as Reported to the United Network for Organ Sharing (UNOS) and the International Pancreas Transplant Registry (IPTR).* Rev Diabet Stud, 2016. 13(1): p. 35-58.
[57] Zion Market Research
[58] *'The Artificial Pancreas Device System'*, US FDA (March 2018)

Medtronic launched its MiniMed 670G System in July 2017. As of February 2018, the company reported that it was being used by over 20,000 patients and had received strong positive feedback from both patients and physicians.[59] Revenue from company's diabetes group has registered double-digit growth since the launch of MiniMed 670G System. These early trends indicate a positive adoption of any new technology that could offer convenience in administering insulin while assuring safety.

However, MiniMed 670G System is not devoid of its shortcomings. It needs regular user actions. The sensors that are implanted in the body have to be changed every 7 days, and need regular calibration, before meals and bedtime. Insulin in the system needs to be refilled every 2 to 3 days.[60] To counter competition, Kadimastem would have to develop the device such that it could be positioned as a true 'artificial pancreas' in the sense that it could work independently without major interference form patient or physician. Dosing should be comprehensively monitored by in-built sensors and insulin and glucagon be administered as per requirements. A minimum user action, if any, should be required.

Pricing analysis

The price for MiniMed 670G System is $3,700 in the US. Traditionally, the cost of insulin infusion pumps has been reported to be about $4,500, with additional costs for supplies exceeding $1,500 per person per year.[61] With rising pressure from payers who are resisting any new technologies that cost more than current treatments (e.g. inhaled and oral formulations of insulin failed due this reason), Kadimastem would either have to launch their device within the price range of current products, or present a strong case of improvement in quality of life in patients that reduces hospital visits and overall expenditure per patient. Otherwise, the product is likely to face reimbursement resistance from the payer communities in the US and Europe.

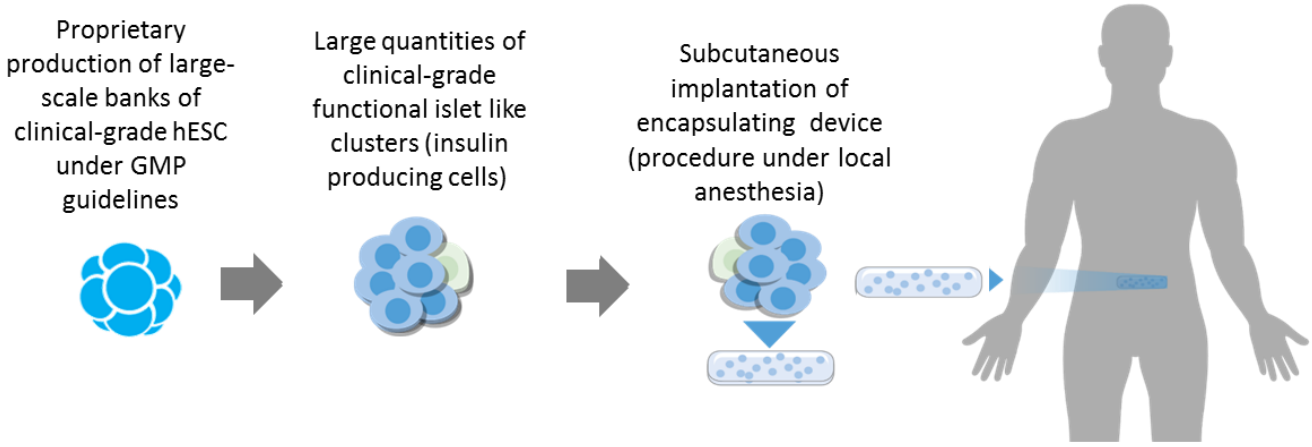
Encapsulin - Kadimastem's Cell Therapy Solution for Diabetes

Kadimastem's cell therapy product contains islet-of-Langerhans-like clusters (ILCs) derived from human embryonic stem cells (hESCs), which produce and secrete insulin and glucagon in response to external glucose levels (Figure 12). Clinical transplantation of islets of Langerhans isolated from the pancreas of a deceased donor into a patient has been shown successful, which can be taken as a proof of concept for Kadimastem's approach. Moreover, Kadimastem's solution overcomes the two major obstacles in this clinical approach: lack of sufficient donor tissue and the use of immunosuppressive drugs. By harnessing the power of cell multiplication, Kadimastem can produce an endless supply of ILCs, ending reliance on deceased donors (Figure 12). Additionally, by encapsulating the cells in an encapsulation device.

[59] *'Medtronic's (MDT) CEO Omar Ishrak On Q3 2018 Results - Earnings Call Transcript'*, Seeking Alpha (February 2018)
[60] Medtronic
[61] *'Comparative Effectiveness and Costs of Insulin Pump Therapy for Diabetes',* The American Journal of Managed Care (June 2017)

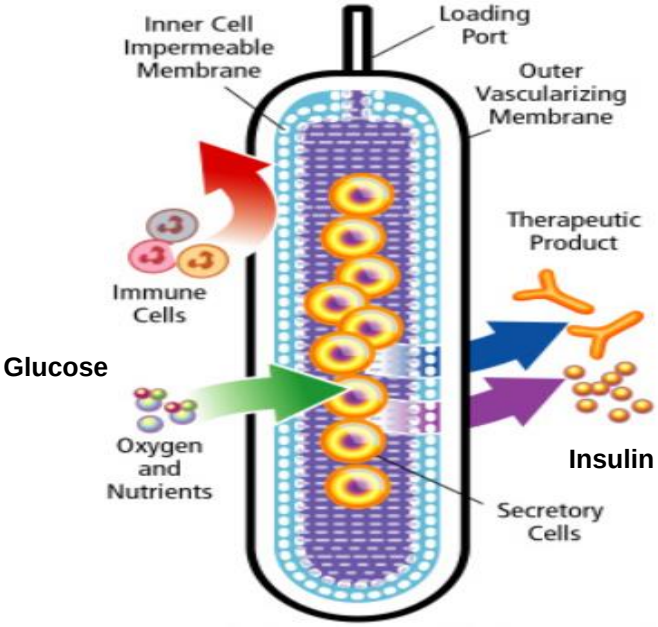
Figure 13), the solution avoids direct interaction between body's immune system and ILC cells. This would overcome the need to supply life-long immunosuppressive drugs. Through the biological and physiological secretion of insulin and glucagon based on a body's requirements, a patient will likely be freed from continuous monitoring of blood sugar levels and injecting insulin. Better overall management of glucose levels is expected to reduce life-threatening complications of diabetes.

Figure 12: Kadimastem's Diabetes Program



Source: Kadimastem

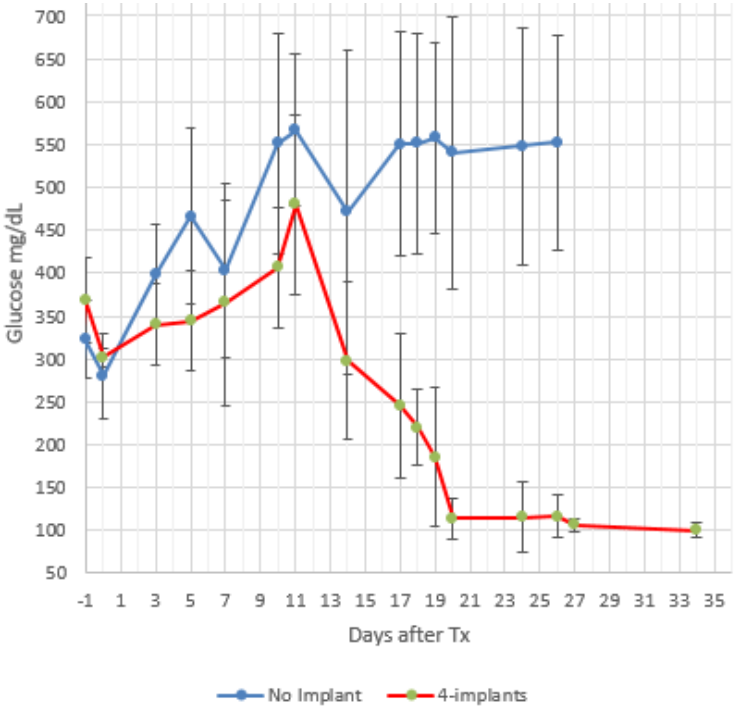
Figure 13: Encapsulation device Protects islet-of-Langerhans Cells from Contact with Immune Cells and Antibodies



Source: TheraCyte Inc.

In animal studies, Kadimastem's ILC cells have shown promising results. A return to normal concentration of glucose in the blood was observed in diabetic mice that received implants (Figure 14). As a next step, the company plans to launch a proof of concept study to establish the efficacy and safety of its cellular product combined with an encapsulation device. Kadimastem is currently evaluating and promoting collaborations in the encapsulation field, in order to select a partner with technological capabilities suitable for application in the company's cell-based product for diabetes treatment. One such collaboration that the company announced is with French medical device company, Defymed.

Figure 14: Impact of Incapsulin in controlling blood glucose



Source: Kadimastem

Financial Valuation & Projections

Financial Analysis – FY2017

Revenues for 2017 were derived from drug screening services generated from the company's agreement with Merck, which expired in July 2017. In 2018 no revenues are forecasted by the company.

Research and development expenses were NIS 14.9M in 2017 compared to NIS 13.1M in 2016. These include costs that are directly attributable to the conduct of research and development programs, including the cost of salaries, employee benefits, cost of materials, supplies, the cost of services provided by outside contractors, including services and expenses related to clinical trials. The 2017 increase is mainly due to the company's ALS clinical trial preparation.

General and administrative expenses decreased to NIS 6.4M in 2017 from NIS 7.5M in 2016. The main decrease is due to options payments to Kadimastem's CEO in 2016 with exercise prices of NIS 10, NIS 11.5 and NIS 13.

Net loss was NIS 21.4M in 2017 similar to NIS 20.0M in 2016.

Since the company's inception, and through August 31, 2017, aggregate losses amounted to NIS 115M. As of December 31, 2017, Kadimastem had NIS 9.5M in available cash, an increase resulting from grants and capital raising conducted during 2017. The company's accountants noted an "on-going" concern in the 2017 financial reports.

Operating activities burned cash of NIS 19.9M in 2017 compared to NIS 13.6M in 2016. Cash used in operating activities in 2017 primarily consisted of net losses resulting from research and development and general and administrative expenses.

To summarize, the company will raise additional capital over the next few months in order to support its clinical development.

Valuation

Clinical development: Kadimastem generates different types of human cells from stem cells. The company holds its stem cell bank in-house which allows it important regulatory and quality assurance control and is more cost-effective than using a CMO. Moreover, in the field of stem cells, it is an important strategic investment. It shields the company from uncertain supply and pricing fluctuations which could arise from third party manufacturers of media, growth factors etc.

The company's focus is on long-term revenues from regenerative medicine for ALS, additional neurodegenerative diseases and diabetes, that are based on human cells. Its business model is a classic biotech company model, i.e. in house development of these indications in early stage phases (1/2a), reaching endpoints results and then co-developing with big pharma through clinical and marketing phases or by out-licensing. The company is at the starting point of its phase 1/2a for ALS and proof of concept for Diabetes.

We assume the following milestones based on Kadimastem announcements, Brainstorm's similar progress and our experience:

AstroRx® for ALS

- Study Start Date: **April 2018**
- Release of top-line data: Primary and secondary outcome data is to be measured for 11 months. Considering they enrolled the first patient on 26th April, we can expect release of top-line data on initial patients by **Q2 of 2019**.
- Initiation of pivotal trial: Study completion date of phase 1/2a trial is expected August 2020. The company will most likely announce the data by the end of 2020 and initiate the pivotal trial in the same year.
- Kadimastem could initiate a pivotal clinical trial in the US by the end of 2020 or the beginning of 2021 which could last for around 2-2.5 years (till the beginning of 2023).
- Considering it generates strong clinical evidence for an orphan indication, it could receive a fast track designation from the FDA, which would enable it to get pass the regulatory review process in about 6 months (mid 2023). In addition the recent 21st century cure act and right to try bills of the US government may raise new market-authorization possibilities and potentially enable the company to receive partial payment in the pivotal trial.
- The company could take another 6 months to establish commercial and marketing operations resulting in **launching the product to market by mid-2024.**

Encapsulin (stem cell therapy for the treatment of diabetes)

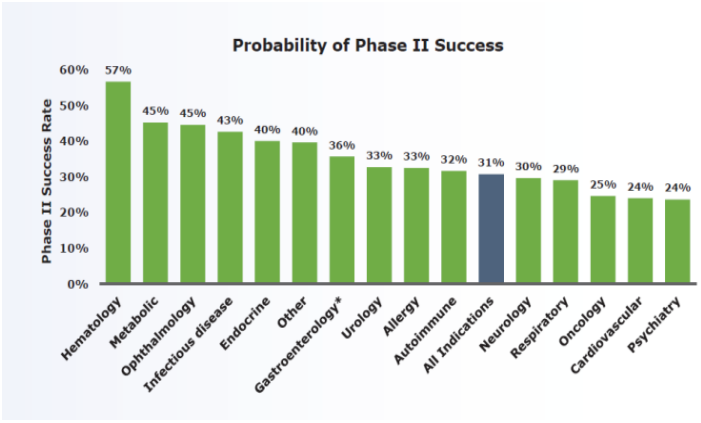
Kadimastem will soon initiate a proof-of-concept study. The company is yet to announce a date for initiating the study. As we have no other approved product with a similar combination, we assume ViaCyte's clinical development pathway that it has undertaken for its product VC-01, which is a medical device encapsulating pancreatic endoderm cells derived from embryonic stem cells for treating type 1 diabetes, will progress along a similar path to Encapsulin by Kadimastem.

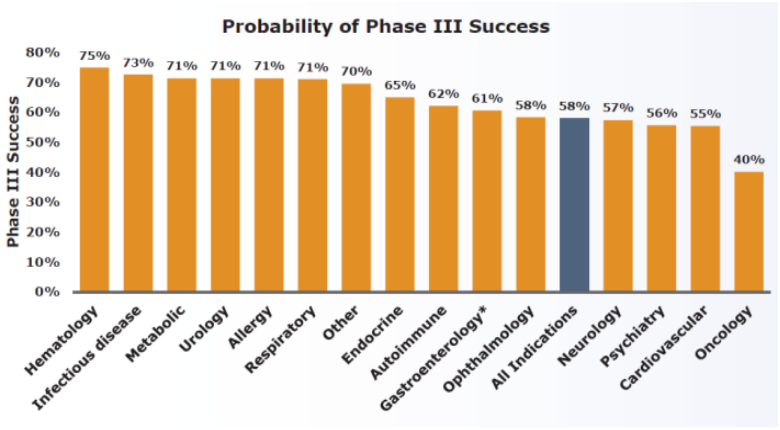
ViaCyte filed an investigational new drug application (IND) with the FDA in July 2014.[62] In October 2014, it initiated a phase I/II study in 65 participants to test if VC-01 combination product can be implanted subcutaneously in subjects with Type 1 Diabetes and maintained safely for two years. It has marked its study completion date as January 2021 and not announced any plans for initiating phase 2 trials.[63] Thus,

[62] ViaCyte
[63] ClinicalTrials.gov Identifier: NCT02239354

we assume Kadimastem's time-to-market will be 10 years for establishing the combination product's efficacy and safety in clinical trials before launching it to market.

Success rates – Kadimastem engages in a high-risk therapeutic area in promoting its indications. Success rate data indicates higher success rates for the metabolic specialty (45%) in comparison with the total average of all indications (31%) from phase II to phase III. Neurology is similar to all indications at phase II. Phase III success rates are higher (71%) for metabolic while for Neurology is lower than all indications (57% Vs. 58%). We address these clinical risks and success rates at each FDA milestone in our rNPV valuation for each indication.





Source: Clinical Development Success Rates, 2006-2015. Biomedtracker 2016.

Recents deals in the stem cell therapy and ALS domains

BrainStorm has its mesenchymal stem cell therapy for treating ALS, NurOwn, under phase 3 clinical trial. BrainStorm has licensed the technology for developing NurOwn under a Research and License Agreement, with Ramot (the technology transfer company of Tel Aviv University). Pursuant to the remuneration terms of the License Agreement, BrainStorm has agreed to pay Ramot royalties of 5% on the Net Sales received by the Company of the Licensed Product. [64]

Deals for developing gene-therapy based medicine for treating ALS

Sangamo entered into a collaboration with pharma giant Pfizer for the development of a potential gene therapy to treat familial ALS with C9ORF72 mutation. Under the terms of the collaboration, Sangamo will receive a $12M upfront payment from Pfizer. Sangamo will be responsible for the development of candidates for gene therapy. Pfizer will be operationally and financially responsible for subsequent research, development, manufacturing and commercialization of the C9ORF72 ZFP-TF program and any

[64] BrainsStorm Q1 2018 SEC Filing

resulting products. Sangamo is eligible to receive potential development and commercial milestone payments of up to $150 million, as well as tiered royalties on net sales.[65]

AveXis and REGENXBIO announced an exclusive worldwide license agreement for AveXis to develop and commercialize gene therapy treatments using REGENXBIO's NAV AAV9 vector to treat two rare neurological monogenic disorders: Rett syndrome (RTT) and ALS. Under the terms of the REGENX License, AveXis has paid or is required to pay an upfront payment of $6.0 million, up to $36.0 million in total milestone fees for the REGENX licensed products, a low double digit royalty percentage on net sales of REGENX licensed products, subject to reduction in specified circumstances; and a lower mid-double digit percentage of any sublicense fees AveXis receives from sublicensees for the licensed intellectual property rights.[66]

Deals for developing stem cell therapy for indications other than ALS - Takeda acquired TiGenix for €520 million ($627 million) in an all-cash deal. The takeover gave Takeda full control of Cx601, a stem cell therapy that was closing in on a European approval in Crohn's disease in January 2018. The therapy eventually got the approval in March 2018. Takeda picked up the ex-U.S. rights to Cx601 for €25 million upfront in 2016. In December 2017, the EMA's drug review group recommended TiGenix's stem cell therapy for approval in the treatment of Crohn's disease patients. That milestone appears to have prompted Takeda to make its move.

In March 2015, Athersys, Inc. (**NASDAQ: ATHX**) and Chugai Pharmaceutical Co., Ltd. (**TYO:4519**) announced a partnership and license agreement to exclusively develop and commercialize MultiStem cell therapy for ischemic stroke in Japan. At the time of the deal, Athersys' proprietary cell therapy product, MultiStem, was being evaluated in a Phase 2 clinical study for ischemic stroke in the United States and Europe, and Athersys had begun preparations for clinical development in Japan, including engagement with the Japanese Health Authority. As part of the collaboration, Chugai will be responsible for the development and commercialization of MultiStem for ischemic stroke in Japan, and Athersys will have responsibility for product supply. Under the financial terms of the agreement, Athersys will receive an up-front cash payment of $10 million from Chugai and would receive additional payments as the program is further advanced. Athersys is eligible to receive milestone payments from Chugai of up to $45 million upon the successful achievement of certain development and regulatory milestones, and sales milestones of up to 17.5 billion Yen (approximately $150 million based on the current exchange rate). Athersys would also receive from Chugai tiered, double-digit royalties on any net sales, as well as payments for product supplied to Chugai.[67] FUJIFILM purchased a 10% equity stake in January 2017 in Cynata Therapeutics, who has allogeneic iPSC-derived therapeutic product (CYP-001) in phase 1 clinical trial for treating graft-versus-host disease, through an investment of $4 million. It also signed a licensing agreement with Cynata for an upfront payment of $3 million, $45 million in milestone payments, and potential $30 million in annual royalties.[68]

Diabetes

In April 2018, Eli Lilly paid $63 million up front to get its hands on Sigilon Therapeutics' islet cell encapsulation technology which is working on "living therapeutics" for Type 1 diabetes, stands to reap an additional $410 million in milestones and royalties. Sigilon launched in 2017 with $23.5 million and the Afibromer technology out of MIT and Boston Children's Hospital. It will be responsible for all development until it files an IND, at which point Lilly will take over the clinical development and commercialization costs and activities for the collaboration, the companies said.

[65] *'Sangamo set to earn more than $160 million in ALS deal'*, The Pharma Letter (March 2018)
[66] Form 8-K Avexis (June 2017)
[67] *'Athersys and Chugai Enter License Agreement and Collaboration to Develop MultiStem® Cell Therapy for Ischemic Stroke in Japan'*, Chugai Press Release (March 2015)
[68] Company Investor Presentation, Cynata Therapeutics (November 2017)

To conclude, we assume 8% royalties upon out licensing, $15M upfront upon successful phase 1/2a results (early 2020) with a total deal structure of $100M. As for Incapsulin, we took a similar royalties structure and based our assumption on similar deals.

R&D costs: We can estimate expenditure on ALS clinical trials based on expenses incurred by BrainStorm during its clinical studies in recent years. Also, we based our estimations on the company's assumptions for each indication as elaborated at the company's financial report for 2017.

Taxes: we assume the company will not pay taxes in our model as it has accumulated losses of more than NIS 115M.

Capitalization rate: We calculate our discount rate at 21.0% based on our CAPM model (see Appendix B).

Main valuation parameters

Indications	Current Development stage	Success Rate Phase I/IIa	Success Rate Phase II	Success Rate Phase III	Regulatory approval success rate	Launch	Exclusivity period
AstroRx®	1/2a	59.1%	29.7%	47.7%	89.0%	2024	2039
Incapsulin	pre-clinical	61.1%	45.2%	71.4%	77.8%	2028	2040

Based on the aforementioned parameters, we evaluate Kadimastem`s pipeline at NIS 76.7M.

Technological Platform Valuation

Kadimastem's product pipeline is supported by the company's broad business and technological base. Valuation of Kadimastem's "technological basis" is in fact a valuation of the company's "residual value". This valuation was conducted using the Feed Rate methodology that is common in the field of life sciences, rather than using the conventional terminal value, normally used by non-life science companies, for the following reasons:

- The terminal value reflects a type of steady state in company sales with a certain fixed growth rate (g) based upon past data. This is not the case for life science companies, where the terminal value is derived from projects in development.

- The terminal value for a given company usually constitutes between 70-80% of its worth. In contrast, the main share of the value of a life science company is attributed to income generated during several years following product launch (for the most part, approximately 6-10 years), after which a certain decline occurs (for example, expiration of a patent, and the emergence of competing products).

The technological platform valuation is based on the average number of new projects that a company can yield annually. Estimating the capitalization value of future projects is based on pre-clinical and clinical development aspects, assessment of unallocated costs, and a higher capitalization rate than the one used during the forecast years, due to the uncertainty of the company's future projects.[69]

Main technology platform valuation points:

- We assume one new project every three years with an average value of NIS 38.4M (equal to the average value of the current pipeline programs)

[69] Bogdan & Villiger, "Valuation in Life Science - Practical Guide", 2008, Second Edition.

- Unallocated costs are mainly G&A and sales costs, with a similar share from the project's value as in the current pipeline programs
- We estimate unexpected costs to be 5% of the average value
- Statutory tax rate is 23%, however we assume Kadimastem will pay low effective tax.
- The capitalization rate is higher than the one used in the pipeline valuation, reflecting the increased uncertainty
- It is assumed that the "platform" generates projects for n years: in our valuation, and based on the average patent period, n=18 years. We therefore subtract from the technological platform value all projects generated after n years (the exceeding projects).

The following formula reflects the value of the technology:

$$\mathrm{V(tech)} = \frac{(fVproject - (1+r)costs)}{r} * 1 - \frac{1}{(1+r)\text{^n}}$$

Main valuation parameters of the technology platform:

Average New Projects per Year	0.33
Project Value ($'000)	38,362
Unallocated Costs ($'000)	-32,090
Unexpected Costs ($'000)	-1,918
Tax	0%
Capitalization	26.0%
Terminal Technology Value ($'000)	5,588
Technology Value - 2018-2035 (NIS, '000)	88
Technology Value ($'000)	5,500

Equity Value

Non-operational assets/liabilities and unallocated costs

As of December 31, 2017, Kadimastem had NIS 9.5M of available cash, with short term credit of NIS 800K. The company also raised NIS 2.8M (gross) on 15 May. Kadimastem's monthly burn rate is approximately NIS 1.6M, thus taking the above into consideration, we evaluate the company as follows:

Pipeline Analysis		**rNPV (NIS,000s)**
AstroRx	ALS	39,084
Encapsulin	Diabetes	37,640
Total rNPV Pipeline		**76,724**
Unallocated Costs		-32,090
Terminal Technology Value		5,500
Enterprise Value		**50,135**
Non-operational assets/liabilities		1,997
Equity Value		**52,112**

Based on the aforementioned parameters, we estimate Kadimastem's equity value at NIS 52.1M.

Sensitivity Analysis

The table below presents Kadimastem's target price relative to the capitalization rate. We set a range of 0.5% change from our CAPM model (see Appendix B). Kadimastem has 61.6M shares.

Sensitivity Analysis - Capitalization Rate vs. target price

Cap. Rate	
23.0%	0.70
22.0%	0.77
21.0%	0.85
20.0%	0.93
19.0%	1.01

We estimate the target price to range between NIS 0.77 and NIS 0.93; a mean of NIS 0.85.

Price Forecast Risks

Biotech companies, particularly those in research and development stages, are relatively high-risk companies. Key risks that may affect Kadimastem include:

Delay/postponement of marketing regulatory approval decisions

In order for Kadimastem to market or out-license its products, it is necessary for them to receive marketing approval from regulatory agencies, such as the FDA (US) and EMA (EU). Our estimates regarding time to market are based on the assumption that these products will successfully complete Phase II and III clinical trials without significant delays. Failure to fulfill the clinical endpoints of these experiments will force the company to conduct additional clinical trials or abandon the development of certain projects. We consider this to be the main risk factor for the company's activity at this stage.

Risks involved in obtaining sources of financing, and stock trading

As a biotech holding company in the research and development stage, with minimal revenue from sales, Kadimastem will be required to conduct fundraising prior to becoming profitable, unless early licensing deals are made. Failure to raise funds, or fundraising under conditions that are not beneficial to the company, may affect its worth. In addition, the low level of tradability may deter some investors from buying Kadimastem stock.

General risks related to similar companies

The value of small companies in the biotech field could, to a relatively high degree, be affected by publications not related directly to their activities. Such publications may refer, for example, to competitors, macro trends in the healthcare sector, and political events.

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Key Executives

Name	Title
Mr. Yossi Ben-Yosef	Co-Founder, Chief Executive Officer and Director
Prof. Michel Revel M.D., Ph.D.	Co-Founder, Chief Scientist, Head of the Scientific Advisory Board and Director
Mr. Yehuda Feinberg	Chief Financial Officer
Dr. Arik Hasson Ph.D.	Executive VP of R&D
Dr. Michal Harel Izrael Ph.D.	VP of R&D for ALS and Neurodegenerative Diseases

Appendicies

Appendix A - Financial Reports

Balance Sheet	NIS 000s	NIS 000s
Current Assets:	**31.12.16**	**31.12.17**
Cash and cash equivalents	944	9,549
Accounts receivable	1,659	911
Total Current Assets	**2,603**	**10,460**
Non-Current Assets		
Restricted cash	585	604
PPE, net	1,575	1068
Total Assets	**4,763**	**12,132**
Current Liabilities		
Short time credit	1,931	772
Accounts payable	8,442	6567
Payments to chief scientist	22	0
Total Current Liabilities	**10,395**	**7,339**
Non-Current Liabilities		
Accounts payable	438	513
Loans	2,486	-
Total Liabilities	**13,319**	**7,852**
Total Equity	**-8,556**	**4,280**
Total Liabilities	**4,763**	**12,132**

Statement of Profit & Loss (NIS 000s) as at 31.12	2015	2016	2017
Revenues	**1,028**	**1,703**	**684**
Costs of revenues	(106)	(134)	(48)
Gross profit	**922**	**1,569**	**636**
R&D expenses	(9,613)	(13,089)	(14,870)
S&M expenses	(340)	(382)	(183)
G&A expenses	(6,390)	(7,467)	(6,420)
Operating loss	**(15,421)**	**(19,369)**	**(20,837)**
Financial income, net	(1,802)	(748)	(766)
Profit before taxes	(17,223)	(20,117)	(21,603)
Taxes	(159)	(144)	(175)
Net loss	**(17,064)**	**(19,973)**	**(21,428)**

Appendix B - Capitalization Rate

Cost of equity capital (ke) represents the return required by investors. The capitalization rate is calculated using the CAPM (Capital Asset Pricing Model). It is based on a long-term 30-year bond with a market risk premium, and based on Professor Aswath Damodaran's (NYU) commonly used sample (www.damodaran.com). As of December 31, 2016, the Israeli market risk is estimated at 6.69%. A three-year market regression Beta is 1.25, according to a sample of 426 companies representing the US biotechnology sector. We used an unleveraged beta of this sample, which is higher than a leveraged beta, due to high rate of cash versus debt. The implied CAPM is 10.7%.

The CAPM model (ke) is estimated as follows:

$$ke = rf + \beta(rm-rf) + P$$

Kadimastem is a small cap company, in which marketability and size premiums need to be considered. Duff and Phelps data from 1963-2016 indicates that an 10.24% premium needs to be added to the CAPM for small cap companies. We therefore estimate the company's CAPM to be 20.98%.

CAPM Model		Value	Source
Long-term (20 years) T-bond	R(f)	2.40%	Israel bond rate (0347)
Market risk premium	R(m)- R(f)	6.69%	based on Professor Damodaran's sample (1/17)
Beta unleveraged	β	1.25	Beta sample of 426 Drugs (Biotechnology) firms (1/17)
Cost of Capital	ke	10.7%	
Size Premium		10.24%	Duff and Phelps data, 10dz.
CAPM	CAPM	**20.98%**	

Appendix C – Team Bios

Kobi Hazan is the Lead Analyst at Frost & Sullivan Research & Consulting Ltd., a subsidiary of Frost & Sullivan in Israel. He has over 14 years of experience in capital markets, including; research, analysis, investment advisory, and management. Mr. Hazan served as a Fund Manager for provident and mutual funds at Analyst Ltd. and, since 2012, he owns and manages the Amida Israel Fund, a hedge fund specializing in Israeli equities. Kobi holds an Economics and Management degree from The College of Management Academic Studies. He is licensed as an Investment Advisor in Israel.

Dr. Tiran Rothman is Head of Operations at Frost & Sullivan, Israel. He has over 10 years of experience in research and economic analysis of capital and private markets, obtained through positions at a boutique office for economic valuations, as chief economist at the AMPAL group, and as co-founder and analyst at Bioassociate Biotech Consulting. Dr. Rothman also serves as the Economics & Management School Head at Wizo Academic College (Haifa). Tiran holds a PhD (Economics), MBA (Finance), and was a visiting scholar at Stern Business School, NYU.

Dr. Anna Cirmirakis joined Frost & Sullivan Transformational Healthcare team as a Healthcare consultant in February 2015. She works primarily with biotech, pharma and diagnostics companies on a wide range of strategic projects including product evaluation, market analysis as well as competitive intelligence. Before joining Frost & Sullivan, Anna worked at Pharmaceutical giant GlaxoSmithKline (GSK) for four years. Prior to her role as a consultant she earned a BSc in Human Genetics and a PhD in biotechnology from University College London. Anna is a specialist in the field of monoclonal antibody production with keen interest in regenerative medicine, immunotherapies and biologics.

Shiva Joshi - Have over 6 years of experience in providing business consulting to global pharmaceutical, medical devices, and healthcare companies. Consulting assignments include opportunity assessment for new product launch, market sizing and forecast, competitive intelligence, supplier benchmarking, engagement models and best practices etc. Shiva has worked across different therapeutic areas, such as oncology, respiratory, and neurology for both emerging markets (including India, Brazil, China, and Saudi Arabia) and developed economies (such as the US, the EU, and Japan).

Daniel Grunstein is a Consulting Analyst at Frost & Sullivan in Israel and has been working on the TASE program for the past 14 months. Daniel has five years of work experience in research and international business development in Australia and Israel. Daniel holds a BA (Economics) from the University of Sydney, and an MBA (Innovation & Strategy) from Tel Aviv University.

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