Argenica Therapeutics Limited

(AGN $0.64) Speculative Buy - Initiation of Coverage

EUROZ HARTLEYS

Analyst	Date	Price Target
Seth Lizee	**7th April 2022**	**$1.00/sh**

The Future of Stroke Treatment?

Investment case

Argenica Therapeutics Ltd (AGN) is a clinical stage pharmaceutical company developing novel therapeutics for stroke and other types of neural injury.

The company's lead candidate, ARG-007, aims to reduce brain tissue death after stroke and improve patient outcomes. The treatment landscape is prime for disruption with new solutions needed. AGN's novel neuroprotective therapeutic is backed up by over 7 years of preclinical research. The company is now looking to start human trials with its Phase 1 study targeted to kick-off this quarter.

The prize, should ARG-007 be clinically successful, is huge. We believe the stock will trade up with the delivery of upcoming catalysts (refer below), including the initiation of phase 1 trials. If successful, phase 2 studies in the primary indication of stroke could be quickly set in motion, with possible secondary indications following. If AGN can delivery successful clinical outcomes, we believe the stock can trade above our price target, potentially significantly higher.

We initiate coverage on Argenica Therapeutics Limited with a Speculative Buy recommendation and Price Target of $1.00/sh.

Key points

- **Large Addressable Market** – An estimated 15 million people suffer from a stroke each year, of which two thirds either die or are left permanently disabled. The high mortality rate makes stroke the second leading cause of death globally, killing over 6.1 million people in 2019 alone. The direct and indirect costs of stroke are estimated to be US$841 billion per annum globally.
- **New Treatments Needed** – Current stroke treatments face various limitations, in addition to only addressing the underlying cause, and not the brain cell damage invoked. The standard of care fails to adequately address the time critical nature of stroke, with life-saving interventions only occurring once a patient is in hospital, sometimes many hours after a stroke. This time lost in the delay of treatment can impact patient recovery, and is associated with increased mortality.
- **Solution: Neuroprotection as a Treatment** – AGN's lead candidate, ARG-007, looks to address the current gaps in treatment with the aim to be administered in the field by paramedics. The drug is being developed to provide neuroprotection to reduce brain tissue death following a stroke, providing physicians more time to treat and improving patient outcomes.
- **Extensive Preclinical Research** – ARG-007's efficacy and safety in stroke is backed up by over 7 years of preclinical research, with a total of 24 published journal articles on the compound. Preclinical studies are comprehensive, covering various injury (stroke) and animal models (including non-human primates).

Argenica Therapeutics Ltd		Year End 30 June
Share Price	**0.64**	**A$/sh**
Price Target	**1.00**	**A$/sh**
Valuation	1.00	A$/sh
Shares on issue	82.3	m, diluted
Market Capitalisation	52.7	A$m
Enterprise Value	44.6	A$m
Debt (Dec'Q)	0.0	A$m
Cash (Dec'Q)	5.3	A$m
Unpaid cap	2.7	A$m
Turnover	210k	sh/day
12 Mth Hi-Lo	1.02-0.18	A$/sh
Balance date	June 30th	

Directors & Management

Mr Geoff Pocock	Non Exec Chair
Dr Liz Dallimore	CEO & MD
Dr Samantha South	Exec Dir
Mr Terry Budge	NED
Ms Liddy McCall	NED
Ms Emma Waldon	CFO & Co Sec
Prof. Bruno Meloni	CSO

Company Details

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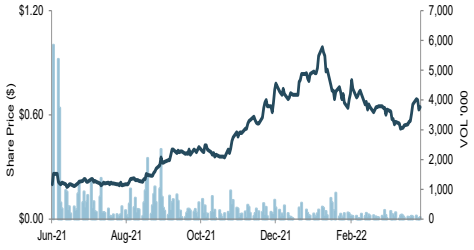
Share Price Chart



Disclaimer

Euroz Hartleys declares that it has acted as underwriter to and/or arranged an equity issue in and/or provided corporate advice to AGN during the last year. Euroz Hartleys has received a fee for these services.

This analyst declares that he has a beneficial interest in AGN.

Euroz Hartleys has received an allocation of shares and/or options as part of our fee for the provision of Corporate services for AGN. These holdings are in escrow and may present a potential benefit to Euroz Hartleys when released from escrow.

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- **Solid Efficacy** – ARG-007 showed a 65.2% reduction in brain tissue death 24 hours post stroke in non-human primates (with a 69.7% reduction at 28 days). This is significantly better than its closest competitor, NA-1, which only showed a 44% reduction at the same time.
- **Excellent Safety Profile** – ARG-007 has shown to be safe and well tolerated across preclinical studies, additional literature on the broader drug class suggest a similar safety profile.
- **Secondary Indications** – AGN has preclinical research showing efficacy in secondary indications, including hypoxic ischaemic encephalopathy (HIE), traumatic brain injury, and global brain ischemia. These have large addressable markets in addition to being in need of better treatments.
- **Experienced board and management** – Extensive background across development and commercialisation. Board and management are well aligned, owning 19.1% of the company.
- **Attractive valuation** – AGN trades at a 36% discount to our $1.00/sh. Valuation.
- **Multiple upcoming catalysts** – We note a number of short to medium term catalyst lie ahead.

	CY'2022			CY'2023				
Key Catalysts	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Significance
Stroke								
Full Pharmacokinetics	■	■						
GLP Safety & Toxicology	■	■						Required for Phase 1 Study
Pre-study activities	■	■						
HREC Approval	■	■						Approval of Phase 1 Study
Phase 1 (stroke)		■	■	■				
Preliminary Results		X						Evaluation of Safety & tolerability
Final Results			X					
Phase 2 (stroke)				■	■	■	■	Evaluation of Efficacy & safety
Other Indications								
Preclinical Research	■	■	■	■	■	■	■	Evaluation of secondary indications

Source: EHL Estimates

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Risks

We outline key risks to our investment case below:

- **Clinical Development** – As a preclinical pharmaceutical company there is significant risk surrounding clinical outcomes. The success of the upcoming phase 1 trial is critical to the future of ARG-007 and AGN. Failure of this upcoming trial risks halting the development of ARG-007 for stroke, as well as any other potential secondary indications. Beyond this, there will continue to be risk surrounding clinical outcomes of later trials (i.e. Phase 2 and 3). The company has worked to offset this risk as much as possible through completing an extensive amount of preclinical studies.
- **Competition** – While there are not a large number of competitors, the development of a superior therapeutic alternative is a risk to the commercial potential of ARG-007. We have extensively evaluated key competitors in this report.
- **Funding** – AGN is currently cashflow negative and will likely require additional capital to fund development programs, there remains the usual risks around timing of any future funding requirements.
- **Regulatory** – Achieving regulatory approval in key jurisdictions will be critical towards development and commercialization of ARG-007. Failure to be granted these approvals will impact AGNs ability to develop or commercialize ARG-007.
- **Intellectual Property** – AGN maintains an extensive intellectual property portfolio, loss or issues surrounding these patents could impact the business.
- **Key Personnel** – The company has a number of experienced key personnel, including the Chief Scientific Officer who discovered and has led the development of ARG-007. Loss of any key individuals could slow the development process.
- **Commercialization** - Clearly a commercial outcome cannot be guaranteed; this risk will decline as the company progressively develops and validates its product(s).
- **COVID19** – There is a risk COVID-19 may disrupt timelines.

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Valuation and Price Target

We initiate coverage with a Speculative Buy recommendation and $1.00/sh. Price Target.

Our valuation is derived through a risked NPV (rNPV) of AGN's clinical program in stroke. We view this as the most appropriate methodology, as it evaluates the programs successful value and accordingly risks it based on its stage of clinical development.

Further justifying our investment case, we have considered ASX listed peers and M&A activity in recent years.

On balance, we believe there is a highly asymmetrical investment opportunity present. Whilst we acknowledge there is considerable risk at this early stage of development, the upside from successful clinical outcomes could be worth many multiples of the current market valuation.

rNPV – Risked Net Present Value

A summary of our risked NPV (rNPV) is shown below.

We have calculated an equity value of $82.2m or $1.00 per share.

Valuation	Units	Value
Asset Value (NPV)	A$m	1,260.4
(x) Risking (r)	%	5.9%
Risked Valuation (rNPV)	A$m	74.2
(+) Net Cash	A$m	5.3
(+) Unpaid Capital	A$m	2.7
Equity Value	A$m	82.2
(/) Diluted SOI	m	82.3
Equity Value/share	**A$/sh.**	**1.00**

Source: EHL estimates

We have modelled the successful **asset value of ARG-007 in the primary indication of stroke**, this calculated using an NPV of forecasted free cashflows. We forecast cashflows using the following assumptions:

- Peak market share & uptake curve
- Pricing
- Economic period
- Gross Margin; and
- Development capital required

We detail these assumptions and forecasts on page 27.

We have ascribed **no value for secondary indications** of hypoxic ischaemic encephalopathy, traumatic brain injury, or global brain ischemia. We will look to eventually incorporate these as clinical development progresses. We further note these indications have large market opportunities.

We have calculated our NPV using a **conservative 25% discount rate, we note there is scope to reduce this as the company de-risks.**

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We have risked our NPV by the statistical likelihood of approval, this being the cumulative probability of clinical success (i.e. successful Phase 1, 2, 3 and NDA). This figure is based on the average historical phase success in neurology indications between 2011 and 2020. These figures are shown below:

Phase Success	Phase I to II	Phase II to III	Phase III to NDA	NDA to Approval	Cummulative
Neurology	47.7%	26.8%	53.1%	86.7%	5.9%

Source: BIO, Informa Pharma Intelligence, and QLS Advisors

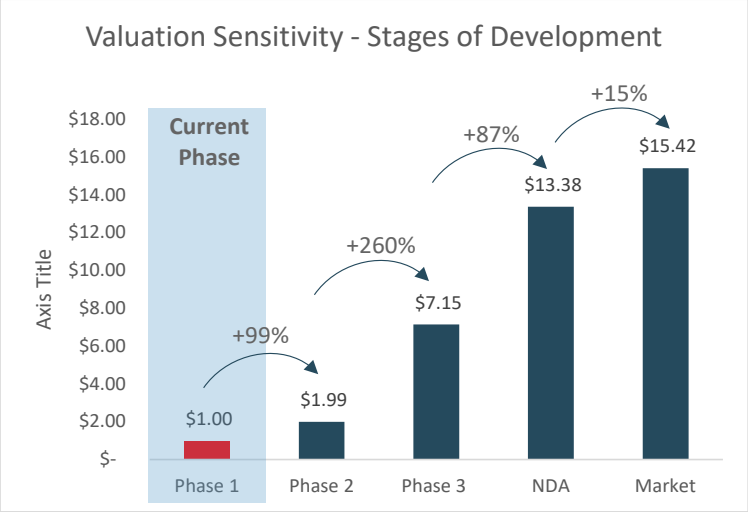
The cumulative probabilities at different stages can be calculated as shown below. Based on AGNs current stage, we have risked our valuation by 94.1% (5.9% probability).

		Future Phase				
		Phase 1	Phase 2	Phase 3	NDA	Market
Current Phase	Phase 1	100.0%	47.7%	12.8%	6.8%	5.9%
	Phase 2		100.0%	26.8%	14.2%	12.3%
	Phase 3			100.0%	53.1%	46.0%
	NDA				100.0%	86.7%
	Market					100.0%

Source: BIO, Informa Pharma Intelligence, and QLS Advisors

We note, our analysis of AGN's preclinical research suggest there is a much higher chance of passing the Phase 1 clinical trial than the ~47.7% probability suggested by these statistics. However, in constructing a conservative valuation, we have applied this conservative risking; further highlighting the upside to our valuation.

Accordingly, our Valuation and Price Target progressively increases as the company passes through successive clinical trials, as a function of de-risking. We have attached below a sensitivity of our rNPV valuation at different stages of clinical development (obviously requires previous stages to be successful). This assuming no change in discount rate or dilution.



Source: EHL Estimates

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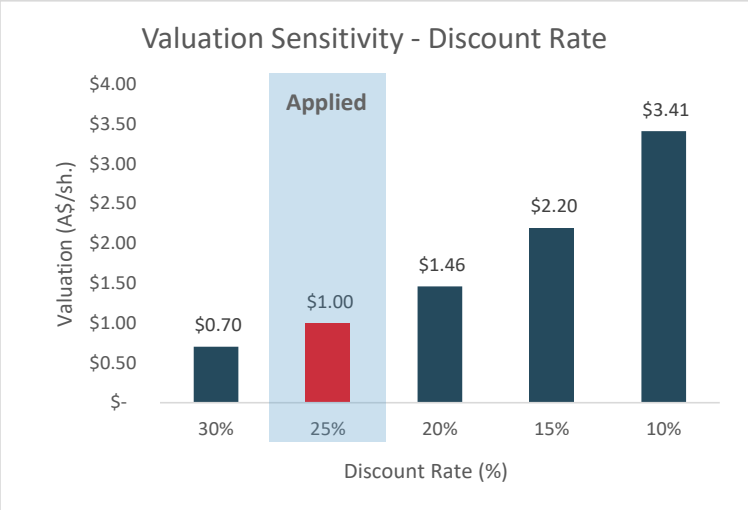
Clearly, there is significant value uplift if AGN can successfully progress the clinical development of ARG-007, from the current preclinical stage through to approval. Additionally, successfully clearing phase 1 should de-risk any secondary indications of ARG-007, potentially offering further value upside.

We have further included a sensitivity analysis of the discount rate used in our rNPV valuation, this shown below.



Source: EHL Estimates

Similarly, there is huge upside as AGN de-risks (through reducing discount rates).

Neurology M&A Activity

We can explore M&A activity in the broader neurology space as an indication of the value potential for AGN, and more specifically ARG-007.

In the last decade there have been a number of transactions in the space, with deals listed below ranging from US$140 million to US$3.5 billion.

Target Name	Buyer Name	Year	Country (Target)	TV* (US$m)	Stage of Lead Product	Indication(s)
Avanir	Otsuka	2015	US	3,500	Phase 2	Alzheimer's, Parkinson's, anti-psychotic
Prexton	Lundbeck	2018	Netherlands	1,100	Phase 2	Parkinson's
NeuroDerm	Mitsubishi Tanabe Pharma	2017	Israel	1,100	Phase 3	Parkinson's
Disarm Therapeutics	Eli Lilly	2020	US	1,360	Preclinical	Alzheimer's, ALS, MS, Neurodegenerative diseases
Prevail Therapeutics	Eli Lilly	2020	US	1,040	Phase 1/2	Parkinson's, Neurodegenerative diseases
Chase Pharmaceuticals Corp	Allergan	2016	US	1,000	Phase 2	Alzheimer's
Rodin Therapeutics	Alkermes	2019	US	950	Preclinical	Neurodegenerative disorders
Cynapsus Therapeutics	Dainippon Sumitomo	2016	Canada	624	Phase 3	Parkinson's
Azur Pharma	Jazz Pharmaceuticals	2012	Ireland	580	Market	CNS (inc. schizophrenia), womens health
Civitas	Accorda	2014	US	525	Phase 2	Parkinson's
XenoPort	Arbor Pharmaceuticals	2016	US	467	Market/Clinical Development***	CNS, Parkinson's, Alcoholism
Heptares	Sosei	2015	UK	400	Market/ Clinical Development**	Various (inc. Alzheimers, ADH, etc), COPD
Biotie Therapies	Acorda Therapeutics	2016	Finland	363	Phase 3	Parkinson's
Envoy Therapeutics	Takeda	2012	US	140	Preclinical	CNS, Parkinson's, Schizophrenia
Average				**939**		

** Overall Transaction Value*
*** Products in market for COPD*
**** Products in market for RLS*

Source: Company announcements, News articles, EHL estimates

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The transactions listed above are across various neurodegenerative diseases, and at various stages of development. We believe these are indicative of the potential for novel stroke treatments such as ARG-007, with similar demands for new treatments wanted and large addressable markets.

These transactions indicatively demonstrate the significant upside possible for AGN, every transaction listed would imply multiples of the company's current valuation.

Furthermore, there is activity across the development spectrum from preclinical through to marketed drugs. This highlights the potential for AGN to realise value, potentially well before its in market or even approved.

Listed Peers

We explore ASX listed peers below.

Ticker	Name	Therapeutic Area(s)	Stage	Mkt Cap	EV
PYC	PYC Therapeutics	Occular/ CNS	Preclinical	291.8	248.2
RCE	Recce Pharmaceuticals	Anti-Viral/ Anti-Bacterial	Preclinical/Phase 1	184.2	168.4
EMD	Emyria	Various	Preclinical/Phase 1	109.3	100.6
IVX	Invion	Oncology	Preclinical	107.0	93.5
PAB	Patrys	Oncology	Preclinical	58.3	45.6
VBS	Vectus Biosystems	Anti-fibrotic	Preclinical	64.5	61.3
NSB	Neuroscientific Bio.	Alzheimers, Neurology	Preclinical	45.7	36.2
EX1	Exopharm	Exosomes	preclinical	40.4	31.1
NYR	Nyrada	Cardiovascular/ Neurology	Preclinical	42.5	31.4
ALA	Arovella Therapeutics	Oncology	Preclinical	32.1	27.8
**Fully diluted*					
			Mean	***97.6***	***84.4***
AGN	**Argenica Therapeutics**	**Stroke, HIE, TBI**	**Preclinical**	**52.7**	**44.6**
			Discount	***-46%***	***-47%***

Source: company announcements, IRESS, EHL estimates

Peer comparisons are difficult, especially for highly differentiated pharmaceutical companies. However, as a broader exercise we have compiled preclinical stage ASX listed pharmaceutical companies.

AGN trades at a 46% discount to the mean market capitalisation.

These peer comparisons indicatively show the value potential for AGN. We further believe AGN is well positioned, coming to the table with a number of strengths, such as:

- Large addressable market, limited competitors, demand for new therapies
- Extensive preclinical research
- Acute disease (i.e. faster development timeline)
- Potential for multiple indications (i.e. HIE, TBI, GBI)

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Downside Valuation

Rounding off our analysis we can explore the worst-case scenario, this downside outcome would imply AGNs upcoming phase 1 clinical trial does not succeed. In the case the phase 1 fails, we would expect AGN falls back down towards cash backing. The company is backed by circa $0.10/sh. (fully diluted) in cash and unpaid capital. This highlights the risks involved.

Price Target and Recommendation

Our $1.00/sh. Price Target per our analysis is based on the risked development of AGN's clinical program in stroke.

The staged success of AGNs clinical program should de-risk the asset and translate into progressively higher valuations, outlining the potential upside beyond our current price target.

The significant risks surrounding unsuccessful outcomes from clinical programs further drive our **Speculative Buy Recommendation.**

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Company Overview

Argenica Therapeutics Ltd (AGN) is a clinical stage pharmaceutical company developing novel therapeutics for stroke and other types of neural injury.

The company's lead candidate, ARG-007, is a neuroprotective peptide being developed in the primary indication of stroke. The aim is to reduce brain tissue death after stoke and improve patient outcomes. AGN is targeting to initiate its first in human phase 1 clinical trial this quarter.

ARGENICA THERAPEUTICS

Source: company website

Founded in 2019, the Perth based company was incorporated with the goal to develop and commercialize ARG-007.

ARG-007 was originally discovered and developed by world-leading researchers out of the University of Western Australia and the Perron Institute for Neurological and Translational Science. A total of 24 peer review journals have been published over the last 7 years on ARG-007 demonstrating safety and efficacy in ischemic stroke, in addition to:

- Traumatic Brain Injury (TBI)
- Hypoxic ischemic encephalopathy (HIE); and
- Global Brain Ischemia

Stroke

Stroke is an acute medical condition where brain tissue is starved of blood and oxygen resulting in cell death. Depending on the level of brain damage caused it can lead to numerous complications, including death.

Non-fatal complication of stroke can result in various temporary or permanent disabilities, which include:

- Paralysis or loss of muscle movement
- Difficulty talking or swallowing
- Memory loss or thinking difficulties
- Emotional problems
- Pain/numbness
- Changes in behaviour and self-care ability

Every stroke is different, the outcome of those affected will depend on various factors which include:

- Type of stroke
- Location of brain damage
- The amount of permanent damage
- Health/wellbeing before the stroke

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The risk factors of stroke include:

- High blood pressure
- Smoking
- High cholesterol
- Diabetes
- Obstructive sleep apnoea
- Cardiovascular disease
- Personal or family history of stroke

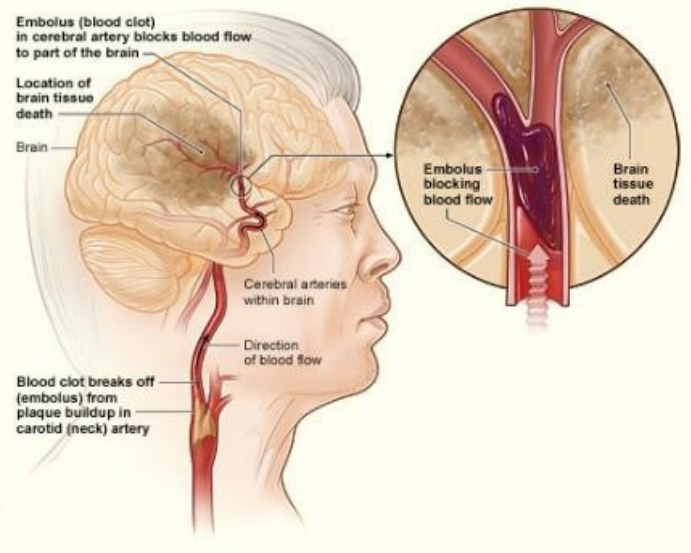
There are two distinct types of stroke:

- Ischemic; or
- Haemorrhagic

The signs and symptoms are the same, however treatment is different depending on type of stroke.

Ischemic Stroke

This is the most common type of stroke, representing 87% of all strokes. This type of stroke occurs when a blood vessel in the brain is blocked, this is typically the result of a blood clot or a piece of plaque. As shown below:



Source: National Heart, Lung, and Blood institute (NIH)

The loss of blood flow initiates a series of events known as an ischemic cascade. This series of biochemical reactions can begin within seconds to minutes and can last for hours to days, even once blood flow has returned to the brain.

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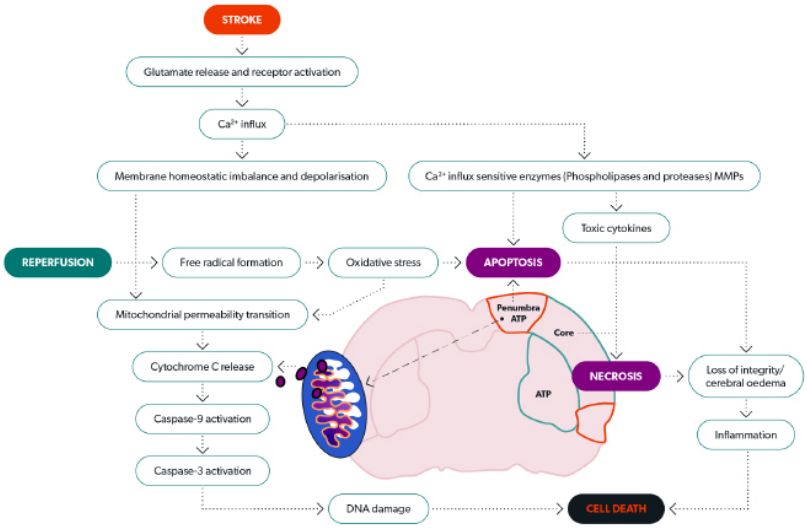
The ischemic cascade despite its name is not always linear. This complex process is detailed in the diagram below:



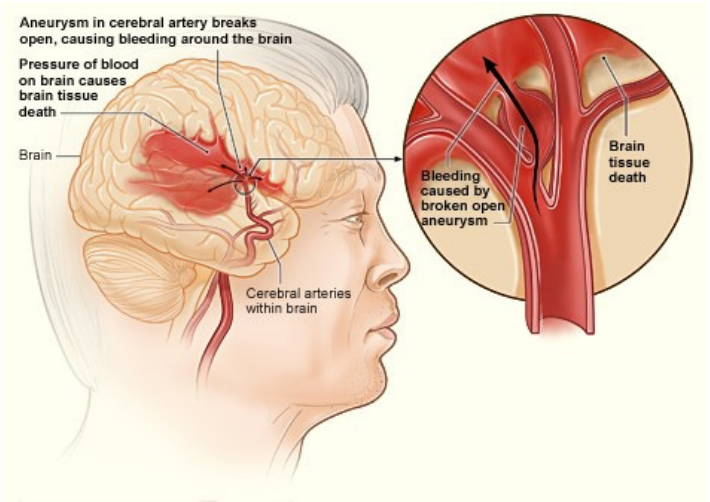
Source: Company website

Broadly speaking, the initial ischemic stroke, as well as the subsequent restoration of blood flow (reperfusion) leads to a cascade of events, the final outcome being cell death. As stated previously, the complications of the stroke will depend on the location and severity of cell death in the brain.

Haemorrhagic Stroke

This type of stroke occurs when a blood vessel breaks open, either in the brain or on top of it. Haemorrhagic strokes are less common, representing 13% of strokes.

A diagram of this is shown below:



Source: National Heart, Lung, and Blood institute (NIH)

The bleed in or around the brain results in swelling, this can compress the brain. The compression can directly distort or injure brain tissue, in addition to potentially restricting blood supply to areas of the brain. This loss of blood flow can result in cell death in the same way as an ischemic stroke.

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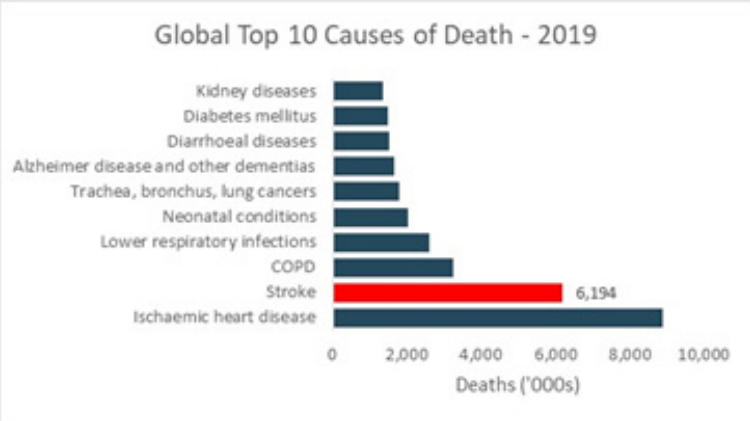
Prevalence

The global burden of stroke is both massive and growing. According to the World Health Organization (WHO), there is an estimated **15 million people who suffer from a stroke each year**, of these roughly:

- 5 million will die; and
- 5 million will be left permanently disabled

The high mortality rate makes stroke the second leading cause of death globally, only behind heart disease. In 2019, there were 6.1 million deaths from stroke globally, shown below:

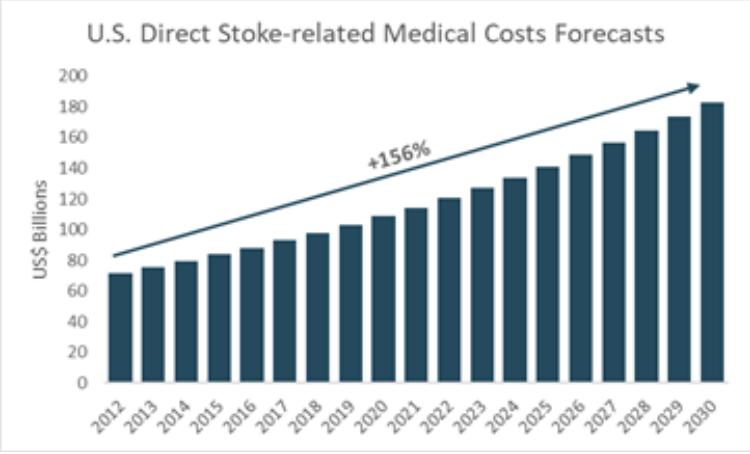


Source: World Health Organization (WHO)

The level of permanent disability is just as substantial, as outlined previously these can be significant and life altering impairments. It is estimated **only 10% of stroke sufferers will recover 'almost completely'.**

The economic burden of stroke is just as significant, both in terms of direct treatment and rehabilitation costs, as well as indirect costs of underemployment and premature death.

Globally, stroke is estimated to directly and indirectly cost ~US$891 billion per annum (2017). In the US alone, total direct stroke-related medical costs were US$71.5bn (in 2012), a figure which is forecasted to reach +US$183 billion by 2030.



Source: EHL estimate; Gorelick PB, 2019

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Current Treatment Pathway

How a stroke is treated will vary based on whether it is an ischaemic or haemorrhagic stroke. As a result, the standard of care begins with diagnosis. Doctors must move quickly to first determine which type of stroke a person is having, this will likely involve a computed tomography (CT) scan or other imagining.

Source: Company prospectus

Treatment can only begin once the type of stroke is identified. It should be noted that brain damage cannot be reversed, rather stroke treatment looks to resolve the underlying cause and stop further damage. The cause either being:

- A clot (ischemic stroke); or a
- Brain bleed (haemorrhagic stroke)

In the case of an ischemic stroke, the most common type of stroke, physicians look to restore blood flow to the brain. Doctors can treat an ischemic clot in one of two ways:

- Thrombolysis – Drug which dissolves blood clots and restores blood flow; or
- Mechanical thrombectomy – Medical procedure that surgically removes the clot

Thrombolysis involves an intravenous (IV) injection of a drug which can dissolve blood clots, known as a recombinant tissue plasminogen activator (or tPA for short). There are three types of tPAs in the market, including alteplase (Activase), tenecteplase (TNKase), and Reteplase (Retavase). Alteplase is the only FDA approved tPA for acute ischaemic stroke.

Despite its strengths, tPa comes with limitations and risks. The drug must be administered within 3hrs (sometimes up to 4.5hrs) after the initial stroke event, after which point the risks outweigh the benefits. Additionally, tPA may not always be effective against larger clots, such as clots found in the larger blood vessels at the base of the brain (25-30% of all strokes). However, the American health association still recommends its use even if a mechanical thrombectomy is being considered.

The main risk with tPA is that it can cause uncontrolled bleeding. Hence the huge risks if incorrectly administered to someone having a haemorrhagic stroke, where tPA can have the opposite effect and actually make the stroke worse (possibly leading to death).

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Given this, it is clear why a powerful and potentially life-saving drug like **tPA cannot be administered on site (i.e. by first responders) prior to the diagnosis of the type of stroke** sustained. This further contributes to its limited real world use (circa 3-15% of strokes).

Mechanical thrombectomy involves a surgical procedure where the clot is removed manually. This can address some of the gaps in tPA and as stated can also be done in conjunction to the tPA treatment.

Treatment for haemorrhagic stroke is more complex in that it involves addressing both the initial bleed in addition to the subsequent pressure caused by the fluids in the brain, the later causing the brain damage. This will typically involve some form of surgery. We won't go beyond this as the focus of this research is on ischemic stroke (the primary indication for ARG-007).

The Gap in Treatment

Roughly 1.9 million brain cells die every minute that goes by following a stroke. The current treatment pathway fails to adequately address the time critical nature of strokes, as lifesaving intervention only occurs once a patient is in hospital.

In terms of patient outcomes, time lost by the delay of treatment can lead to vastly different outcomes. Greater time to treatment is associated with increased mortality due to increasing amounts of cell death. A recent US retrospective cohort study (Man S, Xian Y, Holmes DN, et al) in 61,426 acute stroke (ischemic) patients illustrated this, where a longer door-to-needle (tPA administration) time was associated with:

- Significantly higher all-cause mortality at 1 year; and
- Higher likelihood of all-cause readmission at 1 year

This gap in treatment comes back to the limitations of existing options. As previously discussed there are two main ways to address an ischemic stroke, either through thrombolysis or performing a mechanical thrombectomy.

Clearly the latter has to be done in hospital. As for using a thrombolysis, despite the powerful potential of therapeutics such as tPA, these cannot be administered until the type of stroke is confirmed (which is also done in hospital).

In either case, patients need to be at properly equipped hospital to be treated for stroke. As a result, there can be many hours between the stroke event and medical intervention, this is even longer for those in rural areas. This additional time increases the amount of cell death, as blood flow is not restored.

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New Solution: Neuroprotection as a Treatment

Developing a neuroprotective therapeutic has the potential to completely alter the stroke treatment landscape. A successful drug could provide protection to brain cells in the acute stage of a stroke, this providing physician more time to treat the underlying cause. Additionally, it could possibly address and reduce some of the damaging processes (inflammation, excitotoxicity, oxidative stress, etc) which occur during and long after the underlying stroke is resolved. All together improving patient outcomes. This is exactly what AGN is looking to do with its novel drug, ARG-007.

However, this concept is not new, in practice over the last +40 years there has been over +1,000 different neuroprotectants tested. The bulk of this research occurred in the 1990s, when the space was crowded with large pharmaceutical companies investing hundreds of millions of dollars into researching new therapeutics. Despite all of this, no compound to date has been successful translated from initial Preclinical research into an approved therapeutic. Researchers have theorized a long list of reasons as to why these past drugs have failed, major reasons being:

- **Monofunctional Mechanism of Action** – Most of the drugs previously researched focused on a single mechanism design. It is speculated these compounds failed to work effectively as they only addressed a single part of the complex biochemical reaction which occurs in a stroke. As a result, researchers believe a multimodal mechanism of action is required in developing successful neuroprotective therapeutics.
- **Study Design / Disease Model** – Whilst a broader statement, its also speculated past compounds failed to translate because they were developed on incomparable animal models of stroke, in addition to not effectively capturing the full range of outcome data. Examples of this included assuming neuron chemical injury models would translate into stroke models.

In response to the systemic clinical failures encountered, researchers came together to form an organization to address these issues. Founded in 1998, the Stroke Treatment Academic Industry Roundtable (or "STAIR") was formed to provide new solutions to researchers. In the years since, a myriad of recommendations and guidelines have been provided. AGN in its development of ARG-007 follows these priorities.

At the same time, these past difficulties have resulted in underinvestment in the space, under the pretence that it's a "graveyard" despite the significant progress made (i.e. STAIR). Altogether, this situation has created a huge opportunity for companies like AGN.

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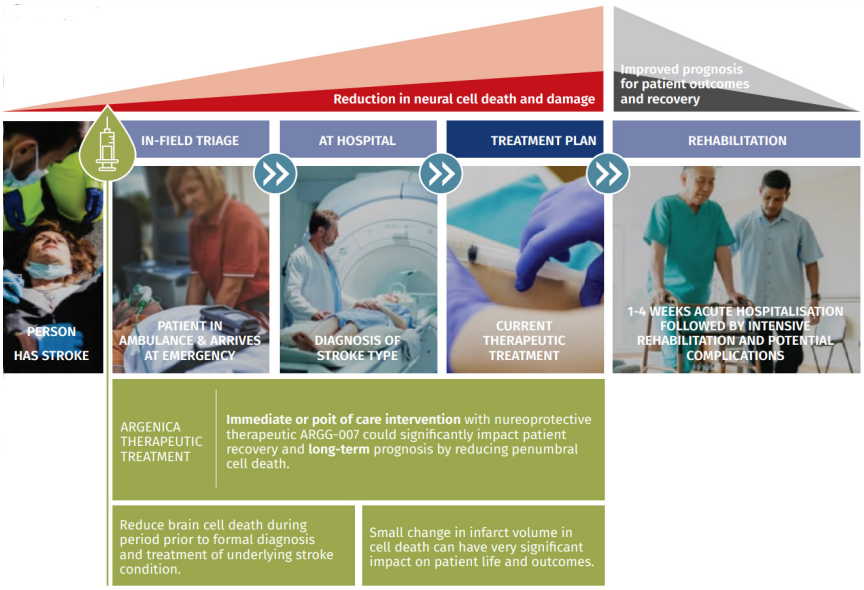
ARG-007

AGN looks to disrupt the stroke treatment landscape with its novel drug, ARG-007. The company is developing ARG-007 to be administered in the field by paramedics to provide neuroprotective treatment prior to a patient's arrival at hospital.

Extensive clinical research has shown ARG-007 can protect vulnerable brain tissue from dying, which could extend the time available for clot removal by thrombolysis and/or thrombectomy, in the process greatly enhancing clinical recovery outcomes for patients post stroke.

This would alter the treatment pathway as follows:



Source: company prospectus

ARG-007 (also known as R18D) is a Cationic Arginine Rich Peptide (CARP). CARPs are an expanding group of drugs with intrinsic neuroprotection capabilities.

The relatively simple molecule is a linear peptide with 18 arginine's.

The compound was initially discovered in 2015, and has been developed by AGN Chief Scientific Officer Prof. Bruno Meloni and his team through the University of Western Australia and the Perron Institute for Neurological and Translational Science. Their initial work on cell penetrating peptides (CPPs) in 2014, specifically poly-arginine rich peptides and their neuroprotective potential is what led to the discovery of ARG-007.

ARG-007 was initially shown to have neuroprotective properties in a 2015 study on various poly-arginine compounds. Various follow up studies found it to be the optimal length poly-arginine peptide, demonstrating the greatest level of efficacy against other candidates (and competitors). In the 7 years since discovery, an extensive amount of preclinical research has been done on the compound. We explore this below.

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Preclinical Research

A core pillar of our investment case centres around the extensive pre-clinical work completed to date on ARG-007.

Over the last 7 years, AGN has accumulated a comprehensive body of research having published 24 peer review journal articles on the compound, with 9 on stroke alone. This research has also followed priorities of the Stroke Treatment Academic Industry Roundtable (STAIR).

The research is diverse in that It covers,

- Various studies (large sample size);
- Multiple animal models;
- Multiple injury models;
- Multiple efficacy endpoints;
- Safety & toxicology (both in vitro and in vivo);
- Mechanism of action;
- Certain interactions/stability (key to real world success); and
- Secondary indications (useful in various ways)

To date, preclinical studies on ARG-007 have demonstrated:

- **Efficacy**: shown to reduce brain tissue death by up to 69.7% (28days after stroke) in non-human primates
- **Safety**: shown to be safe with no adverse side effects, and safe to administer in field (does no exacerbate bleeding in haemorrhagic stroke)
- **Mechanism of action**: targets multiple parts in the ischemic cascade
- **Stability**: Does not degrade when co-administered with tissue plasminogen activators (tPA and TNK)

Overall, this provides AGN a detailed foundational understanding of ARG-007, and in doing so places it in a strong position to translate research into human clinical trials.

We have summarized key figures and findings of these published studies in a table on page 21.

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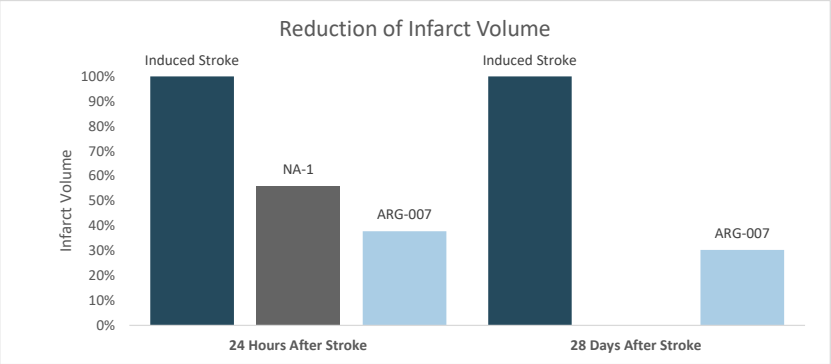
Efficacy

The neuroprotective efficacy of ARG-007 has been demonstrated in the extensive amount of studies conducted by Prof. Bruno Meloni and his team. Data covers various animal models, injury models, and efficacy endpoints. Studies have shown ARG-007 significantly reduces brain tissue death, and improve functional recovery.

The highlight being the 2019 study in non-human primates (monkeys), where **ARG-007 was shown to reduce infarct volume (i.e. Brain cell death) by up to 65.2% and 69.7% at 24hrs and 28 days respectively after stroke.**

This compares to AGNs closest competitor (NA-1), which only recorded a 44% reduction at the 24h point. We explore NA-1 in detail within the competitor's section below.



Source: Company presentation

Equally as significant, the study showed that A**RG-007 improved functional recovery.** The study's treatment group recorded a lower nonhuman primate stroke scale (NHPSS) score at every post-stroke time point.

The study was designed to replicate, as close as possible, the pathological conditions of real-life human stroke. Key study parameters being:

- 20 male cynomolgus macaques
- Transient middle cerebral artery occlusion (MCAO) model, surgically induced for 90 minutes (replicates a stroke with reperfusion, which can cause further damage)
- R18 (i.e. ARG-007, at 1,000nmol/kg) or saline vehicle administered 60 minutes post MCAO

Additionally, AGN has also examined ARG-007's efficacy in rats. A total of 8 studies has been published in various rat models of stroke. Whilst it's not the optimal model, the data is still highly valuable considering the scope and breadth of studies completed. The studies completed cover:

- **Rat Type**: Sprague-Dawley or Wistar
- **Stroke Type**: Permanent or transient MCAO; surgically or chemically induced
- **Stroke Duration** (for transient): from 90mins to 2hrs
- **ARG-007 Administration** (time post MCAO): from immediate to 2hrs
- **Efficacy Endpoints**: physical and function
- **Efficacy Time Assessment** (time post MCAO): from 45mins to 56 days
- **Dosage**: from 30nmol/kg up to 1,000nmol/kg ARG-007
- **Isomer Type**: D-isomer, L-isomer versions
- **Comparison**: evaluated against NA-1 (key competitor), R12, R15, etc

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The table below summarizes key stroke efficacy studies completed in rats; a more comprehensive table of all stroke publications is attached on page 21.

Date	Animal Model	Peptide(s) Analysed	MCAO Type	Induction	Sample size	Dosing (nmol/kg)	Administration (post MCAO)	Assessment (post MCAO)
2016	Sprague-Dawley rat	R18; NA-1	Permenant	Surgical	50	100, 300, 1000	60mins	24hrs
2016	Sprague-Dawley rat	R18; R12; R15	Permenant	Surgical	42	1000	30mins	24hrs
2016	Sprague-Dawley rat	R18; NA-1	Transient (90mins)	Surgical	60	30, 100, 300, 1000	60mins	24hrs
2017	Sprague-Dawley rat	R18; R12W8a;	Permenant	Surgical	23	30	30mins	24hrs
		R18	Permenant	Surgical	21	100	2hrs	24hrs
2017	Sprague-Dawley rat	R18; NA-1	Transient (3Hrs)	Surgical	24	1000	2hrs	24hrs
		R18; NA-1	Transient (2hrs)	Surgical	48	100	Immediate	24hrs
2018	Wistar rat	R18; R18D	Permenant	Surgical	46	300	30mins	24hrs
2019	Sprague-Dawley rat	R18; R18D; NA-1	Permenant	Chemical	122	100, 300, 1000	60mins	56 days
2021	Sprague-Dawley rat	R18; R18D	Permenant	Surgical	8	300, 1000	10mins	45-225mins

Source: various journal publications, EHL analysis

Whilst examining these studies we have focused on physiological outcomes for gauging efficacy. In our view, the small nature and hence complexity in assessing functional outcomes in rats is unlikely to produce consistently useful data, as a result we do not place a significant emphasis on this data.

In the majority of rat studies, ARG-007 led to a statistically significant reduction in infarct volume, as high as 35.1% 24hrs post MCAO (90min transient). Potentially more noteworthy was the equal or superior performance (sometimes significantly better) of ARG-007 against NA-1 (key competitor) in every study completed.

The only study which reported significantly different efficacy results (reduction in infarct volume) was in the 2017 publication, where researchers examined ARG-007 when administered up to 2hrs following MCAO. The three studies done as part of the publication showed negligible reduction in infarct volume for both ARG-007 and its benchmark NA-1 (key competitor). The results of the study from this journal can likely be attributed to the <2hr therapeutic window. However, in other endpoints of the study, ARG-007 lead to a reduction in severity of cerebral edema (brain swelling), and led to improvements of some functional parameters.

Altogether, these studies were highly valuable in showing initial in vivo efficacy of ARG-007, leading the way for research to be translated into a more comparable (to humans) non-human primate stroke model.

In addition to in vivo research, a handful of in-vitro studies have been done on ARG-007. All demonstrated ARG-007 was neuroprotective in various injury models, including:

- Glutamic Acid Excitotoxicity;
- Oxygen-Glucose Deprivation; and
- Oxidative Stress (only unpublished observations)

These studies were also important in designing follow up in vivo rat studies.

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Date	In-vivo/ In-vitro	Animal Model	Study Goal(s)	Peptide(s) Analysed	Disease	Disease Model(s)	sample size [Excluded]	Dosing (nmol/kg)	Reduction in Infarct Volume (%)	Outcome(s)
2015	In-vitro	n/a	Compound Idenfication; Neuroprotective efficacy	R18; Various	Stroke [I]	GAE; OGD	n/a	n/a	n/a	Poly argine-rich peptides shown to be neuroprotective, incl. R18
2016	In-vivo	Sprague-Dawley rat	R18 Dose repsonsiveness when administered 60mins post MCAO	R18; NA-1	Stroke [I]	P; MCAO; [S]	50 [8]	R18 (100, 300, 1000) NA-1 (300, 1000)	R18 (12, 19.7, 24) NA-1 (6.8, 7)	R18 reduced infarct volume at all doses (at 24hrs, statistically significant at 100, 1000 nmol/kg); greater efficacy vs NA-1
2016	In-vivo	Sprague-Dawley rat	Neuroprotective efficacy when administered 30mins post MCAO	R18; R12; R15	Stroke [I]	P; MCAO; [S]	42 [5]	R18 (1000) R12 (1000) R15 (1000)	R18 (20.5) R12 (12.8) R15 (no effect)	Superior R18 neuroprotection efficacy (24hrs Post MCAO) vs R12/15, R18 only one to be statistically significant
2016	In-vivo	Sprague-Dawley rat	Neuroprotective efficacy when administered 60mins post MCAO (90mins, transient)	R18; NA-1	Stroke [I]	T; MCAO; [S]	60 [5]	R18 (30, 100, 300, 1000) NA-1 (30, 100, 300, 1000)	R18 (9.6, 12.2, 24.8, 35.1) NA-1 (7, 16.5, 16.6, 26.1)	Superior R18 neuroprotection efficacy (24hrs Post MCAO) vs NA-1
2017	In-vivo	Sprague-Dawley rat	Neuroprotective efficacy when administered 30mins post MCAO	R18; R12W8a;	Stroke [I]	P; MCAO; [S]	23 [2]	R18 (30) R12W8a (30, 100, 300)	R18 (20.4) R12W8a (Ineffective)	Superior R18 neuroprotection efficacy (24hrs Post MCAO) vs R12W8a
2017	In-vivo	Sprague-Dawley rat	Efficacy with admin 2hrs post MCAO	R18	Stroke [I]	P; MCAO; [S]	21 [5]	R18 (100)	No difference to control	Therapeutic window for R18 and NA-1 to reduce ischemic brain injury would appear to be <2hrs (non sign results), Reduced severity of cerebral edema, and led to improvements of some functional parameters
			Efficacy with admin 2hrs post 3hr transient MCAO	R18; NA-1		T; MCAO; [S]	24 [5]	R18 (1,000) NA-1 (1,000)	No difference to control (Both NA-1 and R18)	
			Efficacy with immediate admin post 2hr transient MCAO	R18; NA-1		T; MCAO; [S]	48 [20]	R18 (100) NA-1 (100)	No difference to control (Both NA-1 and R18)	
2018	In-vivo	Wistar rat	Comparison of neuroprotective efficacy when administered 30mins post MCAO	R18; R18D	Stroke [I]	P; MCAO; [S]	46 [17]	R18 (300) R18D (300)	R18 (12) R18D (33)	Superior R18D neuroprotection efficacy (24hrs Post MCAO) vs R18. No indication of in vivo toxicity at the therapeutic dose used
	In-vitro	n/a	Toxicity assessment	R18; R18D	n/a	n/a	n/a	n/a	n/a	
2019	In-vivo	Sprague-Dawley rat	Effectiveness in improving functional recovery up to 56 days post stroke (Admin. 60mins post)	R18; R18D; NA-1	Stroke [I]	M; MCAO; [E1]	122 [9]	R18 (100, 300, 1000) R18D (100, 300, 1000) NA-1 (100, 300, 1000)	n/a	R18 (1000 nmol/kg) most effective at improving functional outcomes, followed by R18D (300, 1000) and NA-1 (300, 100). Overall suggest R18 may be more effective than NA-1
2019	In-vitro	n/a	Proteomic analysis	R18	Stroke [I]	GAE	n/a	n/a	n/a	Identified plurifunctional mechanism of action
2019	In-vitro	n/a	In vitro cellular uptake and neuroprotective efficacy	R18; O18	Stroke [I]	GAE	n/a	n/a	n/a	Neuroprotective effiacy (R18), further identfication of mechanism
2019	In-vivo	Sprague-Dawley rat	Safety and neuroprotective efficacy in ICH (Admin. 30mins post)	R18; R18D	Stroke [H]	ICH	158 [6]	R18 (30, 100, 300, 1000) R18D (30, 100, 300, 1000)	n/a	Overall appeared to be safe when admin during ongoing bleeding. Neither appeared to have any stat. sign. Effect in reducing lession vols or improv. Func. recovery after ICH
2019	In-vivo	Non-human Primate*	Neuroprotective efficacy when administered 60mins post MCAO (90mins, transient)	R18	Stroke [I]	T; MCAO; [S]	20 [4]	R18 (1000)	R18 (65.2 [24hrs]; 69.7 [28 days])	confirms the effectiveness of R18 in reducing the severity of ischemic brain injury and improving functional outcomes after stroke
2020	In-vitro	n/a	Ability to reduce rtPA toxicity .	R18D	Stroke [I]	OGD	n/a	n/a	n/a	Capacity to reduce cytotoxic effects associated with rtPA
2020	In-vivo	Sprague-Dawley rat	Examine pharmacokinetic and tissue distribution profile of R18D	R18D; 18FR18D	n/a	n/a	nd	R18D (1000) 18FR18D (2.5)	n/a	Neither demonstarted any adverse side effects in relation to safety and tolerability
2020	In-vitro	n/a	Investigate mechanism of anti-excitotoxic properties	R18	Stroke [I]	GAE	n/a	n/a	n/a	Further demonstration of plurifunctional mechanism of action
2021	In-vivo	Sprague-Dawley rat	Impact on infarct Growth and Penumbral Tissue Preservation	R18; R18D	Stroke [I]	P; MCAO; [S]	8	R18 (300, 1000) R18D (300)	n/a	Confirm the superior efficacy and proteolytic stability of R18D. Indicates peptide is likely to retain properties when co-admin with rtPA
	In-vitro	n/a	Proteolytic stability assessment	R18; R18D	Stroke [I]	GAE	n/a	n/a	n/a	
2022	In-vitro	n/a	peptide proteolytic stability and affect on tPA or TNK	R18; R18D; NA-1	Stroke [I]	GAE	n/a	n/a	n/a	R18D not degraded (stable) when co-admin with tPA or TNK, neither does it affect clot thombolysis

GAE: Glutamic Acid Excitotoxicity
OGD: Oxygen-Glucose Deprivation
ICH: Collagenase-induced intracerebral hemorrhage
MCAO: Middle Cerebral Artery Occlusion
P/T: Permenant, Transient

[S]: Surgically induced
[E1]: endothelin-1 (chemicaly) induced
Stoke [I/H]: ischemic or hemorrhagic
**male cynomolgus macaques*

Source: Various Journal article publications, EHL analysis

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Safety and Toxicity

Understanding safety is essential for a successful drug development. As explored later, the evaluation of safety will be the main outcome of AGN's upcoming phase 1 clinical trial in humans.

ARG-007 has been shown to be safe and well tolerated across a number of preclinical studies, both in vitro and in vivo. Additionally, literature on the broader CARP (cationic arginine rich peptides) class of compounds, which ARG-007 is a part of, suggest these compounds are relatively safe.

In various published rat studies, ARG-007 did not show any adverse side effects in relation to safety and tolerability, with no signs of toxicity at the therapeutic dose used.

More recently, AGN has had to undertake further preclinical studies examining ARG-007's safety and toxicity as part of approvals required for the phase 1 trial. These studies are required to be carried out under Good Laboratory Practice (GLP) conditions. These are a set of principles required by regulatory bodies such as the FDA which ensure quality assurance is achieved.

These studies are more of a formality, considering they have already been done, just not in GLP conditions. Nevertheless, they should further validate ARG-007's safety, by again evaluating and understanding:

- Pharmacokinetics;
- Genotoxicity;
- Toxicokinetics; and
- Safety pharmacology

In February, AGN released GLP genotoxicity studies which showed ARG-007 will not likely pose a genetic or carcinogenic risk to patients, and does not cause any structural damage to chromosomes in mammalian cells.

Prior to this, AGN released results from preliminary non-GLP toxicology studies confirming the parameters in which AGN can identify the maximum safe starting dose, as well as determining ARG-007's NOAEL (no observed adverse effects levels). Through these studies, AGN identified the safe dosing range, which importantly exceeds the efficacious dose range of ARG-007.

In July last year, AGN announced highly encouraging results from a pilot Pharmacokinetics (PK) study. The study indicated favourable PK profiles in the dose range of 0.3-10mg/kg, which includes the efficacious dose of approximately 1mg/kg (~350nmol/kg). Additionally, no adverse effects were observed, indicating ARG-007 is potentially safe and well tolerated.

Prior studies in rats have also shown ARG-007 appears to be safe when administered during ongoing collagenase-induced intracerebral haemorrhage (i.e. does not exacerbate bleeding during a haemorrhagic stroke). This is critical in understanding if ARG-007 is to be used prior to stroke determination. This is a solid indication for it's potential use in the field (e.g. by paramedics).

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AGN's recent publication on ARG-007's in vitro interactions with tPA show it does not affect clot thrombolysis (i.e. the process of tPA dissolving clots). This is also crucial, as it shows ARG-007 does not affect the actual treatment of stroke. This is also an indication for its potential integration into standard of care.

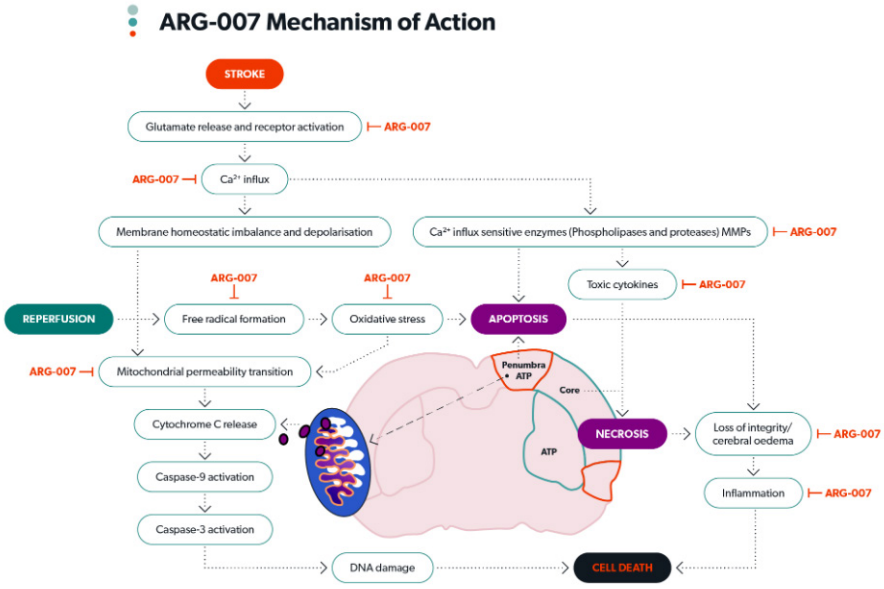
Additionally, based on available clinical research, cationic arginine rich peptides (CARPs) as a class of compounds (ARG-007 is a type of CARP) appear to be safe. Examples of this include well known CARP, Protamine, which has been in clinical use for over 70yrs to reverse the effects of heparin (type of anticoagulant). There have been various other CARP compounds studied over the years (for various indications) which were shown to be safe in humans.

Plurifunctional Mechanism of Action

Addressing stroke requires therapeutics which can target multiple parts of the complex ischemic and excitotoxic cascade of events, as discussed, monofunctional drugs have not previously been successful in providing neuroprotection in stroke patients.

ARG-007 is ideal in that it has a plurofunctional mechanism of action, affecting neuronal excitotoxicity, calcium influx and mitochondrial dysfunction, as well as reducing the activation of damaging proteolytic enzymes.

These targets shown in the diagram below:



Source: Company website

This multimodal mechanism of action has been demonstrated across a number of preclinical studies on ARG-007. This is further illustrated in literature on the broader class of cationic arginine rich compounds (CARPs), with studies suggesting an unpresented number of properties.

These properties greatly enhance the neuroprotective potential of ARG-007, increasing the probability of an effective clinical translation.

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Proteolytic stability

ARG-007 has been shown to resist proteolytic degradation (i.e. breakdown of the peptide) when co-administered with thrombolytic drugs alteplase (tPA) and tenecteplase (TNK).

This is a potential overlooked property which means ARG-007 won't be degraded if clot busting drugs are used following administration of ARG-007 and hence can continue to provide neuroprotection post thrombolysis and improve patient outcomes.

AGN successfully validated this in a recent publication evaluating the impact of ARG-007 on tPA and TNK, which follows from an earlier study that confirmed the neuroprotective stability of ARG-007 when incubated with plasmin, an enzyme activated by tPA that dissolves clots.

This compares to studies on competitor neuroprotective peptides that suggested the active peptide used is degraded following administration of tPA, a major limitation that could affect the efficacy and hence the applicability, when tPA is expected to be administered.

Clinical Research

Phase 1 Clinical Study – Q2 CY22

AGN is quickly approaching the targeted kick-off of its first in humans' Phase 1 clinical trial. This study will investigate if ARG-007 is safe, well tolerated and does not cause any adverse reactions, when administered in **healthy volunteers**. Key data outcomes will be:

- Safety;
- Tolerability; and
- Pharmacokinetics

This trial will NOT investigate efficacy, only safety.

Although nothing is without risk, we have outlined the extensive portfolio of clinical evidence and broader scientific literature which suggest ARG-007 to be safe and well tolerated.

Additionally, considering stroke (key indication) can result in death, the hurdles for what's considered "safe" and hence a successful outcome are likely to be more lenient. An example of this would be the safety hurdles of a cancer treatment vs an everyday painkiller, where the later requires upmost safety, in comparison to a cancer drug which can nearly kill the patient.

A successful outcome, will pave the way for AGN to undertake a Phase 2 clinical trial in stroke patients. Additionally, this trial might allow secondary indications (e.g. HIE, TBI, GBI, etc) to be fast tracked directly into Phase 2 studies.

The Phase 1 trial will be structured as a double blind, randomised study where healthy participants will either receive ARG-007 or a placebo. Parameters of the study include:

- Single site (in WA, operated by Linear Clinical Research)
- 32 healthy volunteers, separated into 4 cohorts
- 8 participants per cohort (2 placebo, 6 receiving ARG-007)
- Each cohort will receive a different dose of ARG-007 (ascending dosage)

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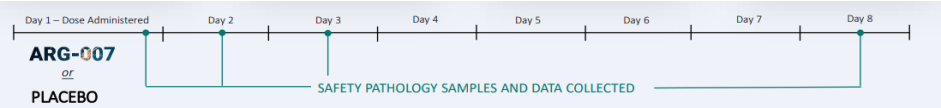
The study will be relatively quick, running for 8 days per cohort, with dosing on day one and data collected at four points. Cohorts will be dosed in a sequential ascending manner. This implies the total study will run for approximately 2-3 months from start to finish, including time between cohorts and follow ups.



Source: Company presentation

Preliminary results should come out shortly after dosing of the initial cohort, after AGN has received approval to move to the next cohort. This providing the market a basic indication of whether the trial was successful (based on initial data). The full analysis and compilation of data including pharmacokinetics (PK) will come after all dosing is completed. From first patient to final report, the Phase 1 trial will take up to 6 months to complete.

Prior to initiating its phase 1 study, AGN needs to compile key data and file an application with the Human Research Ethics Committee (HREC). This includes preclinical safety and toxicology studies completed in GLP conditions (see safety & toxicity section for detail). The indicative timing of this data is:

- GLP Genotoxicity (completed) – Already received
- Pharmacokinetics (ongoing) – Due: Q2CY22
- GLP safety and Toxicology (ongoing) – Due: Q2CY22

Following receipt of these Preclinical study reports AGN can submit its application to HREC. The company has additionally engaged two consultants to provide input and advice on the data package, this should ensure a smooth process with HREC.

In addition to this, AGN will need to complete pre-study activities including clinical site management setup and planning for the recruitment of healthy patient volunteers. The indicative timing of this:

- Completion of Pre-study Activities – Due: Q2CY22

Targeted timing of approvals and the study itself are as follows:

- HREC submission: Q2 CY22
- HREC Approval and Phase 1 study kick off: Q2 CY22
- Preliminary results: Q3 CY22
- Full results: Q4 CY22

Per the prospectus, the cost of the phase 1 study is estimated to be $1.5m.

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Phase 2 Clinical Study – Q1 CY23

Following the successful completion of the Phase 1 study, AGN can look to undertake a Phase 2 clinical study. This second clinical trial would look to primarily evaluate the safety of ARG-007 when administered in stroke patients, with some exploratory efficacy data to be collected.

This will be the trial with both the greatest downside risk, but also greatest upside as it will be the first evaluation of ARG-007's efficacy in human stroke. A successful result will translate into a huge de-risking of ARG-007, bringing the drug a step closer to commercialization.

The company has not provided much detail on potential Phase 2 design, as the structure is likely to be guided based on Phase 1 trial results. We would expect AGN to begin planning immediately following successful preliminary results. Indicatively we would expect:

- 12 to 18 month trial;
- 50-75 patients;
- Multicentre (Australia); and
- Admitted to metro-based patients in the emergency department.

The last part will be especially important, as timing of intervention is likely to greatly affect efficacy outcomes as shown in preclinical research. Optimally, the study would be designed so that ARG-007 is administered as close as possible to the stroke event. AGN looks to manage this risk by administering ARG-007 in the emergency department.

However, it should be noted that such a design will come with a significantly more complex work-flow, and hence risks. The difficulty would come from operating a clinical trial in what's normally a chaotic emergency setting.

This study does not require an FDA IND unless AGN plans on running US clinical sites.

Timing will depend on results of the phase 1 trial, however, indicatively we would anticipate ethics submission required to kick-off the Phase 2 trial around Q1 CY23.

We estimate the Phase 2 to cost approximately $10m depending on the number of sites and patients required.

Phase 3 – CY24+

A Phase 3 trial would be the final evaluation of ARG-007's safety and efficacy in stroke patients. This pivotal study would likely be done with a partner due to its large size and connected costs. As a rough idea, we anticipate the parameters of this trial would include:

- 2-3-year trial (depending on number of sites)
- +500 patients
- Global multicentre trial (Inc. US sites)
- Administered to patients by paramedics

In order to satisfy regulators, this trial would have to be a global multicentre study with sites in the United states (usually required for FDA approval). As a result, AGN will need an IND to complete a Phase 3 study. A trial of this size would likely cost in the order of $70-80m. As a result, we would expect AGN to have brought on a partner to support the costs.

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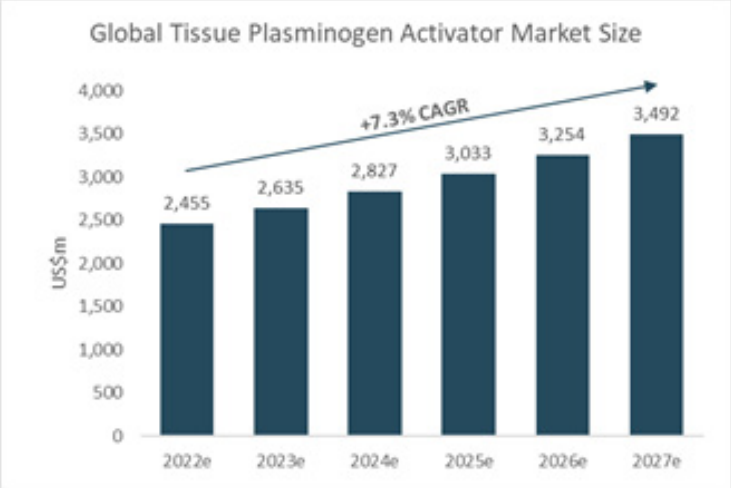
Market Opportunity / Forecasts

The market opportunity for novel stroke treatments is huge. Annually, an estimated 15 million people suffer from stroke globally, the direct and indirect costs of this being upwards of $891 billion per annum. The successful development of ARG-007 as a neuroprotective therapeutic for stroke could improve patient outcomes and potentially yield billions in economic savings globally.

Whilst we acknowledge ARG-007 is still in its initial stages of clinical development, we have indicatively explored below what the therapeutic could be worth if clinical successful and marketed.

Currently, the only therapeutic treatment for ischaemic stroke is tissue plasminogen activators (tPA). The current tPA market is worth US$2.5 billion per annum, this is forecasted to rise to US$3.5 billion by 2027 (7.3% CAGR). This shown below.



Source: Coherent Market Insights

The size of the tPA market provides an indicative idea of what ARG-007 could be worth. Whilst it is a large market, we do believe this represents the lower end of the spectrum. This based on the small market penetration tPA has (as low as 3-5% of strokes), relative to what we believe a successful neuroprotective could attain.

We anticipate ARG-007 could attain a significantly larger market share than tPA, potentially in the order of 25-50%, or even more. This is based on its potential:

- **Universal Application** – Unlike tPA, ARG-007 could be taken by patients with any type of stroke. Preclinical research to date has shown ARG-007 does not exacerbate bleeding during haemorrhagic stroke. Additionally, ARG-007 may be able to provide neuroprotection in various sub-types of ischaemic stroke, and in combination with subsequent treatments (thrombolysis and thrombectomy); and
- **Earlier Intervention** – The goal of ARG-007 is to make it a standard of care and administered by first responders (i.e. Paramedics). This would allow ARG-007 to be accessible in an earlier treatment window than tPA, and as a result be more applicable.

Current tPA pricing indicatively shows what ARG-007 could sell for. As with any pharmaceutical, pricing will vary greatly by region, with the United States typically having the highest pricing.

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In the United States, alteplase (tPA) can cost as much as US$9,197 (for 100mg) per dose. In Europe, pricing is significantly lower, selling for between US$750 up to $1350 (per 100mg) per dose. Indicatively, a pricing model for ARG-007 similar to tPA would not be unreasonable in our view.

AGN patents (discussed in later section) cover key jurisdictions across the United States, Europe, Japan and China. The prevalence of stroke in the regions is as follows:

- United States: 795,000
- Europe: 1.12 million
- Japan: 510,000
- China: 2.5 million

The majority of commercial value would rely in the United States as a result of its higher pricing capabilities. Applying the current tPA pricing would imply a US$7.3 billion total addressable market (TAM) for ARG-007 in the United States alone. Despite lower pricing, the other regions would still amount to very large markets.

Assuming more conservative pricing points, we can estimate the current TAM within AGN's key regions as being circa US$6.2 billion per annum. This shown below:

Region	Pricing (US$/unit)	Prevalence (m/pa)	TAM (US$m)
United States	5,000	0.80	3,975
Europe	1,000	1.12	1,120
Japan	1,000	0.51	510
China	250	2.50	625
Sub-Total (IP regions)			**6,230**
RoW	250	10.075	2,519
Total (Global)			**8,749**

Source: EHL estimates

We estimate the global TAM to be in the order of US$9 billion per annum when including the rest of the world (ROW). This estimate is based on conservative pricing, we note there is scope for it to be much higher.

Clearly, the core driver of value for ARG-007 is the United States. We can sensitise potential annual sales by unit pricing and market penetration, as show below.

		Unit Pricing (US$/dose)							
		$1,000	$2,000	$3,000	$4,000	$5,000	$6,000	$7,000	$8,000
Market Penetration*	5.0%	40	80	119	159	199	239	278	318
	20.0%	159	318	477	636	795	954	1,113	1,272
	35.0%	278	557	835	1,113	1,391	1,670	1,948	2,226
	50.0%	398	795	1,193	1,590	1,988	2,385	2,783	3,180
	65.0%	517	1,034	1,550	2,067	2,584	3,101	3,617	4,134
	80.0%	636	1,272	1,908	2,544	3,180	3,816	4,452	5,088

**Based on 795,000 annual strokes in the U.S.*

Source: EHL estimates

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As part of our analysis and valuation, we have further modelled potential sales and cashflows of ARG-007 (in the indication of stroke). These clearly require the successful development and approval of ARG-007. We have kept our forecasts very simple, with key assumptions including:

- Sales in United States, Europe, Japan
- 7-year commercial life (based on 2034 IP expiry);
- 40% peak market share;
- US$5,000/dose U.S. and US$1,000/dose RoW pricing;
- 80% peak gross margins; and
- Commercial launch in 2028

We further assume the following remaining development costs:

- Phase 1: $1.5m;
- Phase 2: $10m;
- Phase 3: $75m; and
- NDA: $2m

We model unit sales through applying an adoption curve to our peak forecasted market share, adding unit pricing we model revenues as follows:

Source: EHL estimates

Whilst these are clearly quite large figures, they are still less than the forecasted tPA market. In reality, sales of this size for game changing drugs are not infeasible.

We have additionally modelled potential after tax free cash flow generated through applying our forecasted margin, taxes, and remaining development costs. We use these forecasts to calculate our NPV.

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Competition

The competitive landscape is relatively small with only a handful of players, and only one noteworthy competitor.

Nono – NA-1

AGN's main competitor is Canadian based company Nono Inc, which is also developing a neuroprotective therapeutic for stroke. Their lead compound NA-1 (also known as Nerinetide or TAT-NR2B9c) is somewhat similar to ARG-007. It is also a Cationic Arginine Rich Peptide (CARP), however the molecule is more complex in comparison to ARG-007.

The company recently completed a Phase 3 study on NA-1, this was unsuccessful in showing a treatment benefit in the total population. However, patients who received NA-1 but not alteplase (tPA) showed a large absolute benefit. These results indicate a likely interaction between NA-1 and tPA.

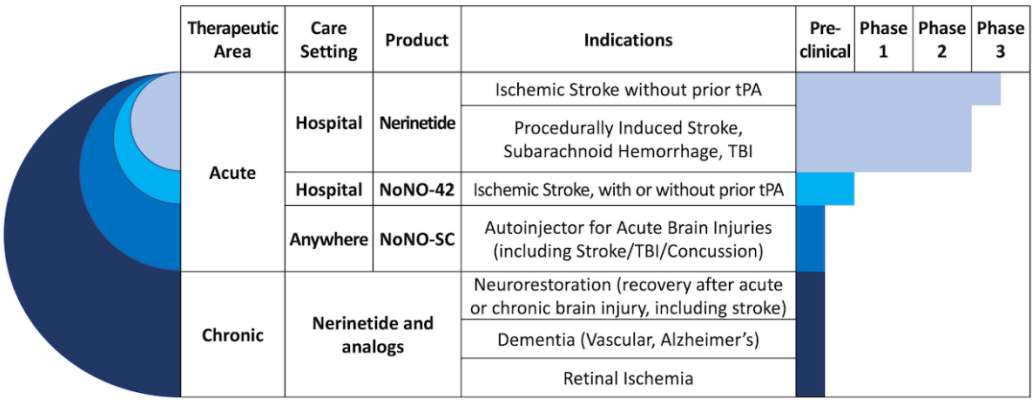
This trial failure is likely due to the fact NA-1 studies to date (including this recent Phase 3) have been on the L-isomer form of the compound, which as we know with ARG-007 is what affects its proteolytic stability. On the other hand, in preclinical research ARG-007 has been shown to be stable when co-administered with thrombolytic drugs alteplase (tPA) or tenecteplase (TNK).

In spite of this setback, Nono is undertaking a second phase 3 trial. This new trial will be done only in patients who receive a mechanical thrombectomy (MT). In theory, this patient population should be successful in showing efficacy, however in practice the work-flow of this will likely cause issues. Determining who or who doesn't have a MT (i.e. Who receives NA-1 in the study) can only be done at the hospital. This situation may increase the time between the stroke event and administration of NA-1, which could impact efficacy. This is in addition to other potential stress points which we won't delve into detail on.

Nono have made a d-isomer form of NA-1, known as Nono-42. However since its technically a new compound, studies need to start from scratch (i.e. preclinical). This essentially places Nono in the same position, if not slightly behind AGN, on the development of neuroprotective therapeutic for stroke.

All of this doesn't even begin to consider preclinical studies which show ARG-007 to be a more effective neuroprotective therapeutic than NA-1. This is best illustrated by AGN's recent non-human primates' study where ARG-007 showed a 65.2% reduction in infarct volume at 24hrs vs the 44% reduction shown by NA-1.

Nono's program pipeline shown below:



Source: Nono company website

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Other Competitors

Outside of Nono, there are handful of other players in the neuroprotective space. These include:

Company: Avilex Pharma

Compound: AVLX-144

Stage: Phase I completed

Description: Developing a neuroprotective therapeutic for acute conditions such as subarachnoid haemorrhage and acute ischemic stroke. AVLX-144 is a type of PDS-95 inhibitor, with the same putative mechanism of action as NA-1. The company is also developing AVLX-147 (preclinical), a second generation tPA resistant version of AVLX-144. Founded in 2012, the private company is based in the Denmark.

Company: DiaMedica Therapeutics

Compound: DM199

Stage: Phase II/III

Description: Developing a synthetic version of human tissue kallikrein-1 (KLK1) for stroke recovery and recurrence reduction. The US listed (DMAC: NASDAQ) company has a market cap of US$74m (A$100m)

Company: Zzbiotech

Compound: 3K3A-APC

Stage: Completed phase II

Description: Developing a genetically engineered variant of recombinant APC, called 3K3A-APC. Designed for the treatment of ischemic stroke, ALS, and diabetic wound healing. Likely susceptible to tPA. The private company is based out of Houston Texas, in the United States.

Company: Athersys

Compound: MultiStem

Stage: Phase III

Description: Developing a stem cell product called Multistem for the treatment of various diseases including neurological ones. The US listed (ATHX: NASDAQ) company has a market cap of US$148m (A$196m)

Company: Lumosa Therapeutics

Compound: LT3001

Stage: Phase II completed

Description: Looking to develop a superior thrombolytic therapy. LT3001 is being designed to restore occluded blood flow without causing haemorrhage. The Taipei listed company has a market cap of A$270m.

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Secondary Indications

Outside of the primary indication of stroke, studies have shown ARG-007 has preclinical efficacy in a number of secondary neural injury indications including:

- Traumatic Brain Injury (TBI);
- Hypoxic Ischaemic Encephalopathy (HIE); and
- Global Brain Ischemia

Additional in-vitro studies suggest ARG-007 could have potential as a neuroprotective therapy for other neurodegenerative disorders, such as Alzheimer's or MS. This is due to the Pathophysiology of these diseases, and the mechanism of action of ARG-007 to act on them.

Traumatic Brain Injury

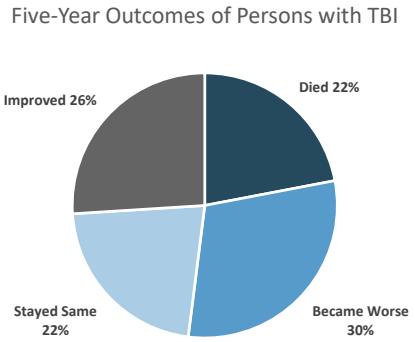
Traumatic Brain Injury (TBI) is a major cause of disability and death globally. TBI occurs typically as a result of a violent blow or jolt to the head, but can also be caused by an object going through brain tissue (e.g. Gunshot wound). The causes of TBI include:

- Falls (most common in developed regions)
- Road traffic accidents
- Violence (e.g. fighting)
- Contact sports
- Explosion blasts/combat injuries

TBI manifest through a primary injury and secondary injury. The primary injury is caused by the external blow or jolt to the brain. This initiates the secondary injury which occurs within minutes to days afterwards, this consisting of biochemical reaction causing neuronal damage.

There are different severities of TBI, ranging from mild which is more or less temporary, to severe which can result in long term complications or even death. Non-fatal complications of TBI include lifelong cognitive, physical, behavioural and communicative deficits.

Outcomes for patients with moderate to severe TBI according to the CDC:



Source: CDC

The scale of the issue is massive, with an estimated 69 million cases of TBI each year globally, however most of these are mild or moderate TBI (81%, 11%). In the US alone, the impact of TBI according to the CDC (2015) is:

- 2.8 million new cases of TBI per year; which includes;
- 2.5 million TBI related hospital visits;
- 288,000 TBI related hospitalisations; and
- 57,000 TBI related deaths

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The economic cost is just as significant, with TBI estimated to cost the global economy US$400 billion per year. In the US alone, indirect and direct medical cost associated with TBI are estimated to be US$76.5 billion per year (in 2010 dollars).

Despite the significance of TBI, strategies for its management are limited to preventative measures, with standard of care consisting of acute neuro-critical care and neurorestorative practices. None of these addresses the secondary neuro-injury and its progression.

Targeting this secondary biochemical process may provide an additional, and potentially more effective treatment, which would complement existing interventions. In this case, any neuroprotective therapeutics which can protect brain tissue likely provide the best opportunity to improve patient outcomes in TBI. Despite this, there are currently no FDA-approved therapeutics for neuroprotection in patients with TBI.

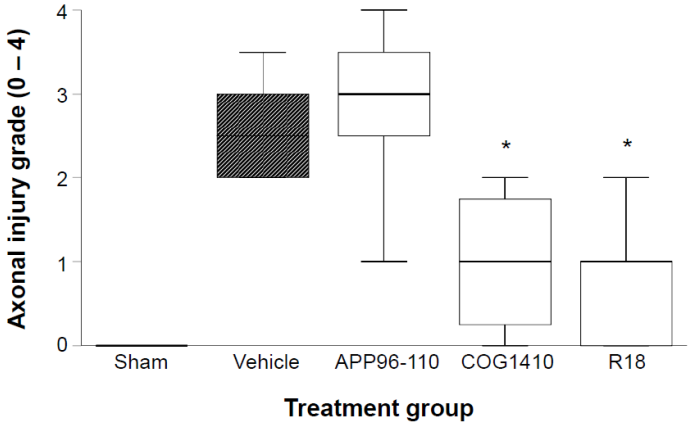
AGN is looking to disrupt this gap in treatment with its novel drug ARG-007. There are 3 published preclinical studies on ARG-007 in TBI, demonstrating efficacy in animal models. We have summarised the results of these studies below:

Date	TBI Injury Model	Animal Model	Sample size	Dosage (nmol/kg)	Axonal Injury	Functional Recovery
2017	weight-drop impact acceleration model	Sprague-Dawley rats	36	300 (30mins post)	Significant reduction	Some improvements
2019	weight-drop impact acceleration model	Long-Evans Rat	40	1,000 (30mins post)	n/a	Significant (for sensorimotor; vestibulomotor)
2020	weight-drop impact acceleration model	Sprague-Dawley rats	26	300, 1,000 (30mins post)	Modest reduction (at 1,000)	Some improvements

Source: Various Journal article publications, EHL analysis

AGN's studies show ARG-007 reduces axonal injury in rat models of TBI with varying levels of functional recovery. However, as previously articulated we don't place much emphasis on functional outcomes in rat models due to their limitations.

Below are axonal injury results from the 2017 study, this shows ARG-007's ability to significantly reduce injury.



Source: Assessment of R18, COG1410, and APP9-100 in excitotoxicity

Altogether, these initial studies indicate ARG-007 can protect the brain following a TBI, and as a result improve patient outcomes. We do however note that at this stage, further studies are warranted to confirm these initial findings.

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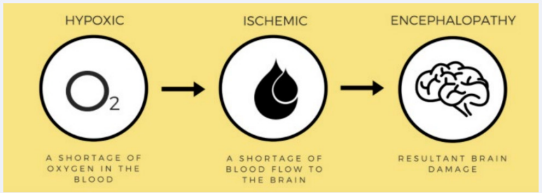
Nevertheless, the market opportunity is huge if AGN is successful in developing a neuroprotective therapeutic for TBI. The scale of the issue suggests the market for such a treatment could be in the order of hundreds of million to billions of dollars per year. These opportunities include potential military applications.

Hypoxic Ischaemic Encephalopathy

Hypoxic Ischaemic Encephalopathy (HIE) is the leading cause of neonatal (i.e. newborns) disability and mortality worldwide. HIE occurs when the brain is starved of oxygen due to lack of blood flow or gas exchange. This can occur immediately before, during or after the birth process.



Source: company presentation

HIE can lead to a number of non-fatal neurological conditions, including:

- Cerebral palsy;
- Epilepsy;
- Intellectual disabilities; and
- Learning disabilities

Treatment options for HIE are extremely limited. Currently the only therapy consists of inducing and maintaining a moderate hypothermia (32-34c) for a period of up to 72 hours. There are numerous limitations with hypothermia therapy, including:

- Only assessed in full term infants (37-40-week gestion), as a result the treatment is not available for preterm (less than 37-week gestation) neonates with HIE;
- 31-55% of infants do not benefit from hypothermia therapy; and
- As a complex process requiring specialised equipment and staff, the therapy is limited to certain hospitals. Non-tertiary, remote or hospitals located in developing countries may not be able to do the procedure.

In developed countries, HIE is estimated to occur in 2.5 of every 1,000 live births. This figure can be as high as every 26 times in developing countries. Furthermore, moderate to severe HIE which requires hypothermia therapy occurs in 1.3 of every 1,000 live births. Altogether, birth asphyxia leads to ~840,000 neonatal death globally, or approximately 1 in 4 neonatal deaths.

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AGN is looking to develop new therapies for HIE with its novel compound ARG-007. The company has completed 3 preclinical animal studies in HIE to date, these shown below:

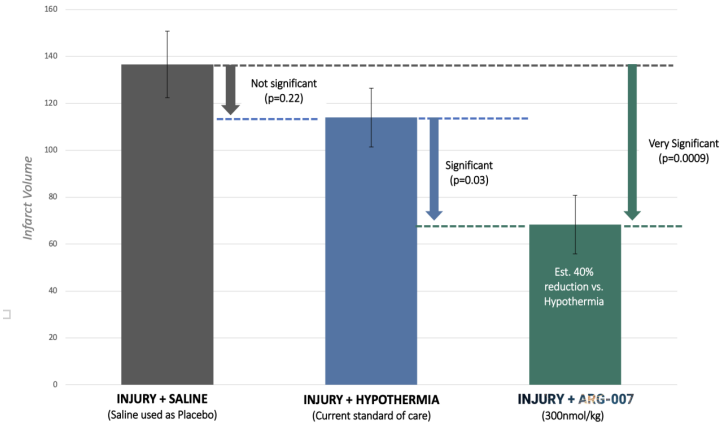
Date	HIE Model	Animal Model	Age (days)**	Sample size	Dosing time delay (mins)	Dosage (nmol/kg)	Infarct Volume Reduction	Behavioural outcomes
2018	Modified Rice-Vannucci procedure*	Sprague-Dawley (Male and female)	7	133	Immediate	30, 100, 300, 1,000	25.3-43.8%	Sign. Improvement
2018	Modified Rice-Vannucci procedure*	Sprague-Dawley (Male and female)	7	195	30	10, 30, 100, 300, 1,000	23.7 - 35.6%	Sign. Improvement
					60	30, 300	Nil - 34.2%	Sign. Improvement
					120	30, 300	8 - 12.8%	Sign. Improvement
2018***	Modified Rice-Vannucci procedure*	Sprague-Dawley	7	n.d.	Immediate	100, 300	up to 50%	n/a

* Common carotid and external carotid occlusion + 8%O2/92%N2 for 2.5 hr
** 7 days equivelant to late pre-term infants
*** Unpublished

Source: Various published journal articles, EHL analysis

AGN's studies show ARG-007 significantly reduces infarct volume (brain cell death) in prenatal HIE models (late pre-term) in rats, in addition to showing significant improvements in behavioural outcomes.

In 2021, AGN announced its third study showing ARG-007 not only reduced the volume of brain tissue death, but that it also significantly outperformed the current standard of care (hypothermia). In this rat study, ARG-007 was shown to reduce infarct volume by up to 50% from the vehicle (saline + injury model), with an estimated 40% reduction vs standard of care. This shown below:



Source: Company announcement

These studies highlight the exciting potential for the use of ARG-007 as a neuroprotective therapeutic in HIE. The company has stated it will now look to progress further efficacy studies in-term animal models of HIE (studies to date have been in late pre-term models). Should these studies also be successful in demonstrating efficacy of ARG-007, then AGN has said it will look to translate the clinical program into HIE in human infants.

The market opportunity for a neuroprotective therapeutic for HIE, is similarly large.

We further note, AGN could potentially seek an Orphan Drug Designation from the FDA for ARG-007 in the application of HIE. This based on the estimated number of HIE cases in the United Sates (we estimate ~10k based on 2.5/1000 incidence rate).

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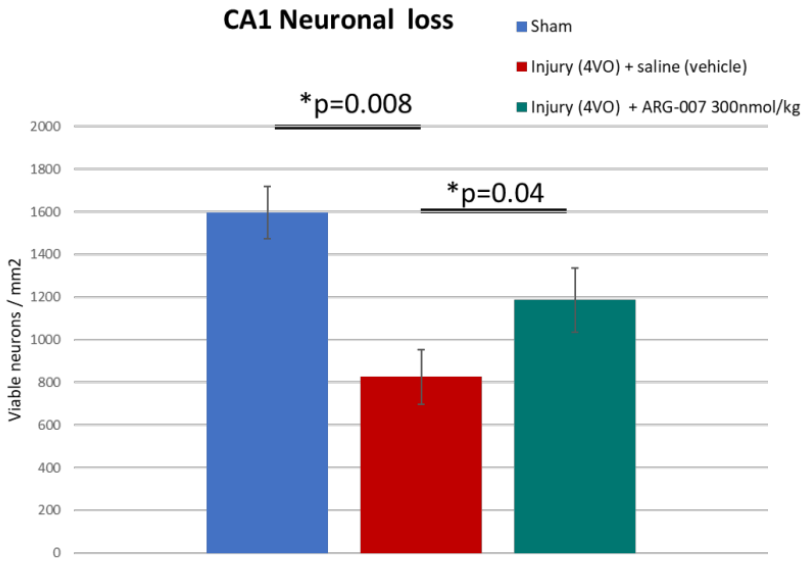
Global Brain Ischemia

Global cerebral ischemia is a condition which can occur following cardiac arrest or from certain cardiac surgeries where cardiac output is decreased. This results in an initial disruption of blood flow, followed by a subsequent restoration once cardiac rhythm is restored. The condition can cause significant brain injury and cognitive impairments in patients.

Despite the risks associated, treatment options are limited. Treatment for cardiac arrest consists of inducing and maintaining a moderate hypothermia (32-34c) for a period of up to 48 hours. However, recent data indicates hypothermia after cardiac arrest provides minimal therapeutic benefit (see Shrestha et al., 2022).

AGN in a recently announced study demonstrated neuroprotective potential of ARG-007 in a rat model of global cerebral ischemia. Results showed ARG-007 reduces brain cell death in CA1 hippocampal neurons compared to a saline control in a four-vessel occlusion (4-VO) animal model of global ischemia. This shown below:



Source: Company announcement

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Intellectual Property Portfolio

AGN maintains a comprehensive intellectual property (IP) portfolio. The IP covers key jurisdictions and is free of any encumbrances.

The company originally executed an IP assignment agreement with the University of Western Australia in January 2020. This transaction was completed in exchange for shares in AGN, the assignment is free of any royalties, milestone obligations or any other encumbrances.

The company has granted patents in key countries which make up some of the largest addressable markets globally. This shown below:

Jurisdiction	Progress	Number	Protection Coverage
Europe	Granted	EU3063168	Exp: 30/10/2034
Japan	Granted	Japan 6495270	Exp: 30/10/2034
China	Granted	ZL2014800719713	Exp: 30/10/2034
US	Granted	US16/041,483	Exp: 30/10/2034

Source: AGN December quarterly update

Patents cover the use of ARG-007 to prevent brain cell death after:

- Stroke (Lead indication);
- Hypoxic Ischemic Encephalopathy (HIE); and
- Traumatic Brain Injury (TBI)

We further note, AGN's patents in the United States also cover the use of ARG-007 in other indications which include:

- Alzheimer's disease;
- Huntington disease;
- Multiple sclerosis;
- Parkinson's disease;
- Motor neuron disease;
- Neuropathic pain;
- Spinal cord injury; and
- Epilepsy

Although AGN hasn't completed any research in these indications, this provides coverage should the company explore these at a later date.

Balance Sheet

AGN finished the recent December quarter with ~$5.3m in cash at bank.

The company has no borrowings.

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Clinical Advisory Board

AGNs clinical advisory board consists of four members. As detailed below per the company's prospectus.

Dr David Blacker – Chairman of the Clinical Advisory Committee

Description: Professor David Blacker is an acute stroke clinician/ neurologist who has previous experience initiating neuroprotection clinical stroke trials in Western Australia and being the local Principal Investigator of a number of national and international acute and secondary prevention stroke studies.

Prof. Blacker is the Perron Institute Medical Director and consultant neurologist and stroke physician.

Assoc. Prof. Paul Bailey – Member of the Clinical Advisory Committee

Description: Assoc. Prof. Paul Bailey is Medical Director for St John Western Australia. Assoc. Prof. Bailey is Perth based, completing his medical degree at the University of Western Australia in 1992, and becoming a Fellow of the Australasian College for Emergency Medicine in 2000. He completed a Biochemistry / Physiology laboratory PhD in 2007 - investigating the functional and structural characteristics of Australian jellyfish venom.

More recently Assoc. Assoc. Prof. Bailey's research focus has been in the areas of out of hospital cardiac arrest, anaphylaxis, emergency department systems and trauma - with 29 papers published in the scientific literature since 2015. In early 2020, Assoc. Prof. Bailey successfully completed the AICD's Company Directors course. Assoc. Prof. Bailey and his team are active participants in the WA Stroke Advisory Group - which has transformed the clinical approach to stroke patients in the prehospital environment in WA.

Prof. Geoffrey Donnan – Member of the Clinical Advisory Committee

Description: Professor Geoffrey Donnan AO is Professor of Neurology at The University of Melbourne and former Director of The Florey Institute of Neuroscience and Mental Health. His research interest is clinical stroke management. He was co-founder, with Prof. Stephen Davis, of the Australian Stroke Trials Network (ASTN) within which there have been conducted numerous investigator driven and other stroke trials. The first of these was the Australian Streptokinase Trial (ASK). He has since been involved in numerous clinical trials of therapy as Chair, Co-chair or Steering Committee member. These include ECASSII and more recently EPITHET. He is currently Co-chair of the EXTEND group of trials, including the recently published EXTEND IA trial of thrombectomy in acute ischaemic stroke. The EXTEND trial itself, in which thrombolysis was safely and effectively given out to 9 hours, was also recently published, again with Prof. Davis.

He was a co-founder of Neurosciences Trials Australia and has a major interest in the imaging of the ischaemic penumbra. The interface between basic sciences and clinical stroke medicine has been a research focus and, in collaboration with Messrs Malcolm Macleod and David Howells, has adapted the meta-analysis technique to assess therapies in animal stroke models. He was Editor-in-Chief of the International Journal of Stroke and is Past President of the World Stroke Organization.

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In 2012 he was appointed an Officer of the Order of Australia for his distinguished service to neurology and research contributions and is the recipient of a number of international awards including the American Stroke Association William Feinberg Award (2007), the World Stroke Organization Leadership Award (2012), Karolinska Institute Award (2012) and Wepfer Award of the European Stroke Congress for excellence in stroke research (2014).

Dr Tim Phillips

Description: Dr Tim Phillips is an Interventional Neuroradiologist with 15 years' experience, currently working at the Neurological Intervention and Imaging Service of Western Australia (NIIS WA) and the Perth Children's Hospital. Prior to returning to Perth he undertook post-specialist fellowship training at the Royal Melbourne Hospital, The Royal London Hospital, Queens Hospital Romford, The National Hospital for Neurology and Neurosurgery, and Great Ormond Street Hospital.

Board and Management

AGN's board of Directors, Key Management are listed below per the company's prospectus.

Board of Directors

Mr Geoff Pocock – Non-executive Chairman

Education/Qualifications: B.Sc., LLB

Shares: 4.4m, Options: 0.5m

Description: Mr Geoff Pocock is an experienced strategy consultant and commercialization professional, with over 20 years' experience across the commercialisation process. Mr Pocock's experience has covered technical roles, executive management as well as significant corporate finance and strategy roles with a number of technology commercialisation ventures.

Mr Pocock is the Principal of Polaris Consulting, a specialist boutique commercialisation strategy and executive services advisory business based in Western Australia, which also provides administrative services to businesses. He is also currently an Executive Director of Osteopore Ltd (ASX: OSX) and Non-Executive Director of EMVision Medical Devices Ltd (ASX: EMV) and former Managing Director/Co-Founder of Hazer Group (ASX: HZR).

Dr Samantha South – Executive Director

Education/Qualifications: B.Sc. (Hons), MBA, PhD

Shares: 2.0m, Options: 1.0m

Description: Dr Samantha South is currently the Senior Commercialisation Officer (Life Sciences) in the Research Development & Innovation office at UWA and has over 12 years' experience in technology transfer in medtech / biotech sector, at the University of Queensland (UQ), Queensland University of Technology and the University of Western Australia (UWA).

Dr South has extensive background in medical research at Weill Medical College at Cornell University (NY), UQ and The Garvan Institute in CNS research. She was also the Preclinical Manager at TetraQ, a preclinical contract organisation, specialising in central nervous system animal models.

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Dr South was the UWA Director on UWA spin-out companies, MiReven Pty Ltd, Eridan Technologies Pty Ltd and OncoRes Medical Pty Ltd and is currently a Director of Rage Biotech Pty Ltd. Dr South is also the WA Ausbiotech Committee Chair and part of the Ausmedtech National Advisory Group and SBE Life Sciences Council.

Mr Terry Budge – Non-Executive Director

Education/Qualifications: B.Ecs, FAICD

Shares: 0.49m, Options: 0.5m

Description: Mr Terry Budge was a Director of Aspen Group Limited from 6 May 2005 to 23 November 2012. He was also Chancellor of Murdoch University from 2006 to 2013 (appointed to Senate 1 June 2004). Mr Budge holds a Bachelor of Economics from Monash University and is a Graduate of the Advanced Management Program from Harvard Business School. He is also a Graduate and Fellow of the Australian Institute of Company Directors and a Senior Fellow of FINSIA. He is currently a non-executive director and Chairman of the Audit Committee of Westoz Investment Company Ltd (ASX:WIC).

Ms Liddy McCall – Non-Executive Director

Education/Qualifications: LLB, B.Juris, B.Com (Hons), GAICD

Shares: 0.13m, Options: 0.5m

Description: Ms Liddy McCall co-founded early state venture fund, Yuuwa Capital LP and has over 20 years' experience as a founder, investor and in management of early stage startups. Her prior experience includes co-founder of iCeutica Inc group, Dimerix Limited (ASX:DXB) and Argus Biomedical Pty Ltd. Previously, Ms McCall was an Associate Director, Macquarie Bank focusing on mergers and acquisitions. Ms McCall has been admitted as a barrister and solicitor in various Australian jurisdictions. Ms McCall is on the Board of various companies including ASX listed AdAlta Limited (ASX:1AD), and unlisted companies, Agworld Pty Ltd, Nexgen Plants Pty Ltd, The Tailor Made Spirits Company Limited and Super Trans Medical Limited.

Key Management Personnel

Dr Liz Dallimore – Managing Director (MD) and Chief Executive Officer (CEO)

Education/Qualifications: B.Sc. (Hons), MBA, PhD

Shares: Nil, Options: 2.5m

Description: Liz Dallimore is a research & development, innovation and commercialisation specialist with over 20 years' experience across Australia and the UK. Prior to joining Argenica Therapeutics, Dr Dallimore was the Director of the WA Data Science Innovation Hub, tasked with working across WA businesses to establish innovative data science projects. Dr Dallimore has also held senior roles in management consulting across Australia, most recently as KPMG's National Director of Research Engagement and Commercialisation. Prior to this she held senior roles with Ernst & Young and PricewaterhouseCoopers.

Dr Dallimore is a co-founder of medical device company Inspiring Holdings, sits on the AusBiotech WA Committee and is a non-executive Director of NERA, a Federal Government Growth Centre. Dr Dallimore has a PhD in Neuroscience jointly completed at Oxford University and the University of Western Australia and has worked as a neuroscientist at the Australian Neuromuscular Research Institute (now Perron Institute). In 2020, Dr Dallimore was recognised at one of Western Australia's Top Women in Tech.

Argenica Therapeutics Limited

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Ms Emma Waldon – Chief Financial Officer (CFO) & Company Secretary

Description: Ms Waldon has diverse accounting, capital markets and corporate governance experience in Australia and the UK and is currently Company Secretary of EMVision Medical Devices Ltd (ASX:EMV) and a number of unlisted companies. Ms Waldon was Company Secretary of Hazer Group Limited (ASX: HZR).

Prof. Bruno Meloni – Chief Scientific Officer (CSO)

Description: Assoc. Prof. Meloni has over 25 years' experience as a research scientist, the last 20 in the field of stroke/cerebral ischemia. His research in the stroke/cerebral ischemia field has focussed on understanding the mechanisms associated with ischaemic brain injury, the identification of potential neuroprotective targets and the development of new therapies. Assoc. Prof. Meloni has experience with designing preclinical stroke trials, and the use of peptides as neuroprotective agents. Assoc. Prof. Meloni is the head of stroke laboratory research at UWA and the Perron Institute.

Top Shareholders

We note the company's top shareholders below:

Top 20 Shareholders	Shareholding	
	m	%
Geoffrey Richard Pocock	4.4	6.0%
University of Western Australia	4.0	5.4%
Perron Institute	3.6	4.9%
Altor Alpha Funds Mgmt	2.6	3.6%
Samantha South	2.0	2.7%
Shane Colley	2.0	2.7%
Ian Middlemas	1.6	2.1%
Shane Wee	1.5	2.1%
James Litis	1.5	2.1%
Xcel Capital Pty Ltd, Asset Mgmt Arm	1.5	2.0%
Bruno Meloni	1.3	1.7%
Ga Skylight Berhad	1.3	1.7%
Helen Sewell	1.2	1.7%
Emma Waldon	1.0	1.4%
Asenna Wealth Solutions Pty Ltd, Asset Mgmt Arm	0.9	1.2%
Pentek Holdings Pty Ltd	0.8	1.1%
Hugh Pilgrim	0.7	1.0%
Kdjama Co Pty Ltd	0.7	0.9%
Quantamatics Pty Ltd	0.6	0.8%
Jacqueline Knuckey	0.5	0.7%
Total	**33.5**	**The**

Source: IRESS, as of 28-Feb-22

The composition of shareholders shown below:

Shareholder Composition	%
Perron Institute	4.7%
University of Western Australia	5.4%
Inventors and Research Team	3.7%
Board, Management & Advisors	19%
IPO shareholders	47%
Other shareholders	21%
Total	**100%**

Source: Company presentation

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