A preliminary prospectus containing important information relating to the securities described in this document has been filed with the securities regulatory authorities in each of the provinces of Canada, except Quebec. A copy of the preliminary prospectus, and any amendment, is required to be delivered with this document. The preliminary prospectus is still subject to completion. There will not be any sale or any acceptance of an offer to buy the securities until a receipt for the final prospectus has been issued. This document does not provide full disclosure of all material facts relating to the securities offered. Investors should read the preliminary prospectus, the final prospectus and any amendment for disclosure of those facts, especially risk factors relating to the securities offered, before making an investment decision.

### ReviveThera.com



**Investor Presentation – November 3, 2014** 



#### **Cautionary Note Regarding Forward-Looking Statements**

This presentation, the preliminary prospectus ("Prospectus") of Revive Therapeutics Ltd. ("Revive") dated November 3, 2014, and the documents incorporated therein by reference contain certain forward-looking information and forward-looking statements, as defined in applicable securities laws (collectively referred to herein as "forward-looking statements"). These statements relate to future events or to the future performance of Revive. All statements, other than statements of historical fact, are forward-looking statements. Often, but not always, forward-looking statements can be identified by the use of words such as "plans", "expects", "is expected", "budget", "scheduled", "estimates", "continues", "forecasts", "projects", "predicts", "intends", "anticipates" or "believes", or variations of, or the negatives of, such words and phrases, or state that certain actions, events or results "may", "could", "would", "should", "might" or "will" be taken, occur or be achieved. Forward-looking information is based on the opinions and estimates of management as at the date the information is given, and is based on information available to management at such time. Forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results to differ materially from those anticipated in such forward-looking statements. The forward-looking statements herein, in the Prospectus and the documents incorporated therein by reference speak only as of the date of such documents or as of the date specified in such statements.

Significant forward-looking statements contained herein, in the Prospectus, and in the documents incorporated herein or therein by reference include: (a) the early stage of development, particularly the inherent risks and uncertainties associated with (i) developing new drug candidates, (ii) demonstrating the safety and efficacy of these drug candidates in clinical trials, and (iii) obtaining regulatory approval to commercialize these drug candidates; (b) the Company's ability to obtain the substantial capital it requires to fund research and operations; (c) factors affecting clinical trials and regulatory approval process of the Company's drug candidates; (d) the Company's ability to find and enter into agreements with potential partners to bring viable drug candidates to commercialization; (e) the Company's ability to obtain and protect the Company's intellectual property rights and not infringe on the intellectual property rights of others; (f) the Company's ability to source markets which have demand for its products and successfully supply those markets in order to generate sales; (g) the proceeds received from the Offering will be expended to achieve the Company's objectives as budgeted in the Prospectus. The material assumptions used to develop such forward-looking statements include: (a) financing will be available for development of new drug candidates and conducting clinical studies, the actual results of the clinical trials will be favourable, development costs will not exceed Revive's expectations, the Company will be able to retain and attract skilled staff, the Company will be able to recruit suitable patients for clinical trials, all requisite regulatory and governmental approvals to commercialize the drug candidates will be received on a timely basis upon terms acceptable to Revive, and applicable economic conditions are favourable to Revive; (b) financing will be available for Revive's research and operations and the results thereof will be favourable; debt and equity markets, exchange and interest rates and other applicable economic conditions are favourable to Revive; (c) actual costs of clinical and regulatory processes will be consistent with the Company's current expectations; the Company will be able to retain and attract skilled staff; the Company will be able to recruit suitable patients for clinical trials; the Company will be able to complete clinical studies on a timely basis with favourable results; all applicable regulatory and governmental approvals for drug candidates will be received on a timely basis with terms acceptable to Revive; debt and equity markets, exchange and interest rates and other applicable economic and political conditions are favourable to Revive; there will be a ready market for the drug candidates; (d) Revive will be able to find a suitable partner and enter into agreements to bring drug candidates to market within a reasonable time frame and on favourable terms; the costs of entering into a partnership will be consistent with Revive's expectations; partners will provide necessary financing and expertise to bring drug candidates to market successfully and profitably; (e) Patents and other intellectual property rights will be obtained for viable drug candidates; patents and other intellectual property rights obtained will not infringe on others; (f) the anticipated markets for the Company's potential products and technologies will continue to exist and expand. The Company's products will be commercially viable and it will successfully compete with other research teams who are also examining potential therapeutics with regards to respiratory and breathing disorders, gout, Rett Syndrome, rare diseases, cognitive dysfunction, and central nervous system disorders; and (g) the amounts actually expended for the purposes described in this Prospectus will not vary and the objectives of the Company will be met.



Material risk factors that could cause actual results to differ materially from the forward looking statements include: (a) Availability of financing in the amount and time frame needed for the development and clinical trials may not be favourable; increases in costs; the Company's ability to retain and attract skilled staff; the Company's ability to recruit suitable patients for clinical trials; timely and favourable regulatory and governmental compliance. acceptances and approvals; interest rate and exchange rate fluctuations; changes in economic conditions; (b) changes in debt and equity markets; timing and availability of external financing on acceptable terms; increases in cost of research and operations; interest rate and exchange rate fluctuations; adverse changes in economic conditions; (c) Revive's drug candidates may require time-consuming and costly preclinical and clinical testing and regulatory approvals before commercialization; the Company's ability to retain and attract skilled staff; the Company's ability to recruit suitable patients for clinical trials; adverse changes in regulatory and governmental processes; interest rate and exchange rate fluctuations; changes in economic and political conditions; the Company will not be adversely affected by market competition; (d) Revive will not be able to find a partner and / or enter into agreements within a reasonable time frame; if the Company enters into agreements, these agreements may not be on favourable terms to Revive; costs of entering into agreements may be excessive; potential partners will not have the necessary financing or expertise to bring drug candidates to market successfully or profitably; (e) Revive will not be able to obtain appropriate patents and other intellectual property rights for viable drug candidates; patents and other intellectual property rights obtained will be contested by third parties; no proof that acquiring a patent will make the product more competitive; (f) The anticipated market for the Company's potential products and technologies will not continue to exist and expand for a variety of reasons, including competition from other products and the degree of commercial viability of the potential product, and (g) the amounts actually expended for the purposes described in this Prospectus and the objectives achieved will vary significantly depending on, among other things, the progress of the Company's research and development programs, regulatory filings, technological advances, activities in anticipation of the commercialization of the Company's products, the terms of any collaborative or licensing arrangements and the status of competitive products. Inherent in forward-looking statements are risks, uncertainties and other factors beyond the Company's ability to predict or control. Please also make reference to those risk factors referenced in the "Risk Factors" section in the Prospectus. Readers are cautioned that the above chart does not contain an exhaustive list of the factors or assumptions that may affect the forward-looking statements, and that the assumptions underlying such statements may prove to be incorrect. Actual results and developments are likely to differ, and may differ materially, from those expressed or implied by the forward-looking statements contained herein, in the Prospectus, and the documents incorporated therein by reference. Forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause the Company's actual results, performance or achievements to be materially different from any of its future results, performance or achievements expressed or implied by forward-looking statements. The forward-looking statements contained herein, in the Prospectus, and the documents incorporated therein by reference, are expressly qualified by this cautionary statement. Accordingly, readers should not place undue reliance on forward-looking statements. The Company undertakes no obligation to update publicly or otherwise revise any forward-looking statements whether as a result of new information or future events or otherwise, except as may be required by law. If the Company does update one or more forward-looking statements, no inference should be drawn that it will make additional updates with respect to those or other forward-looking statements, unless required by law.

#### **Use of Market and Industry Data**

This presentation includes market and industry data that has been obtained from third party sources, including industry publications, as well as industry data prepared by the Company's management on the basis of its knowledge of and experience in the industry in which the Company operates (including management's estimates and assumptions relating to the industry based on that knowledge). Management's knowledge of the industry has been developed through its experience and lengthy participation in the industry. Management believes that its industry data is accurate and that its estimates and assumptions are reasonable, but there is no assurance as to the accuracy or completeness of this data. Third party sources generally state that the information contained therein has been obtained from sources believed to be reliable, but there is no assurance as to the accuracy or completeness of included information. Although believed to be reliable, the Company's management has not independently verified any of the data from third party sources referred to in this presentation or ascertained the underlying economic assumptions relied upon by such sources.

# **Investment Highlights**

- Addressing large markets with unmet medical needs
  - Gout and Rett Syndrome (rare disease)
  - Repurposing existing and proven drugs/orphan drugs focus
- De-risked later-stage clinical assets
  - Known safety (clinical/market use)
  - Patent protection to 2030's
- Secured Pharma development partner for gout
  - Market validation and reduced development risk/cost
- Clear path to commercialization
  - Driven by phase II data and partnerships
- Significant near-term catalysts unlocking value

# **About Revive**

- Clinical-stage company founded in 2012
- Drug repurposing with faster-to-market potential
  - Lower development risk, cost, known safety and manufacturing
  - Example: Viagra<sup>®</sup> (Pfizer) and Thalomid<sup>®</sup> (Celgene)
- Focus on repurposing non-U.S. drugs
  - Advantages of a new drug (i.e. market exclusivity)
- Validate assets in Phase II and seek Pharma deal
- Experienced team and board of directors



# **Team Overview**

#### Management

- Fabio Chianelli, CEO, Director
  - Titan Medical (TSXV: TMD)
  - Generex Biotechnology Corp.
- Carmelo Marrelli, CA, CFO
  - Principal of Marrelli Support Services Inc.
- Dr. Bev Incledon, PhD, VP of R&D
  - Eli Lilly Canada, Director of R&D
- Dr. Robert Terkeltaub, MD, Clinical Advisor/PI
  - UCSD Rheumatology Professor
  - Experienced PI in Gout Clinical Trials

### **Board of Directors**

- Craig Leon, Chairman
  - Titan Medical (TSXV: TMD), Chair/CEO
  - Redwood Asset, COO

#### William Jackson, Director

- Atwill Medical Solutions, CEO
- Covalon (TSXV: COV), CFO, COO, Director
- Titan Medical (TSXV: TMD), Director
- Carlo Sansalone, Director
  - Sanscon Construction, President
- Fabio Chianelli, CEO, Director



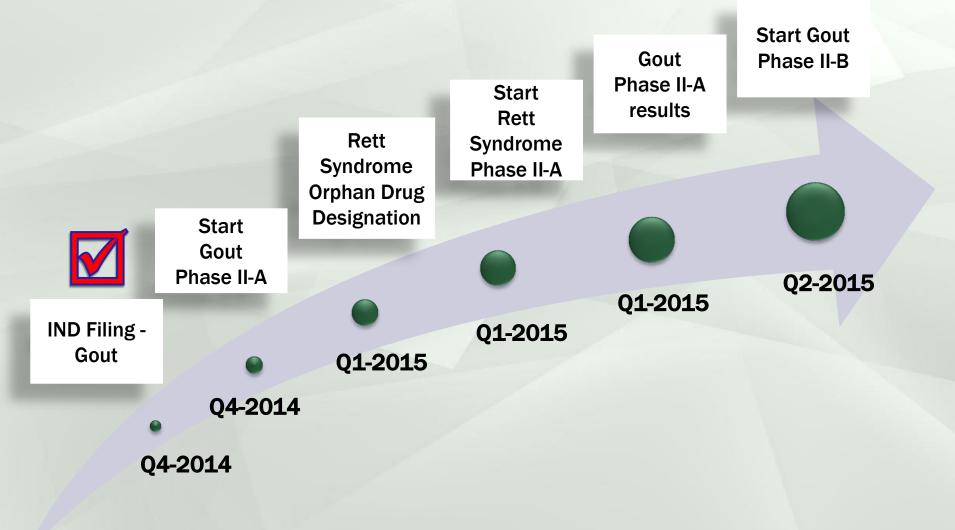
# **Product Pipeline**

De-risked assets, large markets, patent protection 2030's

Product	Indication	Preclinical	Phase I	Phase II-A	Phase II- B/III
REV-002	Gout			Q4/FY	14
REV-003	Rett Syndrome (Rare disease)		Q1/FY20	15	
REV-001	Post-Op Pain (Opioid-induced respiratory depression)	Availat	ble for out-licer	nsing	



## **Near-term Catalysts**





# **Intellectual Property**

#### Gout

- PCT/CA2013/050882 The use of bucillamine in the treatment of gout
- Expires 2033
- Acquired patent assignment from Xenexus Pharma (Xenexus earns 5% from upfront, milestones and royalties that is paid to Revive by Pharma partner)
- Rett Syndrome
  - PCT/GB2013/051213 Treatment of respiratory depression
  - Expires 2033
  - Exclusive world-wide license from Numedicus Ltd

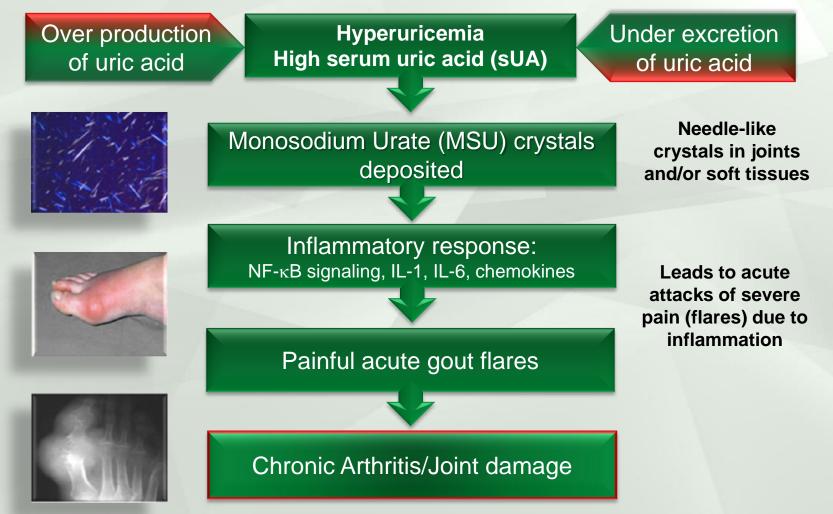


# 1. Gout Opportunity

- Over 8 million adults (~3.9%) in USA with gout and 15 million worldwide with gout (~18 million by 2021)
- Current anti-inflammatory drugs are often contraindicated
- Refractory arthritis increasingly common
- 40%-60% <u>do not</u> reach uric acid lowering target, thus continue to experience acute flares and develop chronic arthritis
- Drug limitations increases healthcare costs, therapy restarts, non-adherence, discontinuations
- Gout prevalence markedly increasing, especially in patients with limited therapy options
- Significant needs for drugs both to control inflammatory arthritis and lower uric acid



# Gout





# **Gout Management Objectives**

Diagnose, Treat and Prevent Acute Gout Flares

Identify, Manage Comorbidities and Causes of Hyperuricemia

Patient Education, Treatment Adherence

Terkeltaub R. Nature Rev Rheumatology, 2010

Rees et al, ARD, 2012

Urate-lowering drugs: Treat to Target of Serum Urate <6 mg/dL <u>At a Minimum</u>



# Pharmacologic Options to **Treat Acute Gouty Inflammation**

#### **First-line options**<sup>1-4</sup> •

- NSAIDs (selective Cox-2 inhibition)
- Systemic glucocorticosteroids
- Oral colchicine (for early in gout flare, lowdose regimen)

### Other options <sup>1-4</sup>

- Intra-articular glucocorticosteroids
- Synthetic ACTH 1,2,5
- **Off-label FDA, approved EMU** 
  - Biologic IL-1 antagonism 1,3,4,6,7

1. \*Terkeltaub RA. N Eng J Med. 2003;349:1647-1655.

- 2. Schlesinger N, et al. Expert Opin Pharmacother. 2009;10:1319-28.
- 3. Terkeltaub R. Nat Rev Rheumatol. 2010;6:30-38.
- 4. Terkeltaub RA, et al. Arthritis Rheum, 2010;62:1060-1068.

ACTH = adrenocorticotropic hormone

1, 2, 5: Schlesinger N. Overview of the management of acute gout and the role of adrenocorticotropic hormone. Drugs. 2008;68(4):407-15.

6: So A, De Smedt T, Revaz S, Tschopp J. A pilot study of IL-1 inhibition by anakinra in acute gout. Arthritis Res Ther. 2007;9(2):R28.

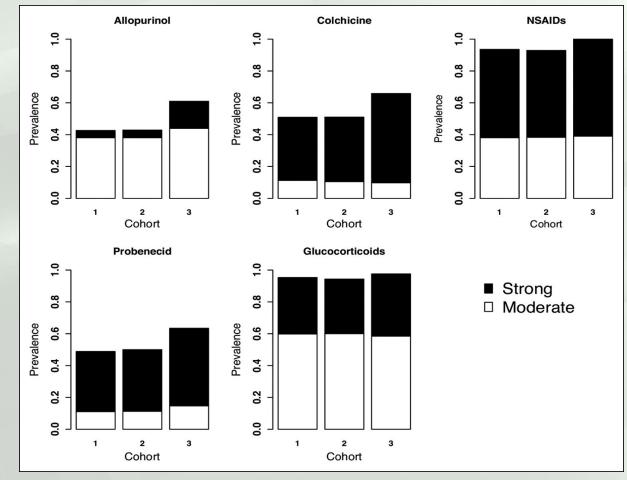
7: Terkeltaub R, Sundy JS, Schumacher HR, Murphy F, Bookbinder S, Biedermann S, Wu R, Mellis S, Radin A. The interleukin 1 inhibitor rilonacept in treatment of chronic gouty arthritis: results of a placebocontrolled, monosequence crossover, non-randomised, single-blind pilot study. Ann Rheum Dis. 2009 Oct;68(10):1613-7.



# Gout and Other Chronic Conditions

- Patients suffering from gout have a high prevalence to show multiple other chronic conditions (Appendix 1) These include:
  - Hypertension (~70-80%)
  - Diabetes Type II (~25-40%)
  - Chronic Kidney Disease (~30-50%)
  - Coronary Artery Disease (~30-40%)
  - Other: GI Tract Disease, Congestive Heart Failure
- Patients with gout harbor multiple comorbidities (Appendix 2)

### Most Gout Patients Harbor Moderate-to-Strong Contraindications to Multiple 1<sup>st</sup>-Line Gout Medications





The American Journal of Medicine, 2011 124, 155-163DOI: (10.1016/j.amjmed.2010.09.012

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# Revive's New Opportunity "REV-002" Indication: Gout

The Drug: Bucillamine (being repurposed from RA to gout)

- Arthritis drug marketed since 1980s in Japan and South Korea
- Promising efficacy in mouse models: lowered inflammation and serum uric acid (Potential dual-acting treatment)

Patent Protected: PCT/CA2013/050882, until 2033

Market Potential: \$1 billion + global sales for new gout drug

<u>Clinical Strategy</u>: Preparing for Phase II-A clinical study in the U.S in Q4/FY14

• Results expected in 1H/FY15

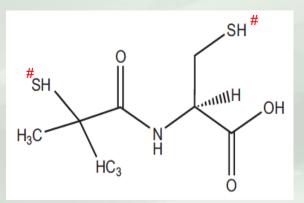


### Bucillamine Anti-Inflammatory Mechanism: Unique versus Current Drugs Used to Treat Gouty Inflammation

- NSAIDs, Colchicine, Corticosteroids
  - Nonselective Therapeutic effects
  - Frequent and potentially serious adverse events, major organ toxicity, and drug interactions
- Bucillamine
  - Dual thiol donor-based inhibitor of inflammation signal transduction (including NF-κB inhibition)
  - Limits multiple cytokine responses central to gouty inflammation (including IL-1, IL-6, TNFalpha, synovial angiogenesis)

## Rationale for Bucillamine in Gout

**Bucillamine** 

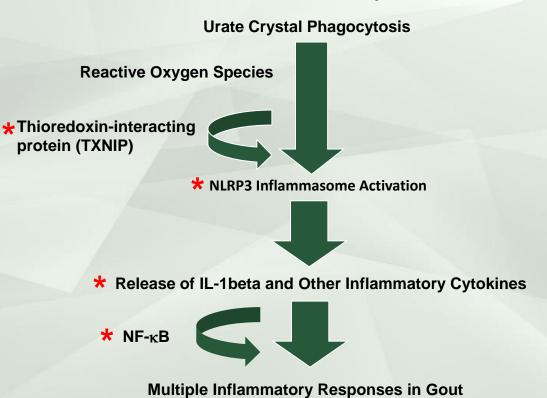


**Bucillamine:** Disease Modifying Anti-Rheumatic Drug With Unique Dual Sulfhydryl Thiol Donor Structure #

Bucillamine Loci of Action in Gouty Inflammation Can Include:

- Thioredoxin-interacting Protein (TXNIP) in NLRP3 Inflammasome Activation
- NF-κB Signaling
- Release and Responses to IL-1 $\beta$  and Other Cytokines Including IL-6 and TNF $\alpha$

#### \*Putative Bucillamine Loci of Inhibitory Effects in Patients with Acute Gouty Arthritis



# Gout Treatment: Bucillamine versus other drugs

	Treatment Effect		More Adverse Events and Drug Interactions In:					
	Flares	Lower Uric Acid	Hyper- tension	Diabetes Type II	CKD	CAD/ HL	CHF	GI Tract Disease
Bucillamine	Yes	Potential*			+/-			
Allopurinol/ Febuxostat	No (+ more early flares)	Yes			+++ (Allopurinol)			
Colchicine	Yes	No			++	++		++
Steroids	Yes	No	+	+++		+	++	+
NSAIDs	Yes	No	++		++++	+++	++++	++++

• Bucillamine, as a repurposed drug, benefits from 20 + years of safety and contraindication data.

• Bucillamine belongs to a different class of drugs and has a different mechanism of action resulting in a potential unique dual-therapeutic action \*based on gout animal studies.

CDK: Chronic Kidney Disease, CAD: Coronary Artery Disease, HL: High Lipids, CHF: Congestive Heart Failure, GI: gastrointestinal 19

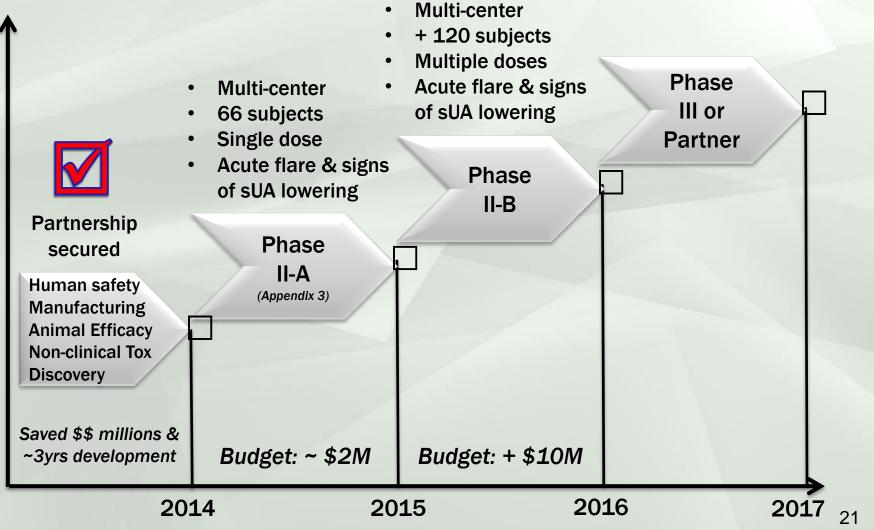
REVIVE
 therapeutics

# **Japanese Pharma Relationship**

### **Gout Partnership Potential**

- Relationship with Japanese Pharma
- Rapidly paves way for commercialization
- Access to clinical, market, manufacturing info, drug supply
- In return, Pharma secured Japan, Korea and Taiwan rights
- Validation of market potential and intellectual property
- Unlocks advantages of a new drug
  - Market exclusivity (i.e. USA and EU)

# **Commercialization Path**



# 2. Rett Syndrome

- Orphan Disease Designation (>200,000 people in US)
  - Rare disease affecting 16,000 in U.S. and 20,000 in EU
  - Experience loss of motor skills, seizures, respiratory dysfunction
  - Girls are mostly affected
- No cure for Rett Syndrome
  - Current therapies focus on symptoms management



# **Revive's New Opportunity**

#### "REV-003" Indication: Rett Syndrome

The Drug: Tianeptine (being repurposed from anti-depressant)

- Anti-depressant drug marketed since 1980s in Europe, Asia and South America
- Encouraging results: Enhanced breathing
- Potential for positive outcomes in behavior, cognition, anti-seizure

Patent Protected: PCT/GB2013/051213, until 2033

Market Potential: \$180-\$360 million on unserved market

Low of 3,000 / max of 6,000 patients at \$60,000 annual cost

Clinical Strategy: Positive animal studies in respiratory rate

- Orphan Drug Designation in Q1/FY15
- Phase II-A study in Europe Q2/FY15



# **Key Financial Information**

Ticker Symbol	RVV (TSX Venture)		
Share Price	\$0.51 (October 31, 2014)		
	18,912,155 common shares		
Capital Structure	775,206 stock options 590,000 @ \$0.66 and 185,206 @ \$0.30		
Market Value	~ \$9,645,200 (October 31, 2014)		
Insider Ownership	59 %		
Cash and cash equivalents	\$1,188,919 (June 30, 2014)		
Monthly Cash burn	~ \$100,000		
Analyst Coverage	Beacon Securities Limited – Doug Cooper, MBA		

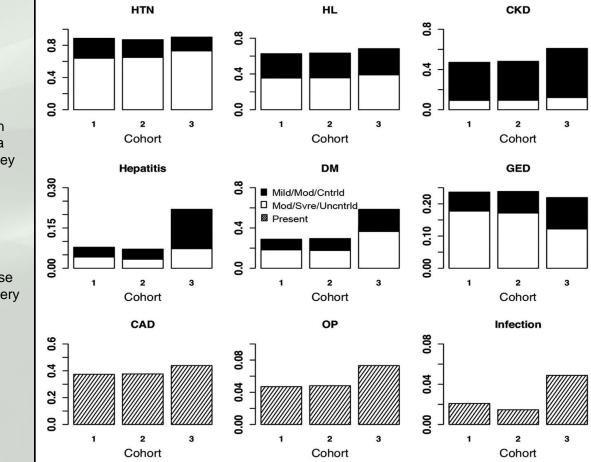


# Appendices

- 1. High Prevalence of Comorbidities in Patients with Gout
- 2. Patients with Gout Harbor Multiple Comorbidities
- 3. Gout Protocol Summary



## 1. High Prevalence of Comorbidities in Patients with Gout



HTN: hypertension

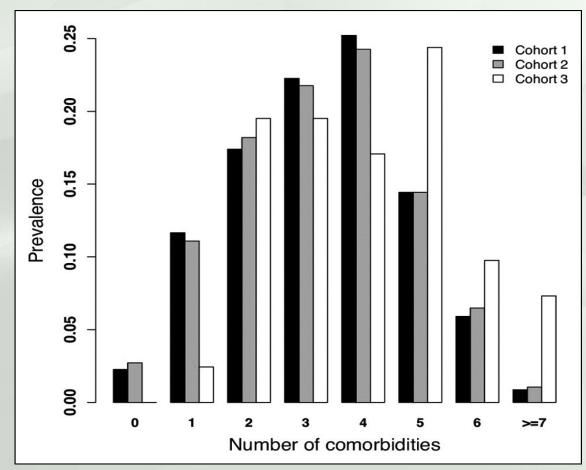
- HL: hyperlipidemia
- CKD: chronic kidney disease
- Hepatitis: chronic hepatitis
- DM: diabetes mellitus
- GED: gastro
   esophageal disease
- CAD: coronary artery disease
- OP: osteoporosis
- Infection: chronic infection

The American Journal of Medicine, 2011 124, 155-163DOI: (10.1016/j.amjmed.2010.09.012

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## 2. Patients with Gout Harbor Multiple Comorbidities





The American Journal of Medicine 2011 124, 155-163DOI: (10.1016/j.amjmed.2010.09.012)

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### 3. Gout Protocol Summary

Title	Bucillamine in Patients with Acute Gout Flares	
Description	Assess the efficacy and safety of bucillamine as compared to colchicine for the treatment of an acute gout flare in patients with moderate to severe gout	
Objectives	Safety of bucillamine in patients with acute gout flare Compare the safety and efficacy of bucillamine vs. active comparator FDA-approved colchicine regimen (1.8 mg over 1 hour)	
Design	Phase II-A, open-label, multicenter parallel group clinical trial designed to compare the safety and efficacy of high and moderate bucillamine and low-dose colchicine treatment in acute gout flare. Eligible patients will be randomized in a 1:1:1 ratio to either Test or Control as follows: Test Arms (Bucillamine high and moderate dose), Control Arm (Colchicine)	
Outcome measures	<ul> <li>Responders [ Time Frame: 72 hours after baseline ]</li> <li>Primary: Responders: ≥ 50% reduction in target joint pain score from baseline at 72 hours without using rescue drug</li> <li>Secondary: Alternative time points, pain metrics, rescue med use</li> <li>Exploratory: Analysis of serum and urine uric acid, and CRP, ESR, IL1beta, IL-6</li> </ul>	

