Zacks Small-Cap Research
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Quantum Genomics Corp. (ALQGC.PA – Paris)

A FRESH Look at Hypertension

Based on our DCF model and a 15% discount rate, Quantum Genomics is valued at approximately €13.00 per share. Our model applies a 50% probability of ultimate approval and commercialization for firibastat in hypertension and a 15% probability for heart failure. The model includes contributions from the United States, European Union and Latin America.

Current Price (7/20/2020)	€2.55
Valuation	**€13.00**

INITIATION

Quantum Genomics is developing lead candidate firibastat for difficult to treat and resistant hypertension (HTN) and heart failure (HF). The BAPAI class drug blocks the conversion of A2 to A3 thereby preventing A3 binding with AT1 receptors which controls blood pressure via a triple mechanism of action.

Quantum is conducting a Ph3 trial for HTN in difficult to treat and resistant populations, a Ph2b trial in heart failure and a Ph1 in 1x/day HTN. We expect another Ph3 safety study for HTN and a Ph3 study in heart failure to start in 2021. The timeline also anticipates a HTN NDA filing in 2023.

HTN is a highly prevalent disease and a material portion of this population does not have the disease under control. Firibastat seeks to address this unmet need via a differentiated pathway complementary to currently approved therapies.

Our valuation assumes a 2023 regulatory submission in the US and EU and subsequent commercialization. Partner Biolab is expected to pursue approval in select Latin American countries and commercialize throughout that region in 2023 and 2024 respectively.

SUMMARY DATA

52-Week High	**5.59**
52-Week Low	**1.51**
One-Year Return (%)	**-52.1**
Beta	**0.84**
Average Daily Volume (sh)	**279,575**
Shares Outstanding (mil)	**20.5**
Market Capitalization (€mil)	**52.3**
Short Interest Ratio (days)	**0.27**
Institutional Ownership (%)	**0.3**
Insider Ownership (%)	**13.8**
Annual Cash Dividend	**€0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2020 Estimate	**N/A**
P/E using 2021 Estimate	**N/A**
Zacks Rank	**N/A**

Risk Level	**Above Average**
Type of Stock	**Small-Growth**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue

(In millions of EUR)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2019	€0.0 A	€0.3 A	€0.0 A	€0.1 A	€0.4 A
2020	€0.0 E	€0.0 E	€0.0 E	€10.0 E	€10.0 E
2021					€12.0 E
2022					€15.0 E

Earnings per Share

	Q1	Q2	Q3	Q4	Year
2019	€0.00 A	-€0.24 A	€0.00 A	-€0.27 A	-€0.50 A
2020	€0.00 E	-€0.31 E	€0.00 E	€0.08 E	-€0.20 E
2021					-€0.29 E
2022					-€0.20 E

INITIATING COVERAGE

We are initiating coverage of Quantum Genomics, (Paris: ALQGC) with a current valuation of €13.00 per share. This present value is based on our estimates for a successful commercialization of firibastat in difficult-to-treat and resistant hypertension (HTN)[1] and heart failure (HF) patients. Firibastat is a Brain Aminopeptidase A Inhibitor (BAPAI) that blocks the metabolization of angiotensin II (A2) into angiotensin III (A3) thereby normalizing blood pressure and supporting heart function.

Control of resistant HTN is Quantum's lead indication and addresses one of the most common conditions around the globe. HTN has increased in prevalence as diets have changed, physical activity has decreased and unhealthy habits such as drinking and smoking persist. The World Health Organization (WHO) estimates that there are 1.13 billion people worldwide with HTN, making it one of the most common conditions in the population, costing an estimated $370 billion worldwide.[2] While there are many products approved to treat the condition, about half of the hypertensive population is unable to keep it under control, even with three or more medications, demonstrating a significant unmet need for an important public health challenge. Quantum's secondary indication is post myocardial infarction (MI) heart failure (HF) which describes a complex syndrome, characterized by impaired ability for the heart to pump blood. Our estimates place global prevalence of post-MI HF at around 50 million people this year which could cost the world over $580 billion per year.[3,4,5,6]

Firibastat works within the renin-angiotensin-aldosterone system (RAAS). The RAAS regulates blood pressure, fluid and electrolyte balance and systemic vascular resistance and is the system in which angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) act. Specifically, Brain Aminopeptidase A Inhibitors (BAPAIs) target not the peripheral but brain-level (central) RAAS that plays a unique role in regulating blood pressure. Brain-level RAAS was already known to modulate systemic tone, but, until now, a formulation allowing BAPAI to cross into the brain had not existed. Brain-level RAAS is of special interest, as, unlike peripheral RAAS, central RAAS also has neural relevance to systemic tone, making it a critical target for difficult-to-treat, resistant or salt-sensitive hypertension and post-MI HF. Firibastat is a prodrug, comprised of two EC33 moieties dimerized via disulfide bond. The prodrug crosses the blood brain barrier more readily than EC33, where it is then cleaved and activated by brain-level reductases.

Quantum's firibastat has a triple mechanism of action which may address high blood pressure in resistant populations. The action of the drug prevents the aminopeptidase A enzyme from converting A2 into A3. A3 will normally bind to angiotensin receptor type 1 (AT1), which raises blood pressure. Without A3, vasopressin release is reduced, sympathetic nerve activity declines and baroreflex action increases. Additionally, A2 is converted to angiotensin-(1-7) rather than A3, which has anti-hypertensive effects. Because HTN and HF are related, many drugs used to treat HTN are implemented in the management of post-MI HF. Brain-level RAAS has been implicated in post-MI cardiac remodeling; thus, firibastat can potentially go beyond current therapies to alter the course of post-MI HF.

Quantum's lead indication is difficult-to-treat and resistant hypertension. Clinical trials in support of this indication employ both once-a-day (tablet) and twice-a-day (capsule and tablet) formulations. After successful Phase I and II (NEW-HOPE) trials, and positive feedback from the FDA regarding Phase III trial design, Quantum partnered with Brazilian pharmaceutical firm Biolab Sanus Pharmaceuticals in a milestone and revenue royalty deal to evaluate and commercialize twice-daily firibastat in Phase III studies (FRESH). Quantum also has planned another Phase III study of firibastat in difficult-to-treat and resistant hypertensive patients (RE-FRESH), expected to commence in 1Q:21, design for which is still underway. The once-a-day formulation has been investigated in Phase I. In post-MI HF, firibastat is currently in A Phase IIb trial (QUORUM) which is evaluating its effects on left ventricular ejection fraction post-MI in comparison to ramipril. End of recruitment is expected 2H:20. Success in both in HTN and HF trials would elevate Quantum's firibastat to an immense patient population in need of innovative therapies.

[1] Difficult to treat hypertension is refers to patients whose hypertension is not controlled despite being treated with two hypertensive classes of drugs. Resistant hypertension refers to patients whose hypertension is not controlled despite being treated with three antihypertensive classes including a diuretic.

[2] Gaziano TA, Bitton A, Anand S, Weinstein MC; International Society of Hypertension. The global cost of nonoptimal blood pressure. *J Hypertens*. 2009;27(7):1472-1477. doi:10.1097/HJH.0b013e32832a9ba3

[3] Reynolds K, Go AS, Leong TK, et al. Trends in Incidence of Hospitalized Acute Myocardial Infarction in the Cardiovascular Research Network (CVRN). *Am J Med*. 2017;130(3):317-327. doi:10.1016/j.amjmed.2016.09.014

[4] Gruppetta M, Calleja N, Fava S. Long-term survival after acute myocardial infarction and relation to type 2 diabetes and other risk factors. Clin Cardiol 2010;33:424–9

[5] Torabi A, Cleland JG, Rigby AS, Sherwi N. Development and course of heart failure after a myocardial infarction in younger and older people. J Geriatr Cardiol. 2014;11(1):1-12. doi:10.3969/j.issn.1671-5411.2014.01.002

[6] https://www.census.gov/popclock/

INVESTMENT THESIS

Quantum's most advanced drug candidate is firibastat. The company's lead indication is difficult-to-treat and resistant hypertension (HTN) followed by post myocardial infarction (MI) heart failure (HF). Firibastat is a Brain Aminopeptidase A Inhibitor (BAPAI) which blocks the metabolization of angiotensin II (A2) into angiotensin III (A3), normalizing blood pressure and supporting heart function. EC33, the main component of firibastat, has long been known to be an inhibitor of aminopeptidase A but had poor penetration of the gastrointestinal and the blood brain barriers, necessary features of an oral, centrally acting drug. Firibastat is able to enter the brain when its EC33 molecules are dimerized, masking the exposed thiol group via disulfide bond. Once in the brain, reductases cleave the dimer, activating the drug. Firibastat works within the renin-angiotensin-aldosterone system (RAAS), specifically brain-level RAAS. RAAS, in general, regulates blood pressure, fluid and electrolyte balance and systemic vascular resistance, and is the system in which angiotensin-I converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) act. Brain-level (central) RAAS plays a unique role in regulating blood pressure, as, unlike peripheral RAAS, central RAAS has neuronal, systemic tone relevance. Practically inaccessible before, brain-RAAS is a promising system to explore in difficult-to-treat, resistant or salt-sensitive HTN and post-MI HF with strong evidence already demonstrated in the lab.

When active, firibastat has a triple mechanism of action. The action of the drug prevents the aminopeptidase A enzyme from converting A2 into A3. A3 will normally bind to angiotensin receptor type 1 (AT1), which raises blood pressure. Without A3, vasopressin release is reduced, sympathetic nerve activity declines and baroreflex action increases. Additionally, A2 is converted to angiotensin-(1-7) rather than A3, which has anti-hypertensive effects. Brain-level RAAS has also been implicated in post-MI cardiac remodeling, where, *in vivo,* firibastat has been shown to alter the course of post-MI HF.

HTN is one of the most common conditions around the globe and continues to increase in prevalence. The World Health Organization (WHO) estimates that there are 1.13 billion people worldwide with HTN, making it one of the most common conditions in the population, costing an estimated $370 billion worldwide.[7] Approximately half of this population remains unable to keep blood pressure under control, even with three or more medications.

MI is a common cause of HF. HF can develop immediately after MI, during hospitalization or after discharge. In 2008, the estimated incidence of MI in the US was 168.6 per 100,000 person-years.[8] Mean survival of patients presenting with MI is estimated to be 10.3 years, implying a prevalence of MI around 1.7% of the US population.[9] Coupled with an estimated 38% of MI patients developing HF, we estimate post-MI HF to be 0.65% of the population, or about 2.1 million in the US in July 2020.[10,11] At a mean cost of about $24,695 per patient presenting with MI,[12] healthcare costs for post-MI HF are $51.9 billion in the US, alone, not including the cost of chronic management of the resulting HF. When extrapolated to the world population of 7.7 billion at an international mean cost per patient of $11,664,[13] the post-MI HF population could be approximately 50 million and cost over $580 billion annually.

Quantum's lead indication is in difficult-to-treat and resistant HTN, for which it is currently exploring both twice-a-day (capsule and tablet) and once-a-day (tablet) formulations. After successful Phase I and II (NEW-HOPE) trials, and positive feedback from FDA regarding Phase III trial design, Quantum partnered with Brazilian pharmaceutical firm Biolab Sanus Pharmaceuticals to evaluate twice-daily firibastat in Phase III studies (FRESH), which should provide the clinical data needed to market globally. Biolab Sanus has exclusive rights to market firibastat in Latin America. Quantum will have to partner with additional firms to enter other markets such as the United States, Europe and Asia. Management has hinted at discussions with potential large pharmaceutical partners such as Bristol Myers Squibb, Merck, Gilead, Bayer, Pfizer, AstraZeneca, Menarini as well as partners in China, Korea and Japan.

[7] Gaziano TA, Bitton A, Anand S, Weinstein MC; International Society of Hypertension. The global cost of nonoptimal blood pressure. *J Hypertens*. 2009;27(7):1472-1477. doi:10.1097/HJH.0b013e32832a9ba3

[8] Reynolds K, Go AS, Leong TK, et al. Trends in Incidence of Hospitalized Acute Myocardial Infarction in the Cardiovascular Research Network (CVRN). *Am J Med*. 2017;130(3):317-327. doi:10.1016/j.amjmed.2016.09.014

[9] Gruppetta M, Calleja N, Fava S. Long-term survival after acute myocardial infarction and relation to type 2 diabetes and other risk factors. Clin Cardiol 2010;33:424–9

[10] Torabi A, Cleland JG, Rigby AS, Sherwi N. Development and course of heart failure after a myocardial infarction in younger and older people. J Geriatr Cardiol. 2014;11(1):1-12. doi:10.3969/j.issn.1671-5411.2014.01.002

[11] https://www.census.gov/popclock/

[12] Nicholson G, Gandra SR, Halbert RJ, Richhariya A, Nordyke RJ. Patient-level costs of major cardiovascular conditions: a review of the international literature. *Clinicoecon Outcomes Res*. 2016;8:495-506. Published 2016 Sep 21. doi:10.2147/CEOR.S89331

[13] Nicholson G, Gandra SR, Halbert RJ, Richhariya A, Nordyke RJ. Patient-level costs of major cardiovascular conditions: a review of the international literature. *Clinicoecon Outcomes Res*. 2016;8:495-506. Published 2016 Sep 21. doi:10.2147/CEOR.S89331

Quantum also has planned another Phase III study of firibastat in difficult-to-treat and resistant hypertensive patients (RE-FRESH), expected to begin in 1Q:21. Study design is still underway. The once-a-day formulation (QD) has been investigated in Phase I. In post-MI HF, firibastat is currently in Phase IIb trial (QUORUM) evaluating its effects on left ventricular ejection fraction post-MI in comparison to ramipril. End of recruitment is expected 2H:20. There is also preliminary work being done in renal failure, a common comorbidity with resistant HTN and HF that limits treatment options. Success in these trials, both in HTN and HF, would elevate Quantum to an immense patient population in dire need of innovative therapies.

Key reasons to own Quantum Genomics shares:

- **First in class, Phase III asset to address an unmet need in difficult-to-treat and resistant HTN**
- **First in class, Phase II asset to address post-MI HF**
- **Sizeable target patient populations with no innovative competitors**
- **Patent protection and global licensing of BAPAI technology**
- **Strong pre-clinical evidence *in vivo***
- **Healthy cash position, runway for approximately one year**
    - **Closed €8 million and access to additional €16 million financing from Negma**

With strong preclinical evidence, partnership with Brazilian heavyweight Biolab Sanus Pharmaceuticals, and a €11 million cash position, Quantum is well positioned to prove firibastat's efficacy in difficult-to-treat and resistant HTN. Dozens of already-generic medications have failed in this indication, but firibastat's novel mechanism of action has shown efficacy in a Phase II study and there are no direct competitors on the horizon. Difficult-to-treat and resistant HTN is represented in an immense population, with associated healthcare costs in the hundreds of billions of dollars. The indication in HTN appears to be bright but is closely followed by another shining example in post-MI HF which has shown promise in preclinical studies and is currently involved in a Phase IIb study.

RAAS, BAPAIs, and Firibastat

Renin-Angiotensin-Aldosterone System (RAAS)

The renin-angiotensin-aldosterone system (RAAS) plays a dominant role in regulating blood volume and vascular resistance using a variety of mechanisms. The three important RAAS components are renin, angiotensin and aldosterone. RAAS is differentiated into peripheral and central RAAS. Generally, peripheral RAAS is of the body, and central RAAS is of the brain, though the brain includes both, separated by the blood brain barrier. Certain parts of the brain, namely the circumventricular organs (CVO), are considered peripheral, as they allow access to peripheral RAAS components. Within most of the brain, however, RAAS components must be independently synthesized.[14] Peripheral RAAS involves a network of organs that work together to regulate blood pressure via electrolyte balance/blood volume and systemic vascular tone. When the kidneys detect that blood pressure has dropped, the proteolytic enzyme renin is released on signal from the juxtaglomerular cells. Renin is secreted from the juxtaglomerular cells in response to several stimuli: renal perfusion pressure, changes in sodium delivery to the macula densa and increased sympathetic nerve activity. As renin travels throughout the circulatory system, it passes through the liver where the enzyme cleaves several amino acids from the prohormone angiotensinogen to form Angiotensin I (A1). A1 does not have biological activity but rather is a precursor to Angiotensin II (A2). The conversion of A1 to A2 takes place in the lung where the angiotensin-converting enzyme (ACE) cleaves an additional two residues to create the A2 octapeptide.

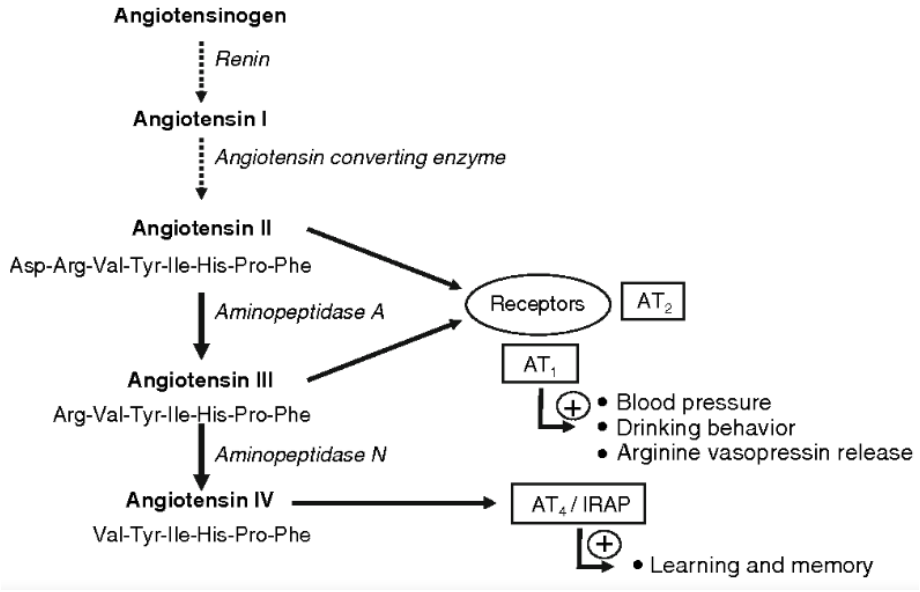
Exhibit I – Octapeptide Angiotensin II[15]

A2 will bind to the angiotensin type I receptors (AT1) where it stimulates vasoconstriction in the arterioles, the renal efferent artery and production of aldosterone from the zona glomerulosa of the adrenal cortex. A2 has several important functions including constricting blood vessels, stimulating sodium transport and acting on the adrenal cortex. These actions release aldosterone which in turn instructs the kidneys to increase sodium and fluid retention, stimulating the release of vasopressin, antidiuretic hormone (ADH), stimulation of thirst centers and other activity. Many current drug therapies for hypertension (HTN) act on A2 and are classified as angiotensin-converting enzyme (ACE) inhibitors. ACE inhibitors block conversion to A2 that binds to AT1, preventing the concomitant rise in blood pressure via multiple pathways.

[14] Jackson L, Eldahshan W, Fagan SC, Ergul A. Within the Brain: The Renin Angiotensin System. Int J Mol Sci. 2018;19(3):876. Published 2018 Mar 15. doi:10.3390/ijms19030876

[15] Serfozo, P. *et al.* Ang II Conversion to Ang (1-7) in the Circulation Is POP Dependent and ACE2-Independent. 2 Dec 2019 Hypertension. 2020;75:173–182

Exhibit II – Schematic of the Brain Renin-Angiotensin System[16]



When A2 reaches the adrenal glands, it stimulates the release of aldosterone, a steroid hormone produced by the zona glomerulosa. Aldosterone causes an increase in salt and water reabsorption into the bloodstream from the kidney and increases stroke volume by the heart. These activities increase blood volume thereby restoring balance.

Brain Aminopeptidase A Inhibitors (BAPAI)

Brain Aminopeptidase A Inhibitors, or BAPAIs, specifically target the brain RAAS which plays a key role in regulating the cardiovascular system. At the brain level, A2 is metabolized into angiotensin III (A3) by the enzyme aminopeptidase A (APA) which cleaves the aspartate amino acid from the N-terminal of the sequence. Now a heptapeptide with affinity to AT1, A3 will bind to AT1 and activate three angiotensinergic pathways involved in blood pressure increase and heart function deterioration.

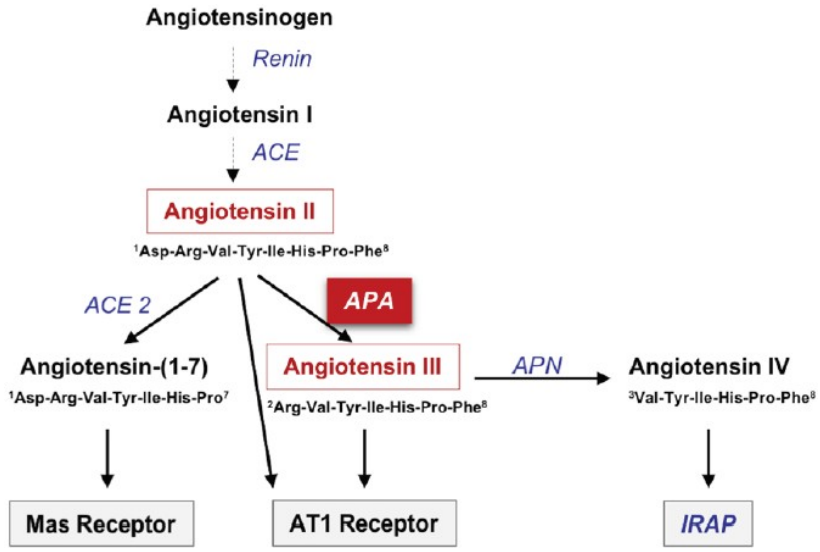
1) Vasopressin from the posterior pituitary gland increases in the bloodstream thereby decreasing diuresis and increasing vasoconstriction,
2) The baroreflex arch is desensitized consequently increasing heart rate,
3) Sympathetic nerve activity is activated, thereby increasing vascular resistance.

A3 is one of the primary effector peptides of brain RAAS which impacts blood pressure. When BAPAIs are administered, the inhibitor is able to block APA conversion of A2 to A3. In the case of the BAPAI firibastat, the molecule is a prodrug which is able to cross the blood brain barrier where it is activated to locally release the inhibitor that blocks enzyme activity. This prevents the production of A3 and its subsequent binding with the AT1 receptors and the resulting blood pressure increase. It also activates alternative enzymatic action via ACE2 which will then sever the C-terminus peptide phenylalanine from A2 and convert it into angiotensin-(1-7), a peptide which can reduce blood pressure and confer protective effects on the heart and blood vessels.[17]

Because BAPAIs inhibit the AT1 receptor pathway and brain AT1 receptor blockade has been shown to inhibit cardiac remodeling that is characteristic of post MI HF, BAPAIs also have the potential to alter the course of post-MI HF through various mechanisms beyond modulating blood pressure.

[16] Bodineau, L., *et al.* Aminopeptidase A inhibitors as centrally acting antihypertensive agents. Published 2007 Medicine Heart Failure Reviews
[17] Santos, R.A. Angiotensin-(1-7). Hypertension. 2014;63:1138–1147. Originally published March 24, 2014.

Exhibit III – RAAS Angiotensin Conversion[18]



Firibastat

Firibastat is a prodrug formulation and dimer of EC33, generated via a disulfide bond. EC33[19] is an APA inhibitor that was developed through the refinement of glutamate thiols where the carboxylate of the side chain of the glutamate thiol was replaced by a sulfonate. This increased the polarity of the side-chain and interaction with the calcium ion, thereby enhancing selective inhibition of APA. Though EC33 has been long known to inhibit APA activity, it could not be used orally as it could not cross the blood brain barrier. The disulfide bond allows the dimerized EC33 to cross the blood brain barrier, allowing daily administration in pill form and defining a new treatment paradigm. After entering the brain, firibastat is cleaved by brain reductases to produce two active moieties of EC33 that then inhibit APA.

Firibastat's mechanism of action disrupts central (brain) RAAS which in turn affects peripheral RAAS, thereby reducing blood pressure and improving cardiac function. Quantum Genomics has produced a video, accessible at the bottom of this page that illustrates the action of the drug in the brain.

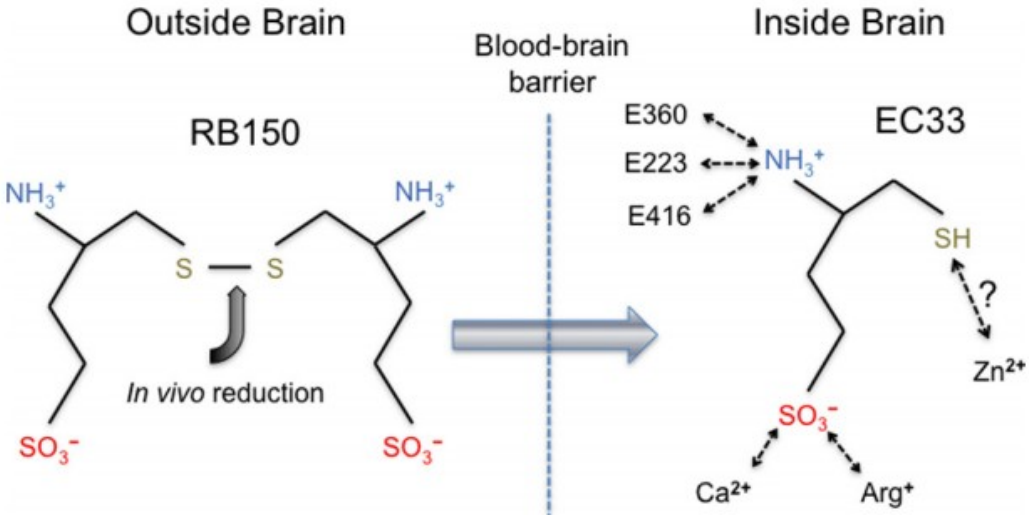
When firibastat blocks the creation of A3, it leads to a normalization of A3 synthesis and favorable regulation of blood pressure. The inhibitor engages a triple mechanism of action enumerated below:

1) Vasopressin secretion decreases
   a. Increases diuresis
   b. Reduces vasoconstriction
2) Activation of Baroreflex arch, a fast acting modifier for blood pressure
   a. Affects heart rate
   b. Adjusts blood pressure
3) Decrease in sympathetic nerve activity
   a. Reduces vascular resistance
   b. Improves cardiac function

Firibastat's mechanism of action is effective in multiple hormone profiles, a characteristic that may provide increased efficacy for individuals with hard to treat HTN such as elderly patients and those of Asian, African and Hispanic descent.

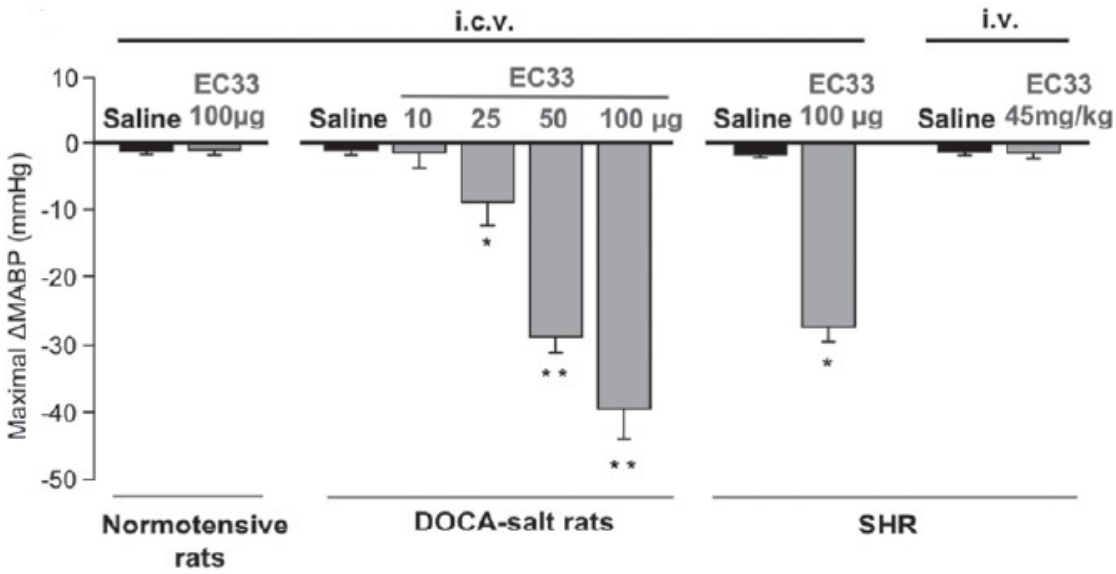
[18] Llorens-Cortes, C., Touyz, R.M. Evolution of a New Class of Antihypertensive Drugs; Targeting the Brain Renin-Angiotensin System. Hypertension. 2020;75:00-00.
[19] (S)-3-amino-4-mercaptobutyl sulfonic acid

Exhibit IV – RB150 (Firibastat) Converting to EC33[20]



Firibastat only provides its blood pressure reduction benefit under conditions of a hyperactive RAAS. *In vivo* studies injected EC33 into rat brains in both normotensive and hypertensive animals. The experiment demonstrated the effect of the drug as an anti-hypertensive agent rather than a hypotensive agent. It also shows dose dependent drug effect. This profile provides activity only when it is needed and used in broader applications such as HF for patients with normotensive blood pressure. As firibastat blocks brain A3 production, it also prevents brain AT1 activation that has been implicated in post-MI cardiac remodeling that causes HF.

Exhibit V – Blood Pressure Effect of EC33 on Normotensive and Hypertensive Rats[21]



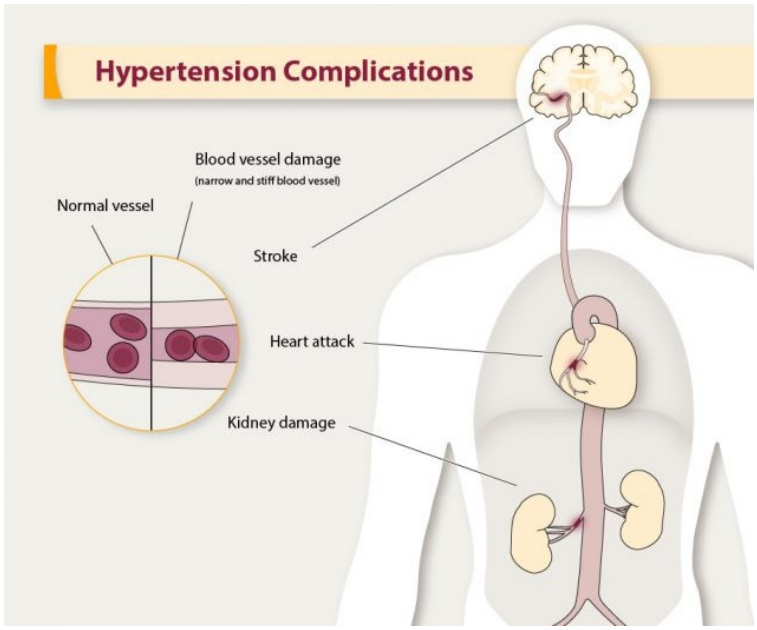
[20] Jian, Y. Structural Insights into Central Hypertension Regulation by Human Aminopeptidase A. Journal of Biological Chemistry July 2013
[21] Llorens-Cortes, C., Touyz, R.M. Evolution of a New Class of Antihypertensive Drugs; Targeting the Brain Renin-Angiotensin System. Hypertension. 2020;75:00-00. MABP: Mean Arterial Blood Pressure; i.c.v.: intracerebroventricular injection; i.v.: intravenous.

Hypertension (HTN), Post Myocardial Infarction (MI) and Heart Failure (HF)

Hypertension

Hypertension (HTN) is a condition where blood pressure is elevated, usually above 140/90 millimeters of mercury (mm Hg) as measured by a blood pressure monitor or a provider. Normal blood pressure averages 120/80 mm Hg. The first number is the systolic pressure, which occurs when the left ventricle pumps blood out of the heart. The second number is the diastolic pressure, which occurs between heartbeats, as the heart relaxes and chambers refill. HTN, when experienced over an extended period of time, can cause a number of health issues including fatal heart attack or stroke. Consistently higher than normal pressure can damage the arteries' inner lining and can reduce their elasticity. If there is a weak area of an artery, high blood pressure can cause a bulge or aneurysm which could burst and cause internal bleeding. There is an extended list of injury that can occur as a result of HTN, including heart damage, such as coronary artery disease, brain damage, such as stroke, kidney failure, sexual dysfunction, vision loss and other conditions. In some cases when blood pressure exceeds 180/120 mm Hg, it is considered a hypertensive crisis that requires immediate medical attention.

Exhibit VI – Hypertension Complications[22]



Incidence/Prevalence

The World Health Organization (WHO) estimates that there are 1.13 billion people worldwide with HTN, making it a common condition. Studies conducted by the National Health and Nutrition Examination Survey during 2017 and 2018 found HTN prevalence of 45% among adults and positive correlation with age.[23] 48.3% of the hypertensive population is able to keep the condition under control,[24] demonstrating an unmet need for an important public health challenge due to its association with cardiovascular disease. Using data collected over the 2013 to 2016 period, the US National Center for Health Statistics estimated that 108 million adults have hypertension. Of this total, an estimated 82 million of the US adults with HTN do not have it under control. The WHO estimates that prevalence of HTN in Europe is just over 40%. Another study found that control is on average under 15% in each of the five[25] European countries investigated.[26] Two studies, EURIKA[27] and EUROASPIRE,[28] identified a proportion of

[22] Source: Centers for Disease Control and Prevention Website. High Blood Pressure Symptoms and Causes, accessed May 2020. https://www.cdc.gov/bloodpressure/images/hypertension-complications-medium.jpg
[23] National Center for Health Statistics. National Health and Nutrition Examination Survey. July 2020
[24] Hypertension Prevalence and Control Among Adults: United States, 2015-2016. NCHS Data Brief, No. 289. October 2017.
[25] These included Sweden, Spain, England, Germany and Italy.
[26] Wolf-Maier, K., *et al.* Hypertension Treatment and Control in Five European Countries, Canada, and the United States. Hypertension. 2004;43:10–17
[27] Borghi, C., *et al.* Lack of Control of Hypertension in Primary Cardiovascular Disease Prevention in Europe: Results From the EURIKA Study. Int J Cardiol. 2016 Sep 1;218:83-88.
[28] Kotseva, K., *et al.* The EUROASPIRE surveys: lessons learned in cardiovascular disease prevention. Cardiovasc Diagn Ther. 2017 Dec; 7(6): 633–639.

hypertensive patients with controlled blood pressure ranging from 27% to 47%. This low level of blood pressure control across the globe highlights the need for new approaches to lower blood pressure.

Treatment

To combat this deadly but conventional disease, a broad variety of treatments have been developed and approved. Treatment spans a wide range and frequently begins with recommendations for lifestyle changes such as weight loss, exercise and a diet high in fruits and vegetables. If this is ineffective, medications such as diuretics, ACE inhibitors, ARBs or calcium channel blockers will be prescribed. There are dozens of medications available for this indication in a wide variety of classes. Despite the varied approaches and choice available, in many cases treatment is ineffective, highlighting the need for new approaches for controlling HTN. Two groups that have more difficulty controlling blood pressure than others are individuals of African descent and those suffering from obesity.

Exhibit VII – Product Classes Used for Hypertension

Classes of Hypertension Medications			
Loop diuretics	Central agonists	Calcium channel blockers	Angiotensin converting Enzyme (ACE) inhibitors
Beta blockers	Alpha-blockers	Alpha-beta-blockers	Angiotensin II receptor blockers (ARBs)
Vasodilators	Renin Inhibitor	Thiazide diuretics	Potassium-sparing diuretics

Risk Factors & Symptoms

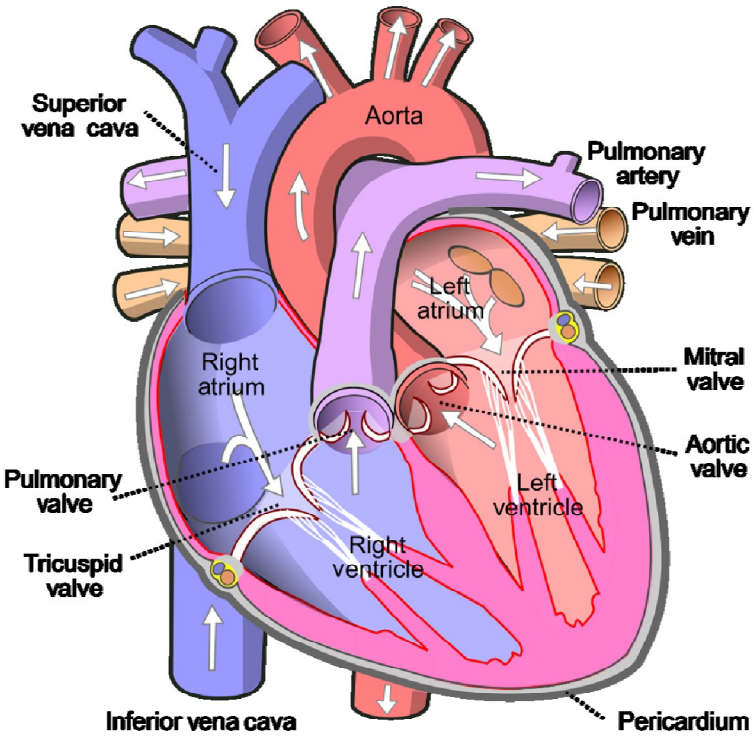
There are a number of risk factors for HTN including obesity, excessive intake of alcohol and salt, lack of exercise, poor sleeping habits, diabetes, stress and others. Family history also plays a role. In some cases, other medical conditions can contribute to high blood pressure such as pregnancy, heart defects and kidney disorders. High blood pressure usually subsides when the underlying condition resolves. One of the reasons HTN is so common is that the symptoms are usually undetectable earning its moniker: the silent killer. In some cases, high blood pressure may cause headache, blurred vision, dizziness and shortness of breath. High blood pressure may also affect the heart which can cause shortness of breath, chest pain and heart attack and can also impact the kidneys, resulting in fluid retention and kidney failure. Since detectable symptoms without diagnostic measurement are uncommon, screening for blood pressure is a routine part of an office visit.

Post Myocardial Infarction (MI) Heart Failure (HF)

Pathophysiology
Heart failure (HF) describes a complex syndrome, characterized by impaired ability for the heart to pump blood, evolving into a condition where the heart is eventually unable to sustain the body with oxygen, even at rest. The heart has four chambers, left and right atria and ventricles, and HF is classified according to which chamber is undergoing damage. The left ventricle is responsible for pumping oxygenated blood to the body and is the common locus of HF. Left-sided heart failure is classified into preserved ejection fraction (HFpEF) or reduced ejection fraction (HFrEF). HFpEF is also known as diastolic HF, where ejection fraction is normal but the left ventricle is unable to fill, while HFrEF is known as systolic HF.[29,30] HFmrEF (mid-range) has been recognized as a potentially distinct entity, with characteristics between the preserved and reduced ejection fractions.[31] HF can be chronic, developing over time, or acute (acute decompensated heart failure), as in the case of myocardial infarction (heart attack).[32]

[29] https://www.mayoclinic.org/diseases-conditions/heart-failure/symptoms-causes/syc-20373142
[30] https://www.heart.org/en/health-topics/heart-failure/what-is-heart-failure
[31] Savarese G, Lund LH. Global Public Health Burden of Heart Failure. *Card Fail Rev*. 2017;3(1):7-11. doi:10.15420/cfr.2016:25:2
[32] Roger VL. Epidemiology of heart failure. *Circ Res*. 2013;113(6):646-659. doi:10.1161/CIRCRESAHA.113.300268

Exhibit VIII – Diagram of the Human Heart[33]



Myocardial Infarction

A myocardial infarction (MI) occurs when an atherosclerotic plaque ruptures, triggering acute ischemic thrombosis resulting in cardiomyocytic necrosis. The most common coronary artery occluded is the Left Anterior Descending (LAD), which supplies blood to the left ventricle.[34] The left ventricle is responsible for pumping oxygenated blood throughout the body. As the infarct progresses, cardiomyocytes continue to necrose, and their ability to contract is weakened, reducing ejection fraction. In cases where HF does not present immediately, HF following MI progresses in the following weeks after the initial infarct. While many patients either present with or develop HF during their hospitalization for MI, some patients even return home from the hospital before they develop HF for the first time.[35] This likely depends on the severity of the infarction with respect to size, duration and location. The heart progressively weakens, undergoing remodeling, where cardiomyocytes apoptose and fibrose.

Post-MI HF

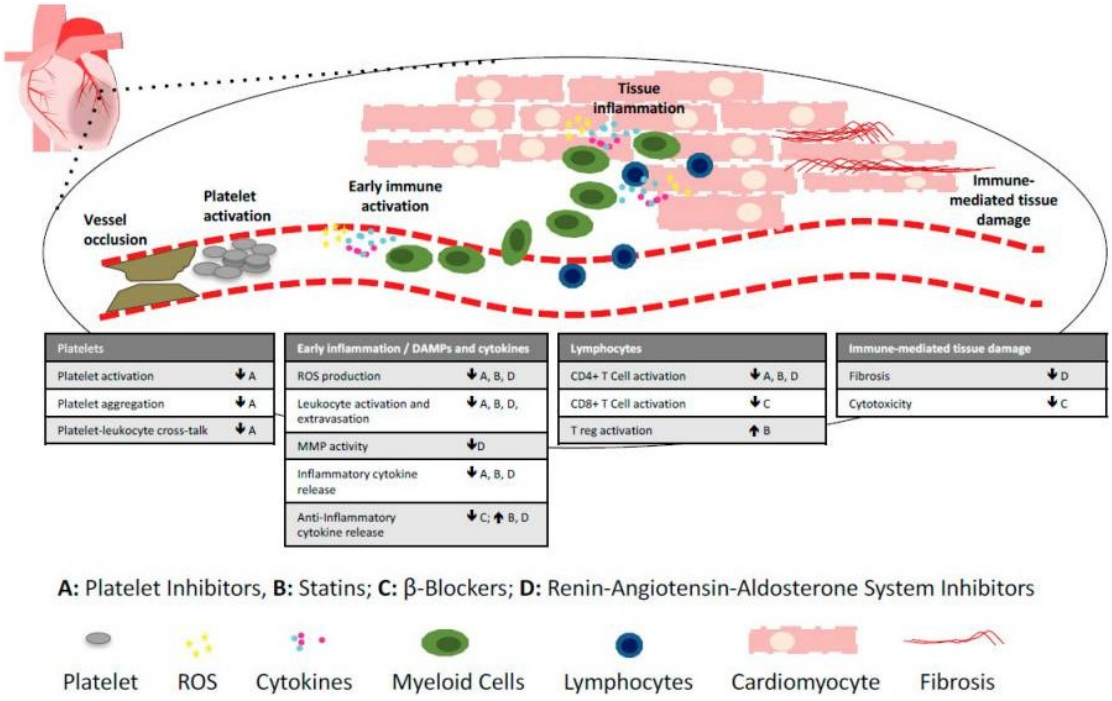
Post-MI fibrotic remodeling stiffens the myocardial tissue, inhibiting the ability of the left ventricle to fill and pump resulting in eventual HF. HF often follows MI and is characterized by cardiomyocytic apoptosis and fibrotic remodeling. The process of post-MI HF is imperfectly understood and complex, with many components, though many mechanistic relationships have been elucidated *in vivo*.[36] While the exact mechanism is not perfectly understood, experiments have implicated multiple systems, including the brain RAAS.

When MI occurs, the infarct sends signals via cardiac afferent reflex, releases cytokines, and causes elevation of circulating RAAS. In the first few hours and days, circulating A2 is elevated, which, through the subfornical organ (SFO), elicits brain-level aldosterone production. In the weeks following the infarction, neurons in the SFO and the nucleus of the solitary tract show elevated activity, which lasts approximately four weeks. The brain-level aldosterone then interacts with mineralocorticoid receptors (MR), triggering the production and release of ouabain-like compounds, most likely in the paraventricular nucleus (PVN) and supraoptic nucleus (SON). Activity in the magnocellular neurons of the PVN and SON has been observed to progressively increase after the initial infarction. Sympathetic cardiac afferent reflex and cytokines released in response to the infarct further stimulate the PVN.

[33] Source: By Wapcaplet - Own work, CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=830253
[34] http://www.vhlab.umn.edu/atlas/coronary-arteries/lad-left-anterior-descending-artery/index.shtml
[35] Torabi A, Cleland JG, Khan NK, et al. The timing of development and subsequent clinical course of heart failure after a myocardial infarction. Eur Heart J. 2008;29(7):859-870. doi:10.1093/eurheartj/ehn096
[36] Westcott KV, Huang BS, Leenen FH. Brain renin-angiotensin-aldosterone system and ventricular remodeling after myocardial infarct: a review. *Can J Physiol Pharmacol*. 2009;87(12):979-988. doi:10.1139/Y09-067

Ouabain-like compounds enhance the activity of angiotensinergic pathways from the PVN, resulting in sympathetic hyperactivity and activation of circulating and cardiac RAAS. The increase in sympathetic activity can be prevented or normalized by blockade of the A2, AT1 receptors, aldosterone, MR, or the ouabain-like compounds. The confluence of sympathetic activity and RAAS elevation may activate cardiac pro-inflammatory cytokines and increase cardiomyocyte apoptosis. At the cardiac level, MR and ouabain-like compound blockade has been shown to attenuate serum and cardiac aldosterone and attenuate increase in ACE and AT1 receptor density. Post-MI cardiac remodeling is characterized by dilation, hypertrophy, and interstitial and perivascular fibrosis. Blockade of brain-level A2, AT1-receptors, aldosterone, MR, or ouabain also shows marked improvement of remodeling and dysfunction. The remodeling begins at the time of the MI, where the inflammatory response signals damage to the tissue, cytokines are elevated and the tissue responds by allowing increased permeability to leukocytes. The leukocytes infiltrate the heart tissue and clear necrotic and apoptotic cells leading to fibrosis and scar tissue formation. The remodeling alters the biomechanical properties of the tissue, and spreads beyond the infarct. Myocardial apoptosis and fibrosis are thought to be driven mostly by inflammation, sympathetic hyperactivity and RAAS.

Exhibit IX – Mechanism of Cardiac Remodeling[37]



As a BAPAI, firibastat can modulate brain RAAS by inhibiting the APA, so that A3 cannot be produced from A2. A3 is a major signaling peptide at the brain level with similar affinity to AT1 receptors as A2. AT1 receptor activation is implicated in post-MI HF sympathetic hyperactivity and cardiac dilation, hypertrophy and fibrosis. In rats, firibastat has been shown to decrease renal sympathetic nerve activity and improve left ventricular ejection fraction and contractility.[38] The drug also has been shown to improve post-MI ejection fraction and decrease HF biomarkers and fibrosis in mice.[39] Finally, in mice that were orally administered firibastat, ejection fraction and contractility improved, while arterial diastolic blood pressure and left ventricle end-diastolic pressure were preserved. *In vivo,* firibastat was shown to be comparable, or superior to representatives of current standard of care including losartan, enalapril, and ramipril.

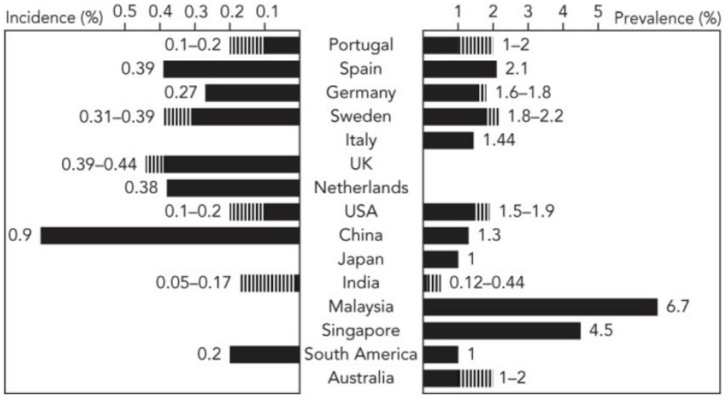
Incidence, Prevalence & Risk

Because HF is a syndrome, rather than a disease, diagnosis can be ambiguous and challenging. For example, the ejection fraction threshold for diagnosing HF ranges from 40% to 50%. Estimates of incidence and prevalence vary

[37] Panahi M, Vadgama N, Kuganesan M, Ng FS, Sattler S. Immunopharmacology of Post-Myocardial Infarction and Heart Failure Medications. *J Clin Med*. 2018;7(11):403. Published 2018 Oct 31. doi:10.3390/jcm7110403
[38] Huang BS, Ahmad M, White RA, Marc Y, Llorens-Cortes C, Leenen FH. Inhibition of brain angiotensin III attenuates sympathetic hyperactivity and cardiac dysfunction in rats post-myocardial infarction. Cardiovasc Res. 2013;97(3):424-431. doi:10.1093/cvr/cvs420
[39] Boitard SE, Marc Y, Keck M, et al. Brain renin-angiotensin system blockade with orally active aminopeptidase A inhibitor prevents cardiac dysfunction after myocardial infarction in mice. *J Mol Cell Cardiol*. 2019;127:215-222. doi:10.1016/j.yjmcc.2018.12.008

among studies due to shifting criteria, data collection methods, and external factors.[40] Global prevalence of HF is estimated to be at least 26 million in 2017.[41] Of the studies compiled, Malaysia had the highest prevalence at 6.7%, China had the highest absolute prevalence at approximately 18 million and relative and absolute incidence at 9 in 1000 people, or approximately 500,000 per year.

Exhibit X – Heart Failure Worldwide[42]



In 2019, the prevalence of HF was estimated to be 6.5 million in the US.[43] The number is expected to increase dramatically to 8 million people by 2030[44] due to rising levels of obesity and metabolic syndrome. In the United States, there are approximately 915,000 new cases of HF each year (about 0.3% of the population), with the incidence in older populations (65+) approaching 1%. After the age of 40, lifetime risk of developing heart failure is 20%.[45] Populations at risk for HFpEF include obese older women, individuals in the upper quartile of NYHA classification,[46] and those who have comorbidities, such as hypertension, diabetes, atrial fibrillation, and valvular disease.

The post-MI HF population is a subset of the total HF population. MI is a common cause of HFrEF. HF can develop immediately after MI, during the hospitalization or later after being discharged. In 2008, the estimated incidence of MI in the US was 168.6 per 100,000 person-years.[47] Mean survival of patients presenting with MI is estimated to be 10.3 years, implying a prevalence of MI around 1.7% of the US population.[48] Coupled with an estimated 38% of MI patients developing HF, we estimate post-MI HF to be 0.65% of the population, or about 2.1 million in the US.[49,50] When extrapolated to the world population of 7.7 billion, post-MI HF population could be approximately 50 million.

Symptoms & Diagnosis

Symptoms of post-MI HF are the same as general HF and include dyspnea, fatigue, weakness, lower extremity edema and rapid or irregular heartbeat. HF symptoms can also include reduced exercise capacity, coughing, wheezing, traces of blood in phlegm, increased night-time urination, and abdominal swelling. In acute HF, sudden dyspnea, coughing blood-tinged, foamy mucus, and chest pain may occur. Symptoms of HF vary with its type and which side of the heart is affected: in left sided heart failure, fluid backs up into the lung and causes shortness of breath, in right-sided, fluid backs up into the abdomen, legs and feet resulting in edema.[51]

HF is classified (Class I-II-III-IV) based on severity of symptoms and heart function deterioration according to New York Heart Association guidelines.[52] Additionally, progression of HF is staged (A, B, C and D) and cannot revert.[53]

[40] Roger VL. Epidemiology of heart failure. *Circ Res*. 2013;113(6):646-659. doi:10.1161/CIRCRESAHA.113.300268
[41] Ponikowski P, Anker SD, AlHabib KF, et al. Heart failure: preventing disease and death worldwide. *ESC Heart Fail*. 2014;1(1):4-25. doi:10.1002/ehf2.12005
[42] Savarese G, Lund LH. Global Public Health Burden of Heart Failure. *Card Fail Rev*. 2017;3(1):7-11. doi:10.15420/cfr.2016:25:2
[43] Benjamin EJ, Muntner P, Alonso A, Bittencourt MS, Callaway CW, Carson AP, et al. Heart disease and stroke statistics—2019 update: a report from the American Heart Association. *Circulation*. 2019;139(10):e56–528.
[44] Mozaffarian D, Benjamin EJ, Go AS et al. American Heart Association Statistics Committee; Stroke Statistics Subcommittee. Heart Disease and Stroke Statistics-2016 Update: A report from the American Heart Association. Circulation. 2016;133:e38–e360. doi: 10.1161/CIR.0000000000000350].
[45] Savarese G, Lund LH. Global Public Health Burden of Heart Failure. *Card Fail Rev*. 2017;3(1):7-11. doi:10.15420/cfr.2016:25:2
[46] The New York Heart Association (NYHA) Functional Classification1. It places patients in one of four categories based on how much they are limited during physical activity. Class I is no limitation of physical activity while Class IV is the inability to perform any physical activity without discomfort.
[47] Reynolds K, Go AS, Leong TK, et al. Trends in Incidence of Hospitalized Acute Myocardial Infarction in the Cardiovascular Research Network (CVRN). *Am J Med*. 2017;130(3):317-327. doi:10.1016/j.amjmed.2016.09.014
[48] Gruppetta M, Calleja N, Fava S. Long-term survival after acute myocardial infarction and relation to type 2 diabetes and other risk factors. Clin Cardiol 2010;33:424–9
[49] Torabi A, Cleland JG, Rigby AS, Sherwi N. Development and course of heart failure after a myocardial infarction in younger and older people. J Geriatr Cardiol. 2014;11(1):1-12. doi:10.3969/j.issn.1671-5411.2014.01.002
[50] https://www.census.gov/popclock/
[51] https://www.mayoclinic.org/diseases-conditions/heart-failure/symptoms-causes/syc-20373142
[52] https://my.clevelandclinic.org/health/diseases/17069-heart-failure-understanding-heart-failure/management-and-treatment
[53] https://my.clevelandclinic.org/health/diseases/17069-heart-failure-understanding-heart-failure/management-and-treatment

The stages range from stage A, when a patient is at risk of developing HF, to stage D, when the condition is most advanced. Blood tests, electrocardiogram (ECG), echocardiograms and stress tests are common. Computerized tomography (CT), magnetic resonance imaging (MRI), chest x-rays and coronary angiogram are imaging techniques that can be used to visualize the condition of the heart. To assess the condition of the heart muscle tissue, a myocardial biopsy can be performed. Catheterization, although invasive, sets the gold standard for assessing ejection fraction.[54]

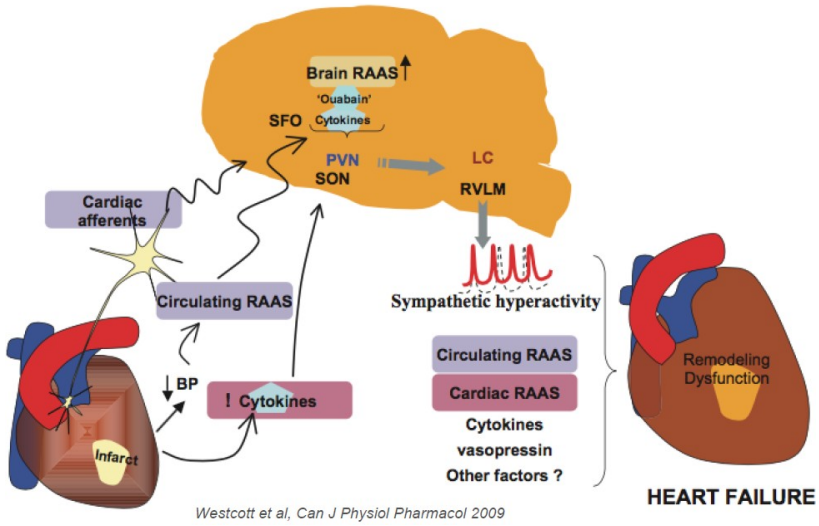
Prevention and Treatment

Lifestyle changes can help to reduce the signs and symptoms of HF and are the first line of defense. This includes exercising, reducing sodium consumption, managing stress and reducing body mass index (BMI).[55] Lifestyle management also includes monitoring areas prone to swelling such as the lower extremities, limiting alcohol intake, and reduction of stress.[56] Prevention of post-MI HF is similar to that of hypertension or general HF. The latest post-MI pharmaco-regimen includes platelet inhibitors, statins, beta-blockers, and RAS inhibitors.[57] The primary goal of routine post-MI pharmacotherapy is to support heart function by ensuring appropriate blood pressure and cardiac output to meet the demands of the body, though several drug classes are now understood to also be modulate the post-MI immune response.[58]

Firibastat in Heart Failure

Preclinical work was conducted to identify the rationale for using firibastat in the treatment of post-MI HF. Firibastat was found to inhibit APA and block the production of A3, which reduced sympathetic nervous system activity thereby improving cardiac left ventricle function in a post-MI rat model. Firibastat was compared to losartan. Results showed an improved ejection fraction as compared to vehicle and losartan.

Exhibit XI – RAAS Effect on Heart Failure[59]



These efforts justified a move into the clinic where a Phase IIa trial was launched to evaluate human safety and a Phase IIb was begun in June 2018 to further assess the efficacy and safety of firibastat compared to ramipril in a trial designated QUORUM.

[54] Roger VL. Epidemiology of heart failure. *Circ Res*. 2013;113(6):646-659. doi:10.1161/CIRCRESAHA.113.300268
[55] https://www.mayoclinic.org/diseases-conditions/heart-failure/symptoms-causes/syc-20373142
[56] https://www.mayoclinic.org/diseases-conditions/heart-failure/diagnosis-treatment/drc-20373148
[57] Panahi M, Vadgama N, Kuganesan M, Ng FS, Sattler S. Immunopharmacology of Post-Myocardial Infarction and Heart Failure Medications. *J Clin Med*. 2018;7(11):403. Published 2018 Oct 31. doi:10.3390/jcm7110403
[58] Panahi M, Vadgama N, Kuganesan M, Ng FS, Sattler S. Immunopharmacology of Post-Myocardial Infarction and Heart Failure Medications. J Clin Med. 2018;7(11):403. Published 2018 Oct 31. doi:10.3390/jcm7110403
[59] Source: Quantum Genomics June 2020 slide deck and Westcott *et al*., Can J Physiol Pharmacol 2009

Research and Development

Preclinical Work

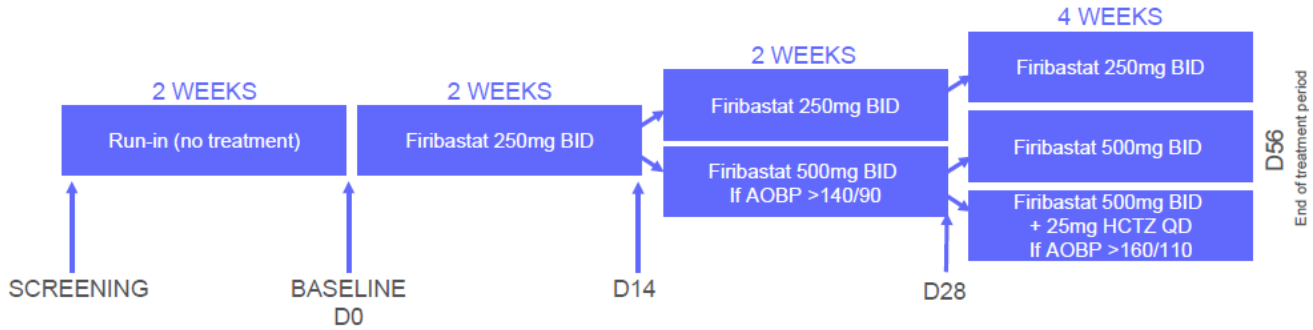
Following initial work where mice received intracerebroventricular (i.c.v.) injections of EC33, Quantum conducted preclinical work in DOCA salt rats where RB150[60] (firibastat) was systemically injected into the models. The results of the research were published in the journal *Hypertension* in 2008. The study was able to demonstrate that EC33 blocked the pressor response of converted A3 and that EC33 did not cross the blood brain barrier in the DOCA salt rat model. The work also provided evidence that aminopeptidase A (APA) was responsible for producing A3 and that A3 was a potential target for the treatment of hypertension. When RB150, a dimer of EC33, created by forming a disulfide bond, was injected systemically in the animal model it was able to block RAAS activity and reduce blood pressure in hypertensive DOCA salt rats in a dose dependent manner. The research also demonstrated that RB150 was able to cross the intestinal, hepatic and blood brain barriers. This study provided evidence that supported the advance of RB150 into clinical trials.

Early Phase Trials for Hypertension

In 2012, a Phase Ia trial was conducted to determine the overall safety and tolerability of firibastat. It was a randomized, double-blind, placebo-controlled study that enrolled 80 healthy volunteers. The study increased the dose up to 2 g.[61] A Phase Ib trial was launched in 2013 which enrolled 44 healthy volunteers for an evaluation of overall safety and tolerability of firibastat up to 750 mg, twice per day without food. Design was randomized, double blind, placebo controlled in multiple ascending doses. Efficacy work began, along with further safety evaluations in a Phase IIa study which included readings from 34 moderate hypertensive patients. Results were favorable with a decrease in ambulatory and office blood pressure (-2.7 mm Hg and -4.7 mm Hg respectively) compared to placebo. The blood pressure decline at the end of the study was a greater magnitude in patients with higher baseline measurements.

With a solid foundation of data in almost 160 patients, Quantum Genomics advanced firibastat into a Phase IIb trial evaluating the effect of firibastat in hypertensive overweight patients of multiple ethnic origins. The open-label, multicenter, dose-titrating study was designated NEW-HOPE (**N**ovel **E**valuation **W**ith QGC001 in **H**ypertensive **O**verweight **P**atients of Multiple **E**thnic Origins) and enrolled 256 participants to measure the effects of the drug over an eight week period of treatment. The population was comprised of at least 50% individuals of African and Hispanic heritage conducted at 38 sites in the United States. The primary endpoint of the study was the change in baseline automated office blood pressure (AOBP) at the end of the study. Secondary endpoints included diastolic AOBP, 24-hour mean ambulatory blood pressure and safety.

Exhibit XII – NEW HOPE Study Design[62]



Results for the Phase IIb trial were favorable with systolic AOBP falling from 154.0 at baseline to 144.4 at the eight week mark, representing a statistically significant 9.5 point reduction in pressure. When examined on the basis of subgroups, decrease in systolic AOBP was similar in those of African descent (-10.5 mm Hg at p<0.0001) and obese patients (-10.2 mm Hg at p<0.0001), which are sometimes classified as hard to treat. All other blood pressure measures declined as well as shown in the following table.

[60] Firibastat is now known internally as QGC001
[61] https://anr.fr/Project-ANR-13-RPIB-0005
[62] Source: Quantum Genomics Corporate Presentation, June 2020.

Exhibit XIII –New Hope Metrics[63]

Hemodynamic Parameter	N	Baseline	Day-56	Change From Baseline	*P* Value
Systolic AOBP, mm Hg	251	154.0±7.3	144.4±14.1	–9.5±14.3	<0.0001
Diastolic AOBP, mm Hg	251	91.5±8.5	87.4±10.1	–4.2±9.4	<0.0001
Office HR, bpm	251	75.6±12.5	76.6±11.4	0.9±12.3	0.22
Systolic daytime ABP, mm Hg	181	151.3±13.2	148.2±14.2	–3.1±13.0	0.0005
Diastolic daytime ABP, mm Hg	181	88.7±9.4	87.1±9.7	–1.6±7.8	0.003
Systolic nighttime ABP, mm Hg	181	137.8±16.3	135.9±17.2	–1.9±14.9	0.11
Diastolic nighttime ABP, mm Hg	181	78.3±10.8	77.5±10.5	–0.9±9.0	0.28
Systolic 24h-ABP, mm Hg	181	146.8±13.4	144.1±14.4	–2.7±12.4	0.002
Diastolic 24h-ABP, mm Hg	181	85.2±9.3	83.8±9.3	–1.4±7.2	0.01

Safety for the patients in the trial was favorable and 36 subjects or 14.1% presented a treatment emergent adverse event. The most common treatment emergent adverse events (TEAEs) were headache (4%) and skin reaction (3%). Nineteen subjects, or 7.5% stopped taking the medication due to adverse events. Of the five serious events that occurred during the study, only one was considered to be related to study medication.

The strong results of the Phase II trial supported a move to Phase III. Firibastat demonstrated efficacy in all subgroups when stratified by age, sex, ethnic origin and weight. The favorable results related to race are particularly important as those of African descent present hypertension that is more difficult to control, occurs with a higher prevalence and with an earlier onset.

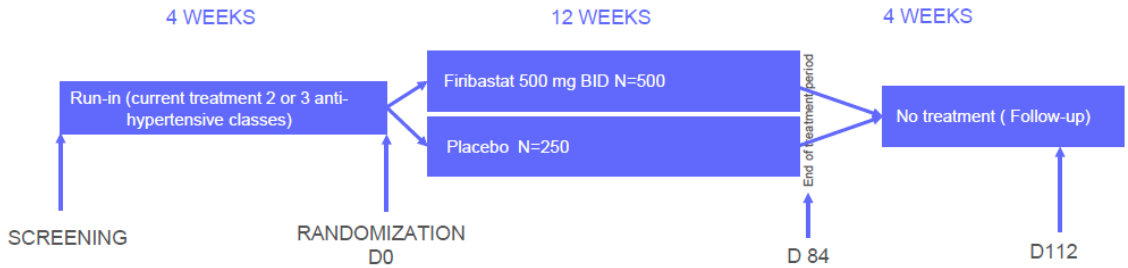
Phase III Trials for Firibastat

Promising *in vivo*, Phase I and Phase II work supported further development of firibastat, advancing the BAPAI into registrational studies. In the summer of 2019, Quantum received favorable feedback from the FDA in an End-of-Phase II meeting to create a development plan and trial design for Phase III studies. Two trials will be run, one for efficacy and one for safety.

Quantum announced the start of its Phase III FRESH (**F**iribastat in treatment-**RES**istant **H**ypertension) in mid-December 2019 that will be conducted in partnership with Biolab Sanus Pharmaceuticals. The 500-subject trial will be a three month, double-blind, placebo-controlled study in difficult-to-treat and resistant hypertension as defined by systolic blood pressure above 140 mm Hg and treatment with two or three anti-hypertensive classes including a diuretic. Study treatment will be 500 mg of firibastat, administered twice per day in addition to currently mandated therapy. The trial will be held at 70 sites around the globe, including hospitals in Europe, the US, Canada and Latin America. Biolab will be responsible for trial costs of 20% (100) of the anticipated subject total and will manage the trials in Latin America.

The primary endpoint for the study is change from baseline in systolic automated office blood pressure (AOBP). Secondary outcomes include measurement of diastolic blood pressure, mean 24-hour ambulatory systolic and diastolic blood pressure.

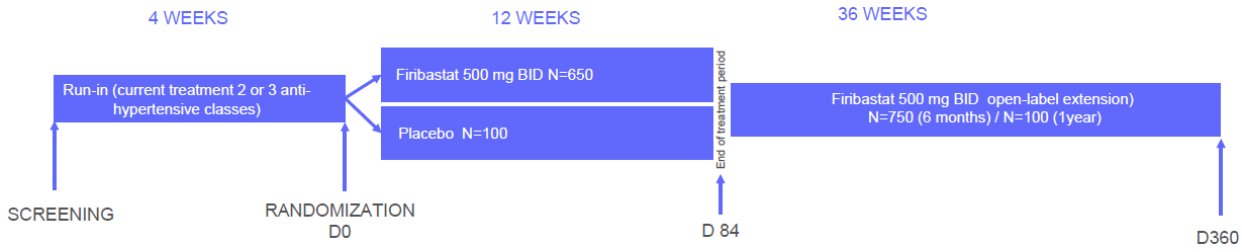
Exhibit XIV – FRESH Study Design



[63] Ferdinand, K.C. *et al.* Efficacy and Safety of Firibastat, A First-in-Class Brain Aminopeptidase A Inhibitor, in Hypertensive Overweight Patients of Multiple Ethnic Origins. Circulation. July 9, 2019. Vol 140, Issue 2.

Expected to begin in the second quarter of 2021[64] and partially concurrent with FRESH is the RE-FRESH trial, a pivotal efficacy and safety Phase III study, also in difficult-to-treat and resistant hypertensive patients. This effort will enroll 750 patients with AOBP above 140 mm Hg. 650 patients will receive firibastat for six months, and 100 patients will receive firibastat for one year. This trial will also be of randomized, double-blind, placebo-controlled design with firibastat administered on top of current treatment for twelve weeks. There will also be an open-label extension for up to 12 months to further evaluate safety. Trial design is still underway; however, the focus will be on long-term safety.

Exhibit XV – RE-FRESH Study Design



Phase I, Hypertension *Quaque Die (QD)*

A novel once per day (QD) 500 mg formulation of firibastat is being investigated. It is a modified release tablet that provides drug exposure of 1000 mg QD similar to the profile provided by the 500 mg twice per day (BID) product. The early part of the Phase I trial demonstrated a safe and well tolerated drug that was able to be taken with food with no modification of the pharmacokinetic (PK) parameters of firibastat and its metabolites.

The new formulation of firibastat completed a Phase Ia study. The study design was an open-label, non-randomized, five-period fixed sequence enrolling 12 healthy subjects conducted at one site in Nottingham, England. The effort evaluated the pharmacokinetic PK profile of firibastat to determine maximum plasma concentration, time to Cmax and area under the curve (AUC). Secondary outcomes measured drug bioavailability as well as safety and tolerability as measured via various dimensions.

Adverse Events and Safety Profile

Exhibit XVI – Summary of New Hope TEAE[65]

	Patients (%)
Patients with any TEAE	107 (42.0%)
Related TEAEs*	36 (14.1%)
Most common treatment related AEs	
Headache	11 (4.3%)
Skin reaction	8 (3.1%)
AE leading to discontinuation	19 (7.5%)
Headache	4 (1.6%)
Skin reaction	3 (1.2%)
Hypertension	3 (1.2%)
Dizziness/presyncope	4 (1.6%)
Diarrhea	2 (0.8%)
Other	3 (1.2%)
Serious AE	5 (2%)
Related serious AE	1 (0.4%)

AE indicates adverse event; and TEAE, treatment-emergent adverse events.

*Investigator determined.

In the Phase II NEW-HOPE study, 255 patients were considered in the safety population and 36 of the subjects (14.1%) reported a related TEAE. The most common events included headache (4.3%), skin reaction (3.1%) and dizziness (1.6%). 19 subjects in the group discontinued treatment due to adverse events and five serious adverse events occurred during the study. However, only 1 of these serious events, which was a case of erythema multiforme, was considered to be related to firibastat. No deaths were reported in the study.

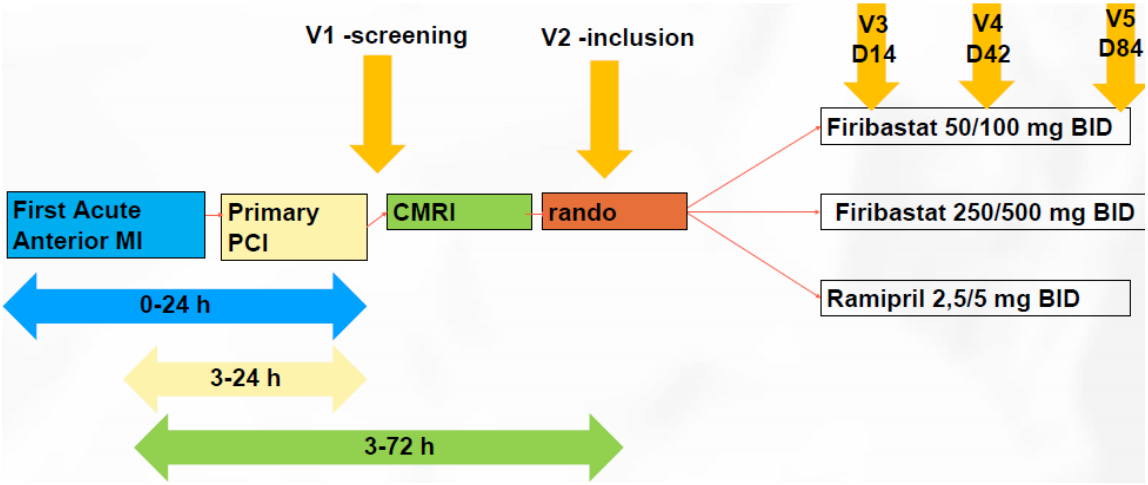
Phase IIb, Post Myocardial Infarction Heart Failure

A 294-patient Phase IIb trial was conducted to characterize safety and efficacy of firibastat in patients after acute anterior myocardial infarction (MI). Subjects were required to have a diagnosis of first acute anterior MI and a primary percutaneous coronary intervention (PCI) within 24 hours after MI. The trial was structured to compare three parallel groups including firibastat at 100 mg BID and 500 mg BID, and ramipril 5 mg BID over a three month treatment period. The primary endpoint of the trial was change in baseline of left ventricular ejection fraction. The trial was conducted at 38 hospitals throughout Europe and is expected to provide topline results in 2H:20. Assuming successful results from the Phase IIb, we anticipate regulatory

[64] As guided in the June 2020 corporate presentation.
[65] Ferdinand, K.C. *et al.* Efficacy and Safety of Firibastat, A First-in-Class Brain Aminopeptidase A Inhibitor, in Hypertensive Overweight Patients of Multiple Ethnic Origins. Circulation. July 9, 2019. Vol 140, Issue 2.

meetings and trial design efforts in support of a Phase III study launching in 2021.

Exhibit XVII – Phase IIb Post-MI HF Trial Design[66]



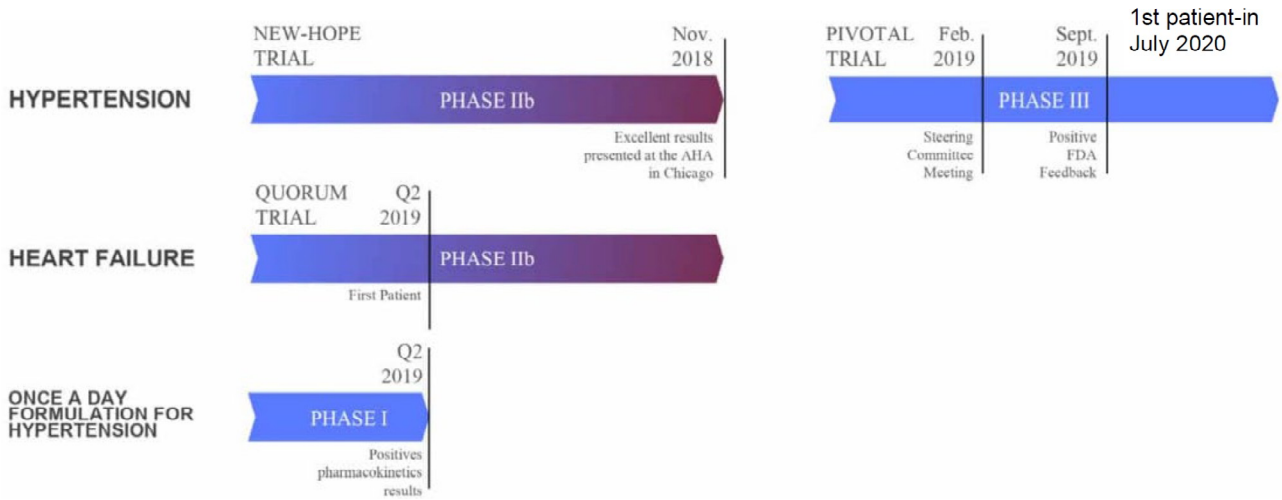
Other Portfolio Candidates

Quantum is also examining firibastat in renal failure and is conducting a PK Phase I study in two cohorts. The 28 patients involed in the trial will be evenly split between those with end stage renal failure and healthy individuals. The goal of the early stage clinical investigation is to assess the need of dose adjustment in the renal impaired population. It will also determine the PK paramenters of the drug using a single oral administration of 500 mg. The metabolites of firibastat (EC33 and QGC515) will be compared between impaired and healthy subjects.

Development Pipeline

Quantum's pipleine consists of one drug with various formulations pursuing multiple indications. The drug is being investigated in difficult-to-treat and resistant hypertension, heart failure, renal failure also in once per day formulations. Firibastat is currently in one Phase III trial for hypertension, one Phase II trial for heart failure and Phase I trials for QD formulation hypertension and renal failure.

Exhibit XVIII - Quantum Development Pipeline



Partners and Collaborators

Biolab Sanus Pharmaceuticals is one of the five largest pharmaceutical companies in Brazil and the region's leader in cardiology and arterial hypertension. The company operates four pharmaceutical production facilities (plants) in Jandira, Taboão da Serra, Bragança Paulista, and Rio de Janeiro. Together, these facilities manufacture over 100

[66] Source: Quantum Corporate Presentation, June 2020.

million units of product per year. In addition, the company has research and development facilities in Itapecerica da Serra and Mississauga, Ontario. It has one distribution center in Extrema and headquarters in São Paulo. Across the company, there are 3,200 employees, and the sales team alone consists of 1,400 representatives. The company features a portfolio with over 100 products, substantial investment in research and development and commitment to over 50 international partnerships.

Biolab Pharma was founded in 1997 with the acquisition of their Taboão da Serra plant, and they began by producing four drugs, Vasopril, Quinoflox, Lipless and Cilvular. Through the 1990s, they expanded their portfolio to include new drugs, open their Itapecerica da Serra R&D center, and merge with Sanus Farmacêutica. In the 2000s, Biolab continued adding products to its portfolio, launching several innovative products, expanded into dermo-cosmetics, and acquired its Jandira production facility. Finally, the 2010s marked a period of considerable growth for Biolab; the company continued to launch innovative products, its portfolio growing to over 100 products and its salesforce growing to over 1000 representatives; the company acquired laboratories and production facilities, opened its distribution center in Extrema, and its second R&D center in Mississauga.[67]

Intellectual Property

Quantum holds a global portfolio of patents and maintains exclusive and worldwide licenses for three patent families owned by Inserm, Centre national de la recherche scientifique (CNRS) and Paris Descartes University. Quantum's rights to patents provide protection for firibastat up to 2031 and are eligible for a five year extension. The company is conducting additional research and development to identify new candidates that may be protected by upcoming patent applications.

Exhibit XIX – Key Quantum Patents

	Patent family 1 (granted)	Patent family 2 (granted)	Patent family 3 (granted)	Patent family 4 (filed)	Patent family 5 (filed)	Patent family 6 (filed)
APPLICANTS	Inserm CNRS (exclusive WW license)	Inserm CNRS Université Paris Descartes (exclusive WW license)	Inserm CNRS Université Paris Descartes (exclusive WW license)	Quantum Genomics	Inserm Quantum Genomics	Quantum Genomics
AREA OF INVENTION	Concept of BAPAI to treat hypertension (active ingredient patent)	QGC001 for the treatment of hypertension and related diseases	QGC006 for the treatment of hypertension and related diseases	QGC001 trihydrate form (current product) for the treatment of hypertension and related diseases	QGC011 for the treatment of hypertension and related diseases	QGC001 L-lysine form for the treatment of hypertension and related diseases
STATUS	Granted	Granted	Granted	International application Granted	International application Granted	International application Granted
EXPIRATION DATE	14/01/2019	16/07/2023 *	06/08/2024 **	07/11/2031*	21/12/2032 *	10/22/2033 *

Corporate Milestones

Quantum is conducting multiple clinical trials for multiple cardiovascular indications. Below we list key milestones that have occurred in the last year and anticipated future events.

- First patient enrolled in Phase III FRESH study – July 2Q:20
- Final results of PK study in firibastat renal patients – 3Q:20
- Final results of PK study with firibastat table formulation – 3Q:20
- Completion of Phase IIb QUORUM (heart failure) study recruitment – 4Q:20
- Bridging PK/PD study for 1x/day in hypertension – 1H:21
- Pivotal Phase III efficacy and long term safety (REFRESH) study – 1Q:21
- Readout from Phase IIb QUORUM study – 1H:21
- Launch Phase III study for heart failure – 2H:21

[67] https://www.biolabfarma.com.br/en/nossa-historia/

- Complete Phase III efficacy (FRESH) study – 2H:22
- New drug application for firibastat – 2023

RISKS

All investments contain an element of risk which reflects the uncertainty of a business and what it will ultimately achieve. Some investments exhibit higher predictability, with current cash flows and established sales. These enterprises will have a lower level of perceived risk while other companies that are developing an undefined, new technology have a much higher level of perceived risk.

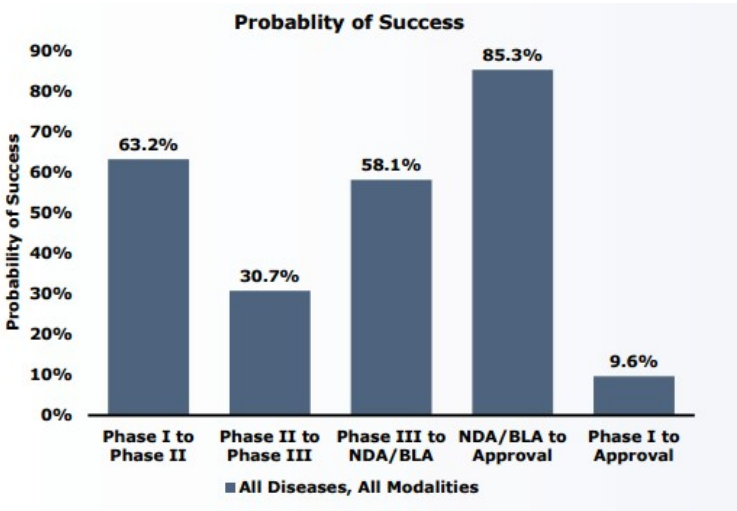
The biotechnology space includes companies at both ends of the spectrum, from mega-cap pharmaceutical powerhouses that have multiple products currently generating revenues, to small operations with a handful of employees conducting pre-clinical studies. Many of the risks faced by the large pharmaceutical companies and smaller biotechnology-focused firms are similar; however, there are some hazards that are particular to smaller companies that have not yet established themselves or their products.

For smaller early-stage companies, investing in drug development is a lengthy process. The timeframe for conducting pre-clinical research to eventually commercializing a drug can take from 12 to 15 years or even longer given market and company-specific conditions. And with, on average, only one in one thousand compounds eventually making it to the market from the preclinical stage, the risks are substantial.

Even if a company has a strong, experienced team that is developing a therapy with a high likelihood of success and a large addressable market, securing funding may be difficult. Access to financing comes and goes in cycles. During periods of improving confidence, capital may be easy to obtain; however, during a liquidity crisis or a period of heightened risk perception, even companies with bright prospects may be in trouble if they are dependent on the financial markets to fund their work. If capital is needed to sustain operations and it is not readily available, the company may be forced to suspend research and development, sell equity at a substantial discount to previous valuations and dilute earlier shareholders. A lack of funding may leave potentially promising therapies without a viable route to progress or force a company to accept onerous terms.

Sponsors must navigate the regulatory approval process in the jurisdiction where they seek to commercialize. Success is uncertain and may take years depending upon the needs and desires of the determining authority. Substantial expense is undertaken to bring a molecule or compound through clinical trials and address all of the regulatory agencies' concerns. Companies that have a long history of research success in drug development, with opinion leaders and experts advocating for the product in the field are important factors that can help mitigate this risk. Previous success with the FDA or other regulatory agencies is another attractive attribute for a sponsor. Some accelerated pathways to approval are available such as those outlined in the Orphan Drug Act and the Breakthrough Therapy designation; however, changes in sentiment or perceived safety for pharmaceuticals drugs could change the regulatory environment to demand a more thorough process and these pathways may be extended or additional requirements may be put in place.

Exhibit XX – Success of Phased Trials and Regulatory Approval[68]



[68]Clinical Development Success Rates 2006-2015. David Thomas, Justin Burns, John Audette, Adam Carroll, Corey Dow-Hygelund, Michael Hay.

Clinical Trial Risk
The future of the company is dependent on the data produced from expensive clinical trials. There are four programs underway in all stages of clinical development. Due to the cost, magnitude and complexity typical of Phase III trials, partners are often sought out to help finance and manage them. Partners may have competing demands which can adversely affect the work they are managing on behalf of Quantum. CROs and subcontractors must abide by strict execution and trial parameters that if violated can jeopardize trial execution or data validity. Subcontractors supervise and execute research, biometric and pharmacovigilance, which are complex tasks. Patient recruitment may be difficult. Though hypertension and even difficult-to-treat and resistant hypertension populations are large and likely to support trial enrollment, there can be challenges related to recruitment. Clinical investigational centers need sufficient capacity and the candidate drug needs to be manufactured according to current Good Manufacturing practices (cGMP) and available to administer. Finally, the data itself needs to achieve statistical significance to justify regulatory approval.

Financial Risk
Pre-revenue biotech firms rely primarily on equity issuance to fund their operations. The duration of drug development is considerable, and can last as long as 12-15 years before a single dose is sold. Funds can be sourced through debt or grants and tax credits; however, these sources may reduce the flexibility of the company and can create difficulties if debt is unable to be repaid.

Liquidity Risk
At year-end 2019, Quantum Genomics held €11.2 million in cash. The company maintains an equity line with Kepler for up to €24 million, of which €22.3 million has been drawn. With a burn rate of ~€10.7 million in 2019, cash reserves of €11.2M and €8 million in new financing from Negma, capacity should be sufficient to sustain the firm through year end. The capital raised through Negma marks the end of guaranteed structured equity financing through Kepler. Any liquidity constraint challenges subordinate programs, including QUORUM, and Quantum's preclinical work, and may force management to delay or abandon preclinical and clinical programs.

COVID-19 Risk
While the recent pandemic has disrupted the operations of companies worldwide, biotech operations are less tied to the macroeconomy, and clinical trials have been relatively insulated. Quantum's guidance has not indicated any material slowing of the company's operations or clinical trials, in fact, Quantum was able to secure funding through Negma despite the current public health crisis. The pandemic continues to disrupt capital markets, and may interfere with Quantum's ability to partner, or raise funds in the future. An outbreak of coronavirus, especially in areas where Quantum's Phase III may be held, may interrupt or delay clinical trials, which can disrupt data collection and add to cost. Quantum announced in an April release that the end-stage renal trial had been halted based on recommendations from health authorities, but that little impact was expected on the FRESH study.

Market Risks
Successful marketing of approved drug candidates relies on the adoption by patients and providers. The approved drug must have convincing clinical trial data and maintain a favorable reputation amongst prescribers. Marketing is expensive and requires the hiring of an experienced sales force and a presence in the marketing area. Marketed products remain under surveillance and any unexpected adverse effects damage the product's reputation. Furthermore, the risk of a competing or superior therapy is a continuous threat. In the case of hypertension, the industry is mature and there are dozens of generic competitors. If firibastat fails to prove superior to existing medicines in difficult-to-treat and resistant hypertension or post-MI HF, demand will evaporate. Insurance coverage is also important. Rapidly obtaining a preferred position on health plan and payor formularies is critical to achieving target penetration rates. Firibastat competes against dozens of generic drugs, including ACE inhibitors, beta blockers, diuretics and many others which seek to disrupt the RAAS similar to firibastat. If health plans and payors cannot agree on appropriate pricing for the drug and the compound fails to offer a significant benefit above standard of care, especially in lower income geographies where hypertension is more prevalent, firibastat may fail.

Licensing Risk
Quantum currently licenses BAPAI technology for the treatment of hypertension, use of firibastat for treatment of hypertension, and use of QC006 for treatment of hypertension. These licenses enable exclusive worldwide use and expire the later of either the last patent expiration or 10 years from the date of initial marketing in a country. Quantum is required to uphold contractual commitments, remain liquid and conduct product studies.

Regulatory Risk
Quantum's revenues are from tax credits designed to incent innovation in France. Quantum is subject to oversight by the French National Agency for Medicines and Health Product Safety (ANSM) and the European Medicines Agency (EMA). As Quantum's candidates proceed through clinical trials and commercialization, these efforts will fall under the regulatory shield of each authority.

Competitors, Peers and Competing Therapies

Quantum Genomics is developing a first-in-class Brain Aminopeptidase A Inhibitor (BAPAI) and conducting clinical trials for difficult-to-treat and resistant hypertension and heart failure. The BAPAI molecule is first in class and no other companies are pursuing it. The drug competes with current and next generation offerings that target heart disease, hypertension and heart failure. The hypertension drug market is mature with multiple classes of drugs, and multiple candidates in each class. There are two novel therapies on the horizon, still in clinical trials, aprocitentan and LHW090; however, aprocitentan is reported to have difficulty enrolling for its Phase III PRECISION trial, and it appears that LHW 090 is a secondary priority for Novartis.

Aprocitentan is an orally administered dual endothelin receptor antagonist targeting resistant hypertension, for which currently Janssen has exclusive ownership of worldwide commercialization rights. While aprocitentan has been around for 30 years, it is now undergoing Phase III trials (PRECISION) which are estimated to complete in 1Q:21. Aprocitentan is a combination ETA and ETB receptor antagonist, acting on the endothelin system that is activated in hypertension, especially in salt and volume dependent variants.[69]

LHW090 is a neprilysin inhibitor also targeting resistant hypertension developed by Novartis that completed Phase II clinical trials in 2Q:17. Neprilysin inhibitors increase bradykinin levels, an important component in the regulation of blood vessel tone and renal function. Novartis management guides to progress after 2022, indicating that this candidate is likely on the back-burner.

Exhibit XXI – Peers and Competitors[70]

Ticker	Company	Price	MktCap (MM)	EV (MM)	Therapeutic Area
AZN	AstraZeneca	$58.68	$153,998	$165,878	Seloken - Beta-1 adrenoceptor antagonist
BAYRY	Bayer Healthcare	$18.15	$67,703	$102,872	Adalat - Calcium channel blocker
DSKYF	Daiichi - Sankyo	$78.49	$50,429	$43,700	Benicar - Angiotensin II receptor 1 (AT1) antagonist
MRK	Merck	$79.41	$200,439	$214,644	Zebeta - β adrenoceptor antagonist, Cozaar - AT1 antagonist
JNJ	Janssen	$149.60	$394,135	$401,504	Aprocitentan
NVS	Novartis	$88.01	$201,428	$221,945	Diovan & Exforge: A2 receptor blocker/dihydropyridine: CCB
PFE	Pfizer	$36.50	$202,751	$228,699	Norvasc - Calcium channel blocker
SNY	Sanofi	$53.77	$134,648	$134,648	Avapro - Angiotensin II receptor blocker
TAK	Takeda	$17.76	$55,993	$91,441	Azilva - Angiotensin II receptor 1 (AT1) antagonist
Private	Boehringer Ingelheim				Micardis - Angiotensin II receptor 1 (AT1) antagonist
Private	Laboratoires Servier				Hypertension, various pathways: ACE, KCNE1, Thiazide
Private	Menarini				Bystolic - Beta blocker
ALQGC	Quantum Genomics	€ 2.55	€ 52,275	€ 41,111	Hypertension & heart failure. BAPAI firibastat

[69] https://www.idorsia.com/documents/com/fact-sheets-presentations/aprocitentan-investor-webcast.pdf
[70] Price and market capitalization data is as of July 20, 2020.

MANAGEMENT PROFILES

Lionel Ségard, Founder and Chairman

Mr. Ségard was the former CEO of Inserm-Transfert, subsidiary of INSERM (French National Institute for Health and Medical Research). He was also founder and former president of Inserm Transfert Initiative, a seed fund dedicated to healthcare innovative emerging companies. Other roles include founder of the Strategic Council for Innovation where he held the position of secretary general from 2003 to 2005. The Council's goal was to boost French efforts in the field of research and high technologies and include key figures from France's science, industry and financial communities. Mr. Ségard is a biochemist by training and received his degree from the University of South Paris, Orsay.

Jean-Philippe Milon, Chief Executive Officer

Dr. Milon has held several management positions at Bayer HealthCare, and was a member of the Worldwide Executive Committee as head of Global Business Development, Licensing, Mergers & Acquisitions. Previously Dr. Milon was head of the cardiovascular business at Sandoz. He has more than 30 years of experience in Healthcare predominantly focused on the Pharmaceutical Industry and was appointed to Quantum's board in June 2019. He was appointed CEO of Quantum Genomics in April 2018. Dr. Milon received his Doctorate in Pharmacy from the University Paris XI, and holds an MBA from ESCP Europe Campus Paris.

Benoît Gueugnon, Chief Financial Officer

Mr. Gueugnon started with Quantum in July of 2018 and was previously Head of Financial Control at Quantum Genomics. He was a former Senior Financial Auditor at KPMG Paris. Graduated from the Normandie's School of Management and holder of a Master II Audit & Corporate Finance.

Fabrice Balavoine, Vice President, Research and Development

Dr. Balavoine has 20 years of experience in Drug Discovery and Drug Development. He participated in the development of several drug candidates (new chemical entities, peptides and recombinant proteins) that reached clinical stages in different therapeutic areas. Ph.D. in Organic Chemistry from the University Paris-Sud, Master of Science from Ecole Supérieure de Physique et de Chimie Industrielle of Paris (ESPCI) and Executive MBA from the ESSEC & Mannheim Business School.

Bruno Besse, Chief Medical Officer

Dr. Besse has more than 20 years of experience in the pharmaceutical industry, having held several positions in R&D and medical affairs at Aventis and Bristol-Myers-Squibb. His positions were held in the field of cardiology and thrombosis. In the past Dr. Besse was Head-Medical Affairs at Crossject SA, Principal at Aventis Pharma SA and Principal at Boehringer Mannheim. Dr. Besse holds an MD from Paris-Sud University and completed his undergraduate degree at INSEAD. Dr. Besse joined Quantum in March 2017, and has served the company for almost three and a half years.

Financial and Operational Results

Quantum's 2019 year began with the appointment of a steering committee in anticipation for its Phase III pivotal trial in resistant hypertension. The steering committee is composed of Dr. Keith Ferdinand, Georges Bakris, William B. White and Jacques Blacher. Dr. Ferdinand, Principal Investigator for Quantum's NEW-HOPE Study, presented at the first annual Masters of Cardiology conference. He highlighted results from the Phase IIb trial of firibastat, confirming excellent short-term results and emphasizing the inclusion of underrepresented minorities in the trial population. Also in January, Quantum provided guidance on a Corporate Action Plan for 2019, the development of controlled-release tablets for once-daily administration, the launch of QUORUM, and partnership discussion with laboratories as a result of NEW-HOPE trial success.

Two journal articles were published in February: "Specific Inhibition of Brain Angiotensin III Formation as a New Strategy for Prevention of Heart Failure After Myocardial Infarction," in the *Journal of Cardiovascular Pharmacology*, and "Brain renin-angiotensin system blockade with orally active aminopeptidase A inhibitor prevents cardiac dysfunction after myocardial infarction in mice," in the *Journal of Molecular and Cellular Cardiology*. February ended with the announcement that Quantum had completed enrollment for its PK, safety study of modified release firibastat tablets.

On March 20th, Quantum announced positive results from preclinical *in vivo* studies on firibastat, confirming that the drug did not induce toxicity. Quantum closed out March reporting 2018 annual financial results.

In mid-April, Quantum received the first of its regulatory approvals from the French authority to initiate Phase IIb QUORUM study of firibastat in heart failure, a study to be conducted in seven European countries. At the end of April, Quantum disclosed the publication of Phase IIb NEW-HOPE study results in the journal *Circulation*, entitled "Efficacy and Safety of Firibastat, a First-in-Class Brain Aminopeptidase A Inhibitor, in Hypertensive Overweight Patients of Multiple Ethnic Origins: A Phase 2, Open-Label, Multicenter, Dose-Titrating Study." The results indicated that firibastat was effective at decreasing blood pressure in a high-risk, diverse population with reduced response to RAS blockers, supporting further vetting of the compound in this population.

Quantum published another article in *Hypertension* in May of 2019. The article, "NI956/QGC006, a Potent Orally Active, Brain-Penetrating Aminopeptidase A Inhibitor for Treating Hypertension," reported antihypertensive efficacy of QGC006, a compound similar to firibastat but with 10X potency, in DOCA-salt rats, a model used to simulate salt-sensitive hypertension.

In the month of June, Quantum enrolled its first patient in QUORUM Phase IIb study of firibastat in heart failure, selected a formulation from its 1QG3 trial, held its Annual General Meeting and reported the resignation of Jean-Paul Kress from and appointment of Jean-Philippe Milon to the board. The formulation selected in the 1QG3 study is a controlled-release tablet that will enable patients to reduce their intake frequency to once-daily. Jean-Paul Kress' resignation was prompted by his appointment as CEO of MorphoSys.

September 2019 featured the announcement of positive FDA feedback on Quantum's design for its Phase III study of firibastat in resistant hypertension, including parameters for enrollment, screening and dosing. The study would build on the successfully completed Phase IIb study. In mid-September, Quantum launched the study of firibastat in patients with renal failure, a common comorbidity with hypertension. In October, Quantum reported 1H:19 financial results and entered into exclusive negotiations with Biolab Sanus Pharmaceutical. An agreement was signed which provided an exclusive licensing and collaboration agreement to develop and commercialize firibastat in Latin America. In mid-December, Quantum initiated its pivotal Phase III FRESH trials in resistant hypertension.

2020 began with the appointment of Benoît Gueugnon as Vice President of Finance in January, succeeding Marc Karako who left the company. At the end of March, as the coronavirus pandemic began to weigh heavily on the world economy, Quantum reported 2019 fiscal year results and announced new financing through Negma Group for up to €8 million, marking the end of guaranteed structured equity financing from Kepler Cheuvreux. The new financing arrangement can be renewed twice, providing up to €24 million.

The most recent operational updates include the efforts to protect trial participants' safety through the temporary halt of the renal failure trial. During the delay, the company conducted an interim analysis of accumulated data and reported it on May 6th, 2020. Participants that were enrolled prior to the cutoff are attending follow-up visits remotely when possible with treatments shipped to patients' homes for dosing. To prevent a slowdown in patient

enrollment, Quantum is currently identifying additional trial sites in new countries. The FRESH trial enrolled its first patient in July 2020 and the pandemic is not expected to impact enrollment or anticipated timeline.

Analysis of interim results from end-stage renal failure (ESRD) patients showed that firibastat was well-tolerated and no adverse event was observed. Due to the condition of the liver in these patients, the drug is eliminated from the system at a slower rate but this did not increase peak concentration in the subjects. Preliminary conclusions hypothesize that a dose adjustment could allow the use of firibastat in patients with chronic renal failure.

Annual financial results were reported March 26, 2020, for fiscal year ending December 31, 2019. Revenue for the year amounted to €361,135 compared to €71,261 in 2018, which primarily consisted of depreciation writebacks, provisions, transferred charges and other income. Expenses totaled €11.1 million, versus €13.7 million the prior year, mainly due to fewer raw material purchases, a decrease in R&D and lower taxes and depreciation, offset by an increase in inventory, higher wages and a rise in social security charges. Including exceptional income and expenses, net loss for the firm for the year was €9.1 million vs €12 million in the comparable period. Research tax credits were €1.5 million for 2019. Cash balance at the end of 2019 totaled €11.2 million versus €14.8 million at the end of 2018. Following the end of the reporting period, Quantum entered into a loan agreement with Negma Group Ltd. to provide the company up to €24 million. The agreement provided €8 million to Quantum and the issuance of five million warrants to Negma group at the end of March 2020. The relationship with Negma concludes the guaranteed structured equity financing from Kepler Cheuvreux. The loan will limit dilution and provide the funding required to advance research and development efforts.

VALUATION

Quantum's lead candidate, firibastat, is the first candidate in the BAPAI class and is being developed for indications in difficult to treat and resistant HTN and post-MI HF. The drug works by blocking the APA from converting A2 into A3 in the brain thereby activating its three-pronged mechanism of action. Clinical trials are in advanced stages with HTN in Phase III and post-MI HF in Phase IIb trials. Assuming research advances as planned and studies meet designated endpoints, regulatory submission is anticipated in 2023 for HTN and in 2025 for post-MI HF. After an estimated year under consideration by the regulatory authorities in the US, Europe and select Latin American countries, we see a 2024 and 2026 launch in HTN and post-MI HF.

Our estimates for revenues over the 2020 – 2022 period reflect upfront payments from Biolab Sanus, reimbursements from Biolab Sanus for part of the HTN trial cost and subsidy research tax credits from the French government.

HTN is estimated to affect over a billion individuals worldwide and over 100 million in the United States, over 85 million in western Europe and as many as 110 million in the largest Latin American countries.[71] Of this group, we estimate 12% of the HTN population does not have it under control[72] which is the target firibastat population. First sales are anticipated to begin in 2024 with a first year penetration of 0.25% into the near 13 million addressable population in the US. This is expected to rise to 1.25% by 2027 and then drop to 0.5% by 2032 following end of patent protection in the US. We expect a similar penetration profile in the top five EU countries addressable population of near 10 million; however, in Europe penetration remains at 1.25% until 2034 due to additional expected exclusivity in this region. Latin America is also expected to see first sales in 2024, but will see a slightly lower penetration rate into its ~14 million addressable population. Year one penetration is forecast to be 0.15% rising to 1.2% by 2027 where it will remain until 2031. In 2032 and beyond, penetration drops to 0.5%. Net realized revenues are expected to be $6,750 for a year of treatment in the US in the first year of commercialization. Pricing in Europe is forecast at half of US levels and Latin America will be just over 30% of US levels. Drug price inflation is 3%. We assume that Quantum will find a partner to commercialize firibastat in the US and Europe and will receive the normal package of upfront, milestone and royalty payments. We represent the totality in value of this package in a 30% royalty.

HF affects about 6.5 million Americans and about a third of that group falls into the post-MI HF group which is about 2.1 million Americans. In Europe, prevalence is from 1-2%[73] and an estimated 3.9 million individuals in the top five European countries suffer HF and we estimate about a third of this group, or 1.7 million, are in the post-MI HF group. While data on this condition is scarce for Latin America, we estimate that about 2.1 million individuals are in the post-MI HF category in Brazil and Mexico. We see Quantum completing their pivotal trials for post-MI HF in late 2024 followed by a submission to the relevant regulatory authorities. First sales are expected to begin in 2026. We anticipate a 2% penetration in year one rising to 8% penetration by year three, assuming a superior profile for firibastat compared with other therapies. We anticipate sales levels will drop precipitously in the US and Latin America in 2032 but continue at 10% penetration in Europe until 2035. Our assumptions call for a similar arrangement between Quantum and Biolab for post-MI HF as they have for HTN. Cost of treatment will match that used for the HTN indication and also inflate at 3% *per annum*. Royalties of 30% are anticipated

We adjust our forecasts by a probability of success rate for each indication. We apply a 50% chance of ultimate commercialization for firibastat in HTN and a 15% chance of success for commercialization in post-MI HF. As of year-end 2019, net operating losses (NOLs) were €48 million and we expect them to reach near €100 million as first sales begin. We will use the NOL to offset taxes and after it is exhausted, cash taxes of 33% will be levied. Our model reflects exercised warrant shares (0.6 million) and additional issued shares (22.0 million) to reflect further capital raises to fund research and development. Our valuation approach employs a discounted cash flow model. Assumptions include a discount rate of 15%.

Based on the assumptions identified in our discounted cash flow model, we generate a current valuation of €13.00 per share.

[71] There are broad ranges of estimates for the prevalence of HTN throughout the globe that range from 25% to almost 50% as discussed in our prevalence section. We assume 1/3 of the population in each of the three regions that we estimate is hypertensive.
[72] There are broad ranges of estimates for the proportion of HTN patients that range from 9% to almost 50%. We take a conservative approach and use 12% (Persell).
[73] Cowie, The Global Burden of Heart Failure. National Heart & Lung Institute, Imperial College London.

CONCLUSION

Quantum Genomics has introduced a new molecule into the clinic known as a BAPAI which is able to act on brain RAAS and prevent the conversion of A2 to A3. This inhibition has a three pronged effect on the angiotensinergic pathway decreasing vasopressin secretion, activating the Baroreflex arch and decreasing sympathetic nerve activity which act in concert to lower blood pressure. This pathway is especially critical for hypertensive patients in resistant and hard-to-treat categories that are not responding to available therapies. The drug has also demonstrated an improvement in ejection fraction in post-MI HF animal models compared to standard of care.

Quantum's candidate is the BAPAI firibastat which is being developed in two late stage indications. The most advanced is in hard-to-treat and resistant HTN where firibastat is participating in a pivotal Phase III efficacy trial (FRESH) and slated to be in a pivotal Phase III efficacy and safety trial (REFRESH) next year. Based on management guidance, firibastat should be complete with clinical trials and ready for filing with regulatory authorities in 2023 for HTN. The second most advanced indication is in post-MI HF which is being investigated in the Phase IIb QUORUM study.

The populations that Quantum is pursuing are large. There are over a billion persons with HTN around the globe and a large proportion of those do not have it under control. Based on our literature review, post-MI HF has up to 50 million persons that are afflicted. Sales of firibastat in these two indications will primarily be in the US, top five European countries and Latin America. We anticipate partners will commercialize in the US and EU and pay an upfront, milestone and royalty payment to Quantum. An agreement with Biolab has already been signed for commercialization of firibastat for HTN in Latin America, which we anticipate will be expanded to include the indication in post-MI HF. We assume all partnerships will pay upfront, milestones and royalties represented by a 30% royalty.

Firibastat has shown safety and efficacy in Phase II trials, reducing blood pressure by an average of 9.5 mm Hg, with no statistically significant difference in those of African descent or obese patients, which are more commonly hard to treat or resistant populations. Safety was favorable with only 14% of patients reporting a treatment emergent adverse event, mostly consisting of headache and skin reaction. The Phase IIb trial for post-MI HF is underway and expected to report topline results in 2H:20.

We anticipate that Quantum will be able to add sufficient capital through equity issuance, relationships with Negma Group, upfront payments from Biolab Sanus and government funding to advance both of its indications to approval. With favorable results from the trials and a successful new drug application, we see a 2024 launch of firibastat for difficult-to-treat and resistant HTN and a 2026 launch of firibastat in post-MI HF. We apply a 50% probability of commercialization for the HTN indication and a 15% probability of commercialization for the post-MI HF indication, recognizing that failure could occur in the trial outcome.

Key reasons to own Quantum Genomics shares:

- **First in class, Phase III asset to address an unmet need in difficult-to-treat and resistant HTN**
- **First in class, Phase II asset to address post-MI HF**
- **Sizeable target patient populations with no innovative competitors**
- **Patent protection and global licensing of BAPAI technology**
- **Strong pre-clinical evidence *in vivo***
- **Healthy cash position, runway for approximately one year**
    - **Closed €8 million and access to additional €16 million financing from Negma**

Based on our analysis of firibastat and the clinical trial data generated to date, we anticipate a favorable outcome from active and future trials in HTN and post-MI HF. Our valuation work takes into account commercialization of firibastat in the United States, top five EU and Latin America for both indications. The opportunity for firibastat extends beyond the indicated geographies and indications. Our valuation will reflect other opportunities as they become apparent and there is a reasonable assumption they will move forward. As we initate on Quantum Genomics, Corp, our analysis and forecasts generate a valuation of €13.00 per share.

PROJECTED FINANCIALS

Quantum Genomics Corp. - Income Statement

Quantum Genomics Corp.	1HA	2HA	2019 A	1HE	2HE	2020 E	2021 E	2022 E
Total Revenues (€)	€ 285	€ 76	€ 361	€ 0	€ 10,000	€ 10,000	€ 12,000	€ 15,000
YOY Growth	333%	1304%	407%	-100%	12997%	2669%	20%	25%
Raw Materials & Supplies	€ 0	€ 89	€ 89	€ 45	€ 45	€ 90	€ 90	€ 90
Other Purchases & Expenses	€ 3,946	€ 3,853	€ 7,799	€ 6,050	€ 6,050	€ 12,100	€ 17,500	€ 18,000
Taxes	€ 9	€ 2	€ 10	€ 5	€ 5	€ 10	€ 20	€ 20
Wages & Salaries	€ 916	€ 814	€ 1,730	€ 865	€ 865	€ 1,730	€ 2,000	€ 2,100
Social Security Charges	€ 660	€ 385	€ 1,045	€ 500	€ 500	€ 1,000	€ 1,200	€ 1,250
Depreciation & Provisions	€ 7	€ 299	€ 306	€ 5	€ 300	€ 305	€ 306	€ 310
Other Expenses	€ 71	€ 69	€ 140	€ 60	€ 60	€ 120	€ 140	€ 150
Income from operations	(€ 5,324)	(€ 5,436)	(€ 10,760)	(€ 7,530)	€ 2,175	(€ 5,355)	(€ 9,256)	(€ 6,920)
Operating Margin	-1870%	-7119%	-2979%		22%	-54%	-77%	-46%
Financial Income	€ 6	€ 5	€ 11	€ 4	€ 2	€ 6	€ 6	€ 6
Financial Expenses	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
Exceptional Items	€ 304	(€ 181)	€ 123	€ 0	€ 0	€ 0	€ 0	€ 0
Pre-Tax Income	(€ 5,014)	(€ 5,611)	(€ 10,626)	(€ 7,526)	€ 2,177	(€ 5,349)	(€ 9,250)	(€ 6,914)
Provision for Income Tax	(€ 886)	(€ 662)	(€ 1,547)	(€ 1,129)	€ 327	(€ 802)	(€ 1,388)	(€ 1,037)
Tax Rate	17.7%	11.8%	14.6%	15.0%	15.0%	15.0%	15.0%	15.0%
Net Income	(€ 4,129)	(€ 4,950)	(€ 9,078)	(€ 6,397)	€ 1,850	(€ 4,547)	(€ 7,863)	(€ 5,877)
Reported EPS	(€ 0.24)	(€ 0.27)	(€ 0.50)	(€ 0.31)	€ 0.08	(€ 0.20)	(€ 0.29)	(€ 0.20)
Basic Shares Outstanding	16,886	18,065	18,065	20,500	23,000	23,000	27,000	30,000

Source: Company Filing // Zacks Investment Research, Inc. Estimates

HISTORICAL STOCK PRICE

Quantum Genomics Corp. (ALQGC) – Share Price Chart (€)[74]

[74] Source: barchart.com

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