Volition

NYSE:VNRX

Casting a new light on sepsis management

February 2025

Forward Looking Statements and Disclaimer

Statements in this document may be “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, that concern matters that involve risks and uncertainties that could cause actual results to differ materially from those anticipated or projected in the forward-looking statements. Words such as “expects,” “anticipates,” “intends,” “plans,” “aims,” “targets,” “believes,” “seeks,” “estimates,” “optimizing,” “potential,” “goal,” “suggests,” “could,” “would,” “should,” “may,” “will” and similar expressions identify forward-looking statements. These forward-looking statements relate to, among other topics, Volition's expectations related to the size of the market opportunity, the timing of product launches, the timing and success of clinical studies, the timing, completion, success and delivery of data from such studies, the timing of publications, the effectiveness and availability of Volition’s blood-based diagnostic, prognostic and disease monitoring tests, Volition’s ability to develop and successfully commercialize such test platforms for early detection of cancer and other diseases as well as serving as a diagnostic, prognostic or disease monitoring tool for such diseases, and Volition's success in securing licensing and/or distribution agreements with third parties for its products.Volition’s actual results may differ materially from those indicated in these forward-looking statements due to numerous risks and uncertainties, including, without limitation, results of studies testing the efficacy of its tests. For instance, if Volition fails to develop and commercialize diagnostic or prognostic products, it may be unable to execute its plan of operations. Other risks and uncertainties include Volition’s failure to obtain necessary regulatory clearances or approvals to distribute and market future products; a failure by the marketplace to accept the products in Volition’s development pipeline or any other diagnostic or prognostic products Volition might develop; Volition’s failure to secure adequate intellectual property protection; Volition will face fierce competition and Volition’s intended products may become obsolete due to the highly competitive nature of the diagnostics market and its rapid technological change; downturns in domestic and foreign economies; and other risks identified in Volition’s most recent Annual Report on Form 10-K and Quarterly Reports on Form 10-Q, as well as other documents that Volition files with the Securities and Exchange Commission. These statements are based on current expectations, estimates and projections about Volition’s business based, in part, on assumptions made by management. These statements are not guarantees of future performance and involve risks, uncertainties and assumptions that are difficult to predict. Forward-looking statements are made as of the date of this release, and, except as required by law, Volition does not undertake an obligation to update its forward-looking statements to reflect future events or circumstances.

 Additionally, unless otherwise specified, all references to “$” refer to the legal currency of the United States of America.

Speakers

Mr. Gael Forterre

Chief Commercial Officer

Dr. Andrew Retter

MBBS, MRCP, FRCPath (Haem), DICM, FFICM

Clinical Lead in Critical Care Medicine, ECMO and Thrombosis

Chief Medical Officer at VolitionRx, UK

Investment Highlights

Vet Commercial Progress

- Nu.Q® Vet Cancer test now available in 20 countries
- Sold >110,000 tests and test components Q1-Q3 2024
- Received $23 million in upfront and milestone payments to-date
  - Additional $5 million milestone payment (feline) anticipated 2025
  - Simple, low cost, recurring revenue generating tests performed on standard lab equipment
- **Multiple international partnerships launching**

Human Licensing Progress

- Same business model as Nu.Q® Vet – low capex/low opex, leveraging global base of established diagnostic and liquid biopsy companies
- **Clinical Partnering: multiple near-term licensing opportunities progressing**
- **Direct and Indirect sales of CE marked routine clinical product(s) in Europe as hospitals evaluate for routine clinical use**

Strong IP Worldwide

- 81 patents granted
- 129 pending internationally
- Patent coverage up to 2044

Large Unmet Needs

- **Lung Cancer Screening** – screening, prognostics and MRD represent a $1.8B opportunity
- **Sepsis** – testing and monitoring ICU patients alone is a ~$1B+ opportunity
- **Other addressable markets** include Acute Kidney Injury (AKI), Acute Respiratory Distress Syndrome (ARDS) and use in the Emergency Department **>$10B** opportunity

Derisked R&D and Commercial Strategy: First $1 million Revenue 2024

What sets us apart?

- **Our tests are *simple, low-cost* <u>*accessible*</u> routine blood tests**
  - Platform agnostic, can be adapted to any diagnostic workflow
    - Manual, Reference Lab, Specialist Lab and Point of Care

Six Hours

45 minutes

<10 minutes

<15 minutes

- **Our expanding *Intellectual Property* portfolio**
  - 81 patents granted, 129 pending, across 54 patent families[1]

1. IP as of 30th September 2024

Go-to-Market Strategy

Strategy implemented

- **Extensive product R&D conducted** by Volition and its research partners
- **Direct** and **Indirect sales** of CE Marked product(s) Europe as Centers of Excellence hospitals evaluate for routine clinical use
- **Monetize broad IP** through commercial contracts with upfront, milestone payments, royalties and sales of key components

Proven Commercial Model with Nu.Q® Vet

- Published canine clinical evidence in peer reviewed journals
- Launched early access program via Texas A&M GI lab
- Licensed the Vet product via a range of agreements, where partner does all lab, blood and sales work (global, regional and national with

Antech, IDEXX, FUJIFILM, NationWide Laboratories, VPG, vetlab, Vita Genomics

Go to Market Strategy - HUMAN

- Utilize granted CE mark for NETs to drive adoption in the EU working with KOLs and hospital networks for wide-ranging NETs utility. Early revenue (pre-US FDA) clinical use in Europe.

- Focused partner led launch worldwide of product in sepsis on existing widely adopted current platforms, leveraging their sales teams, regulatory work and labs

Commercialization of nu·Q nets

Current European CE marked IVDD Product Strategy

- Very broad granted clinical utility for all NETs related diseases
- Both direct and indirect through IDS, (Revvity) sales of the CE Marked product
- Kits already purchased by three hospitals (centers of excellence) for clinical validation work.
- More than ten other active discussions ongoing across six European countries
- NETosis applications through broad CE granted mark:
  - Sepsis
  - Burns
  - Post-transplant
  - Kidney disease
  - and more…

Focused Sepsis Licensing Strategy

Aim to open up wide scale international adoption on existing platforms, with existing labs and sales pipelines

- ***TAM Sepsis – testing and monitoring ICU patients alone is a ~$1B+ opportunity***
- ***Other addressable markets include Acute Kidney Injury (AKI), Acute Respiratory Distress Syndrome (ARDS) and use in the Emergency Department >$10B opportunity***

Licensing and partnering criteria:

- Large installed base worldwide
- Experience of tech transfer to installed platforms
- Regulatory and clinical affairs management, rollout and funding
- Targeting Royalties, upfronts, milestones and key component sales

Progressing well with several global diagnostic and liquid biopsy companies, aim to sign multiple licensing human deals in 2025 to add to the EIGHT signed for Nu.Q® Vet.

Two underlying principles:

- Low CapEx for partners / Low OpEx for Volition
- Low-cost and routine = **accessible** tests worldwide

Dr. Andrew Retter

MBBS, MRCP, FRCPath (Haem), DICM, FFICM
Clinical Lead in Critical Care Medicine, ECMO and Thrombosis
Chief Medical Officer at VolitionRx, UK

Conflicts of interest to declare

- Employee and shareholder of VolitionRX Limited

The Burden of Sepsis

1 in 5 deaths worldwide are associated with sepsis

Almost **50 million** cases resulting in **11 million** deaths

Over 40% of cases are children under 5 years of age

It's the **number 1...**

Cause of death in hospitals

Cause for hospital readmissions

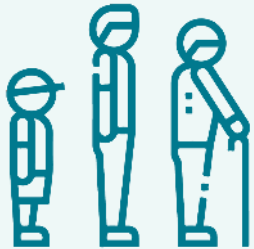
Healthcare cost
($62bn in USA pa alone)

Over **40%** of survivors suffer from long-term physical or psychological effects

Rudd et al, The Lancet, 2020. https://doi.org/10.1016/S0140-6736(19)32989-7

Who is at risk?

Anyone can get sepsis. It is indiscriminate of:



Age

Ethnicity

Socio-Economic status

Unmet Needs

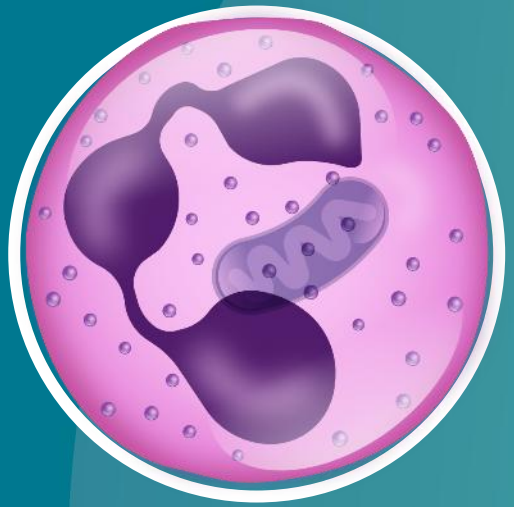
- Current diagnosis is empirical, multi-factorial and subjective.
- CURRENT methods of assessment (SOFA and APACHE II) are both complex & slow.
- Accepted need for **improved diagnostics**[1].

1. Rudd et al. 2020 The Lancet doi: 10.1016/S0140-6736(19)32989-7.

Volition's Mission

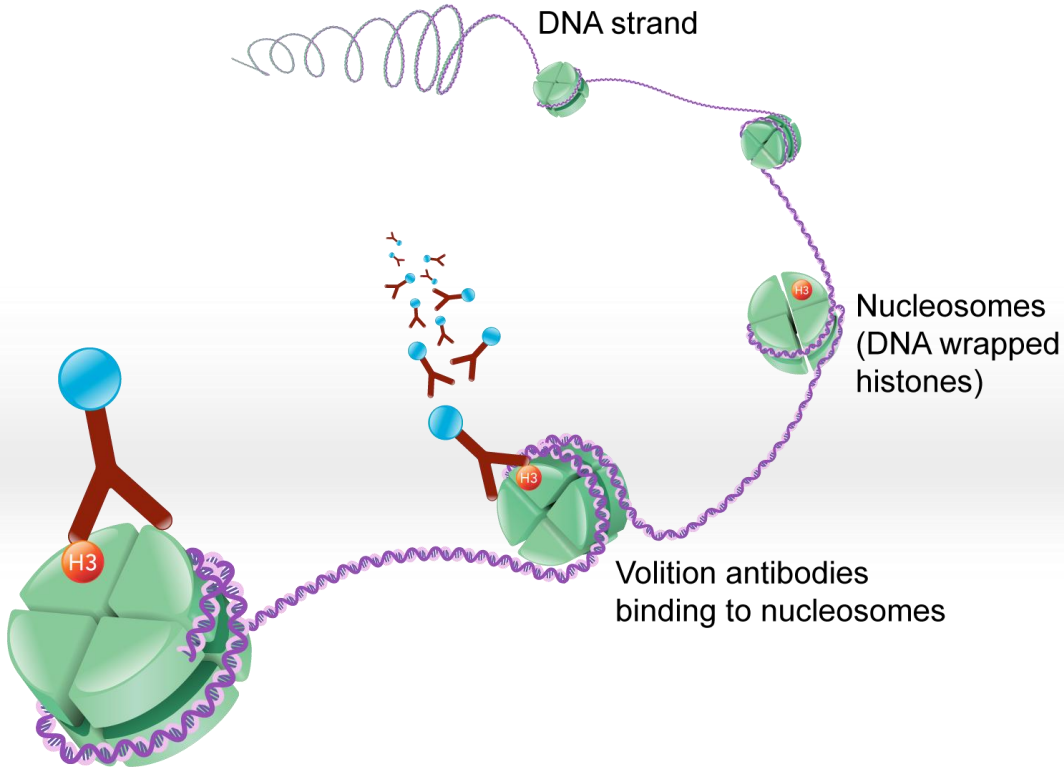
Develop a low-cost, easy-to-use, rapid diagnostic test to save lives and improve outcomes for patients worldwide.

We are here to present Nu.Q® NETs H3.1 assay, a novel, clinically relevant biomarker which has the potential to change the management of patients with sepsis.



Why is H3.1 key: The biology & scientific rationale

Nucleosomes and histones:



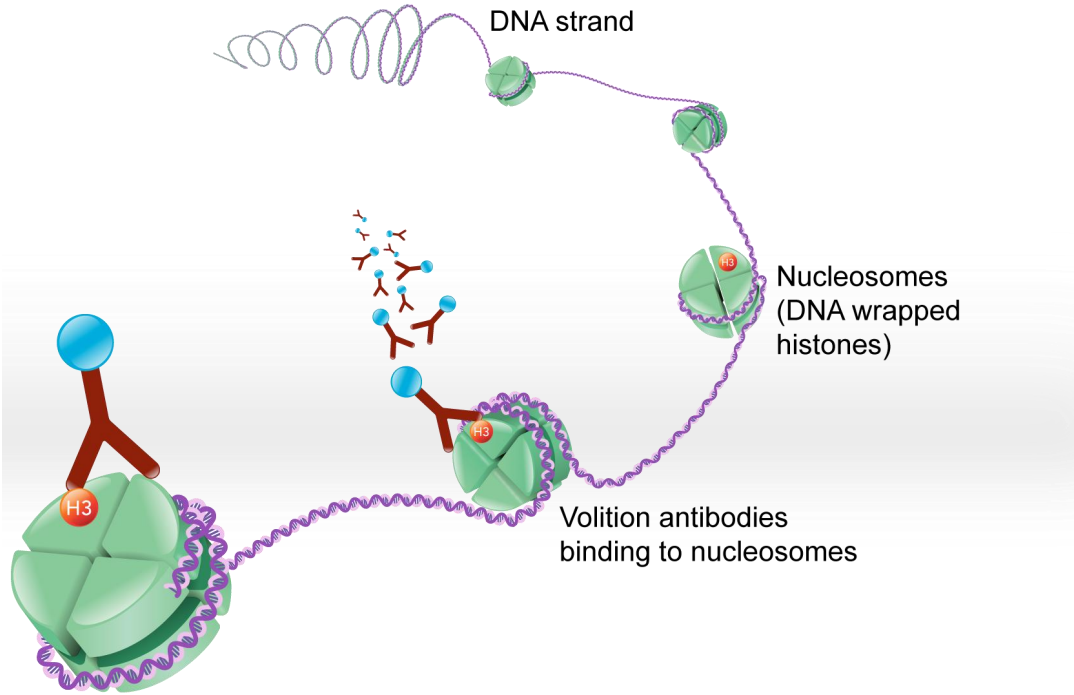
Nucleosomes and histones:

Key message:

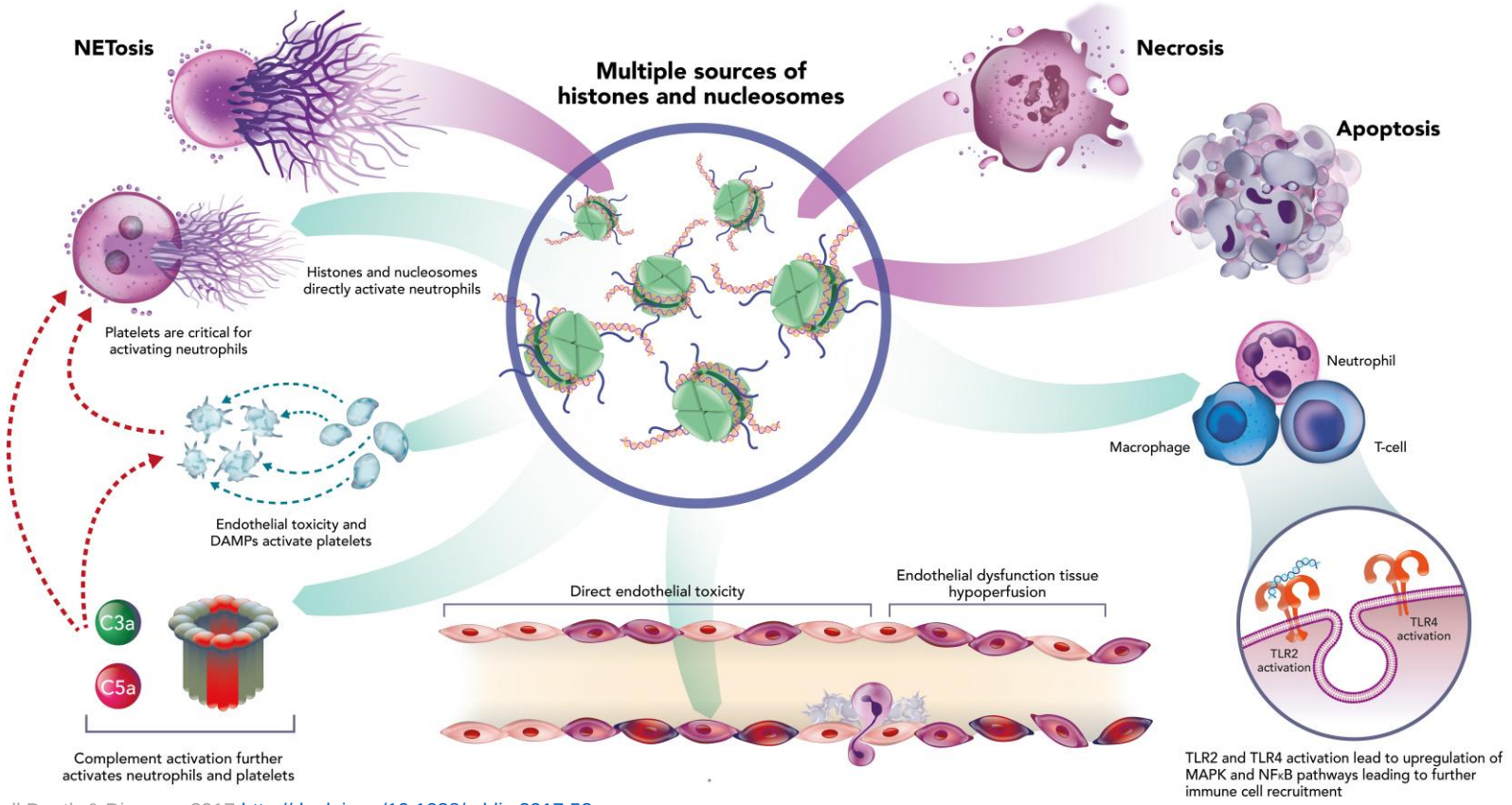
The H3.1 assay can detect nucleosomes using chemiluminescence technology and provide a result within 15 minutes

The lower limit of quantification is 20ng/ml

The upper limit of quantification is 20,000ng/ml



H3.1 as a Damage-Associated Molecular Protein

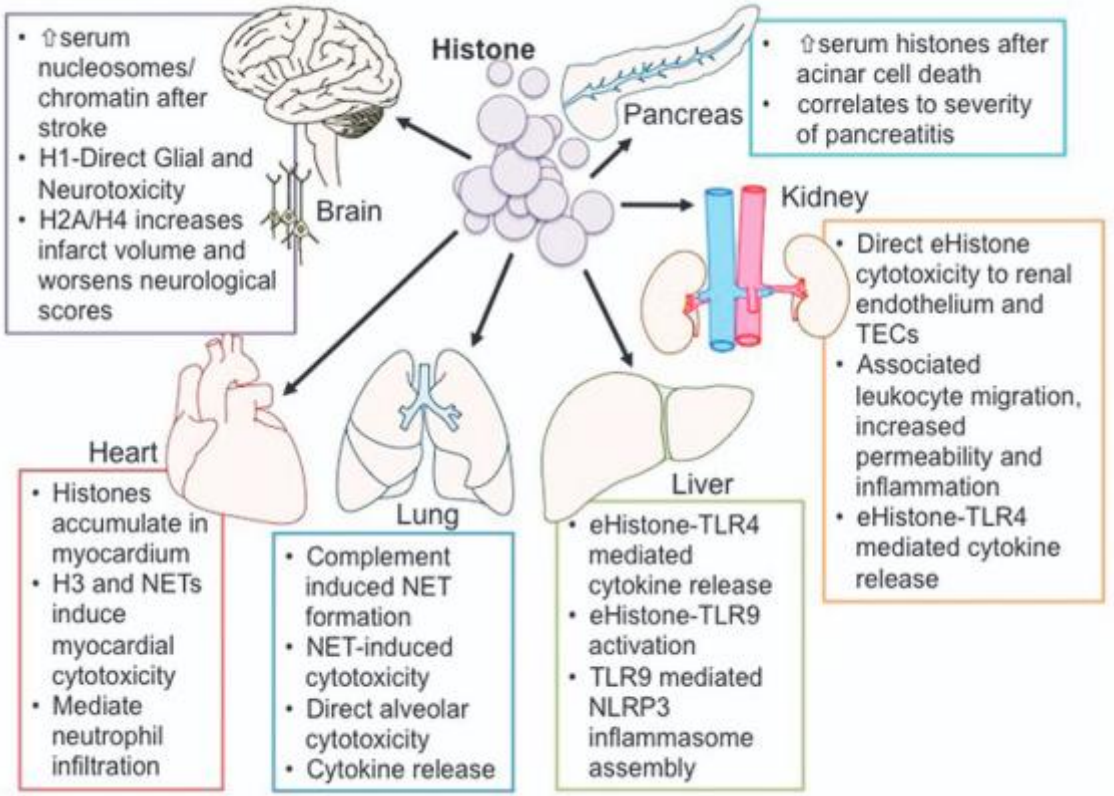


Silk et al, Cell Death & Disease, 2017 http://dx.doi.org/10.1038/cddis.2017.52

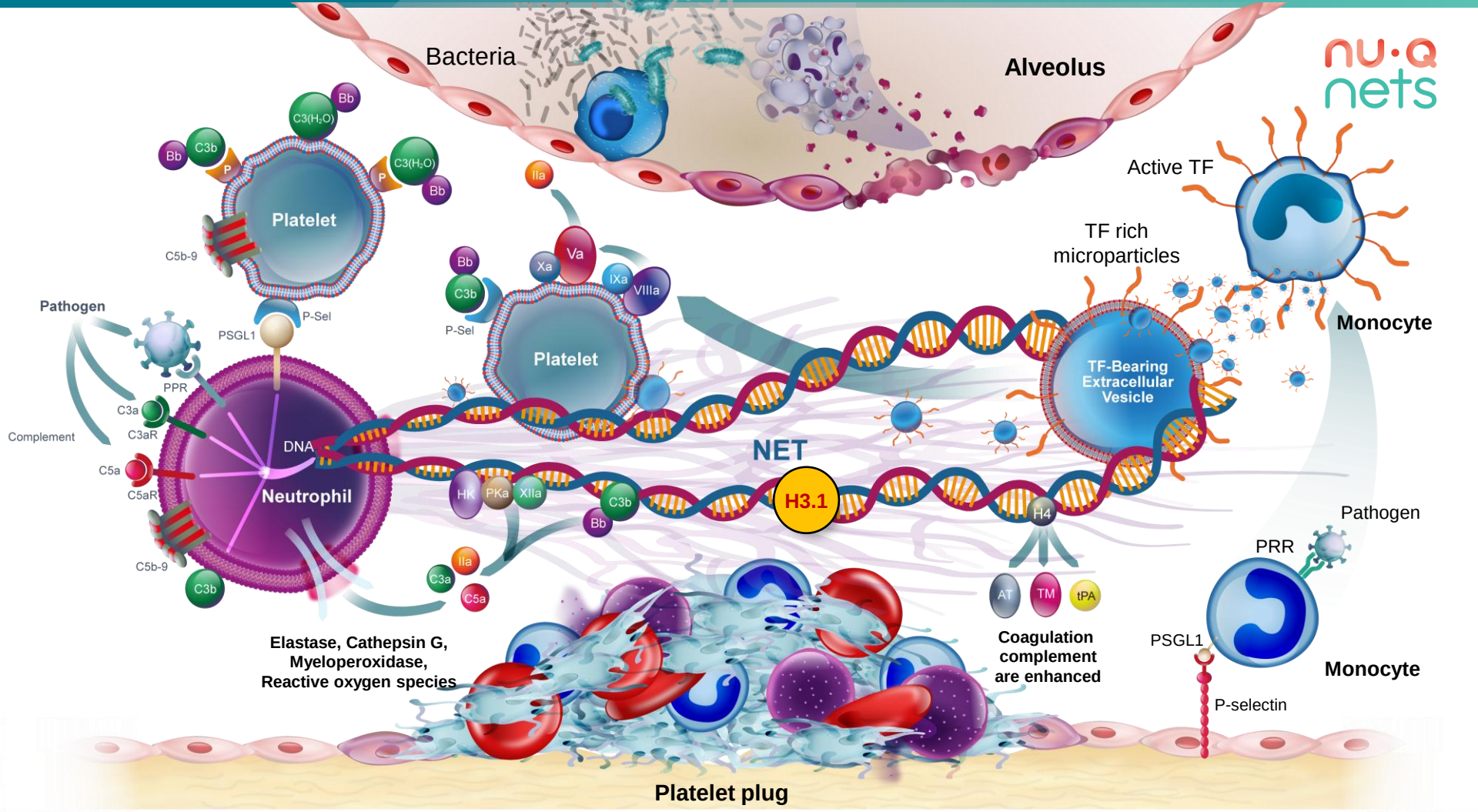
H3.1 sits as a triumvirate of innate immunity, inflammation and coagulation.

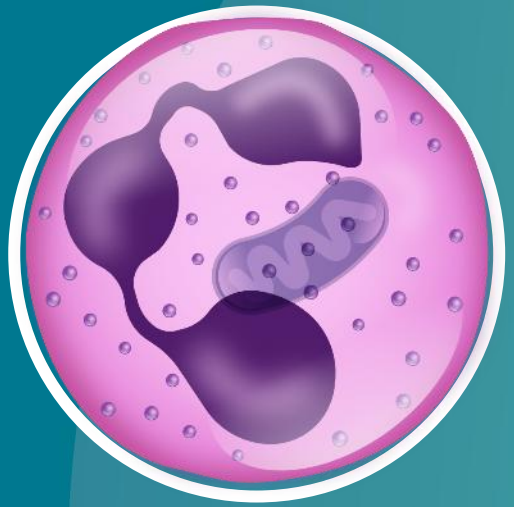
The majority of extracellular pathology is due to the indiscriminate binding of anionic components of the circulation and vasculature.

Extracellular Histones and Organ Injury



Silk et al, Cell Death & Disease, 2017 http://dx.doi.org/10.1038/cddis.2017.52

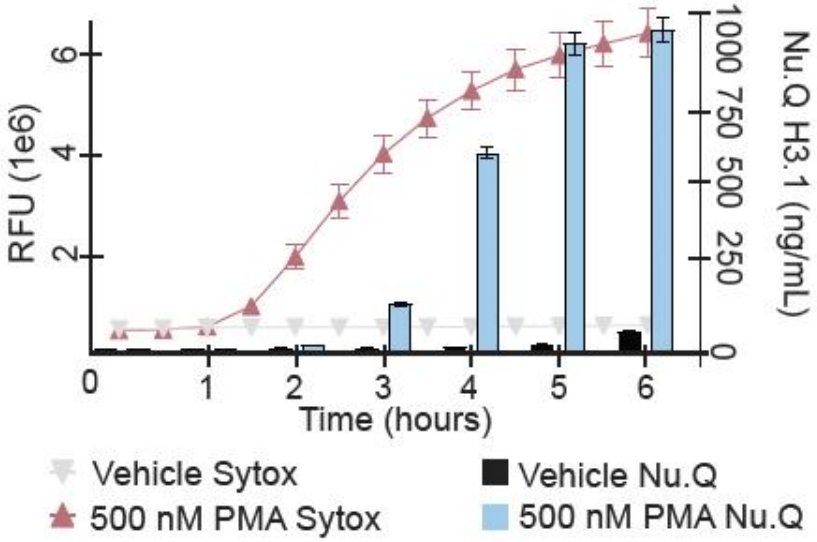

Bacteria
Alveolus
nu·Q nets
Active TF
TF rich microparticles
Monocyte
Pathogen
PSGL1
PPR
P-Sel
Platelet
C5b-9
C3(H2O)
Bb
C3b
P
Complement
C3a
C3aR
C5a
C5aR
DNA
Neutrophil
Va
Xa
IXa
VIIIa
IIa
HK
PKa
XIIa
NET
H3.1
H4
TF-Bearing Extracellular Vesicle
AT
TM
tPA
Coagulation complement are enhanced
Elastase, Cathepsin G, Myeloperoxidase, Reactive oxygen species
PRR
P-selectin
Platelet plug

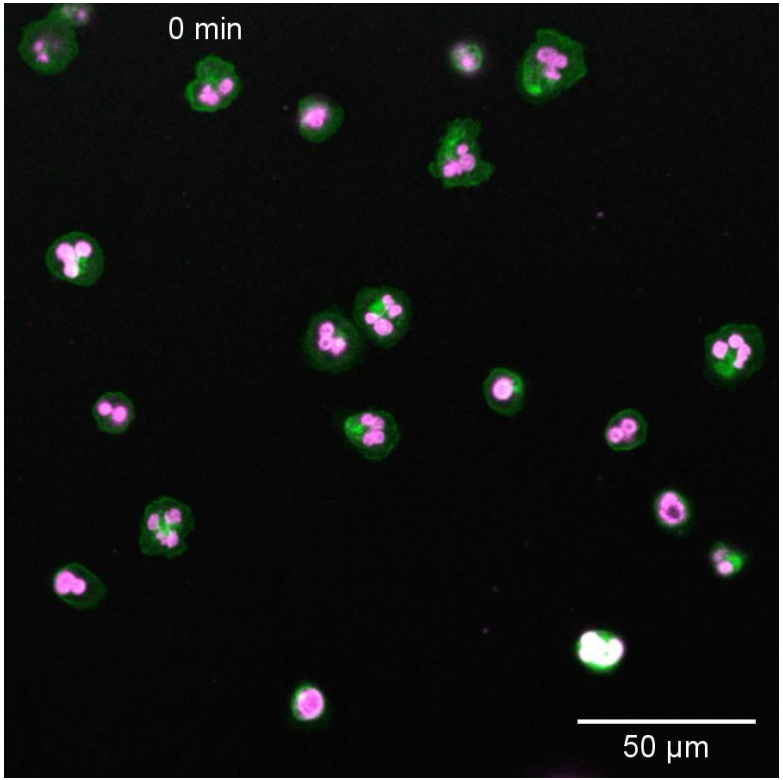


The role of H3.1 in NETosis:

…proving we are measuring what we say we are measuring!

H3.1 Nucleosome Levels Increase With NETosis





Zukas et al, Journal of Thrombosis & Hemastasis, 2024
https://doi.org/10.1016/j.jtha.2024.05.028

JTH Commentary, Sept 2024
https://doi.org/10.1016/j.jtha.2024.06.016

Kinetic Information

H3.1 is not impacted by height, weight, age, sex[1]

H3.1 is not impacted by the circadian rhythm[2]

1. Neumann et al, under review
2. RHU Records Data Set, data on file

Innovation Lab Publications

https://doi.org/10.1016/j.jtha.2024.05.028

ORIGINAL ARTICLE

Rapid high-throughput method for investigating physiological regulation of neutrophil extracellular trap formation

Kieran Zukas[1] | Justin Cayford[1] | Finley Serneo[1] | Brandi Atteberry[1] | Andrew Retter[2] | Mark Eccleston[1] | Theresa K. Kelly[1]

"The NET Effect" - Neutrophil extracellular traps: a potential key component of the dysregulated host immune response in sepsis

Andrew Retter[1,2,3]*, Mervyn Singer[4], and Djillali Annane[5,6,7,8]

Understanding the complex chromatin dynamics in primary human neutrophils during PMA-induced NET formation

Brandi Atteberry[1], Benjamin P. Berman[1,2], Theresa K. Kelly[1] and Justin Cayford[1]*

[1]Innovation Laboratory, Volition America, Carlsbad, CA, United States, [2]Department of Developmental Biology and Cancer Research, The Hebrew University of Jerusalem, Jerusalem, Israel

“The NET Effect” - Neutrophil extracellular traps: a potential key component of the dysregulated host immune response in sepsis

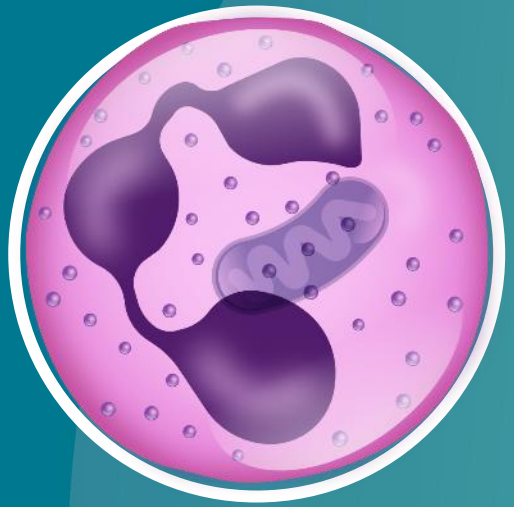
Published Paper

The key take home messages are:

1. Neutrophils are key cells in fighting off invading pathogens. They can swallow up invading micororganisms. They can also eject their DNA in the form of neutrophil extracellular traps (NETs). These webs as DNA can trap pathogens. NETs act as a critical bridge between our blood coagulation system and our immune system.

2. When NETs are released in excess blood vessels become inflamed and damaged. This process is called thromboinflammation and contributes to organ failure by disrupting the blood supply. Targeting excessive release of NETs represents a promising diagnostic and therapeutic strategy.

Retter, Singer and Annane, Crit Care, 2025 https://doi.org/10.1186/s13054-025-05283-0



Clinical Data

Studies at Centers of Excellence: >3000 patients

Study	Country	Description	Cohort Size	Status
SISPCT	Germany	Retrospective analysis of prospectively collected cohort	971 intensive care patients Multiple timepoints	Completed. Manuscript under review. Available on MedRXIV
Amsterdam UMC	Netherlands	Retrospective analysis of prospectively collected cohort	1,713 intensive care patients Multiple timepoints	Completed. Manuscript submitted
RHU RECORDS	France	Prospective, multi-center, placebo controlled, bio-marker-guided, adaptive Bayesian design basket trial	1,500 intensive care patients Interim analysis of 416 patients	Study ongoing
CLUED (CRO organized)	U.S.	Prospective, blinded, longitudinal cohort study.	200 patients (intensive care and emergency department)	Completed. Data on file

Executive Summary: consolidated conclusions

Results from three independent studies totalling over 3,000 patients

These findings are consistent across cohorts[1-3]

An elevated H3.1 level reflects a dysregulated immune response and is associated with:

- a risk of **increased mortality**
- an increased risk of **septic shock**
- an increased risk of **(multi-) organ failure**
- an increased risk of **ARDS**
- an increased risk of **renal failure**

…could be thought of as a Treatable Trait in sepsis management

1. Neumann et al, under review; 2. Daan F.L. Filippini et al. Data on File. Manuscript submitted; 3. RHU Records Data Set, data on file

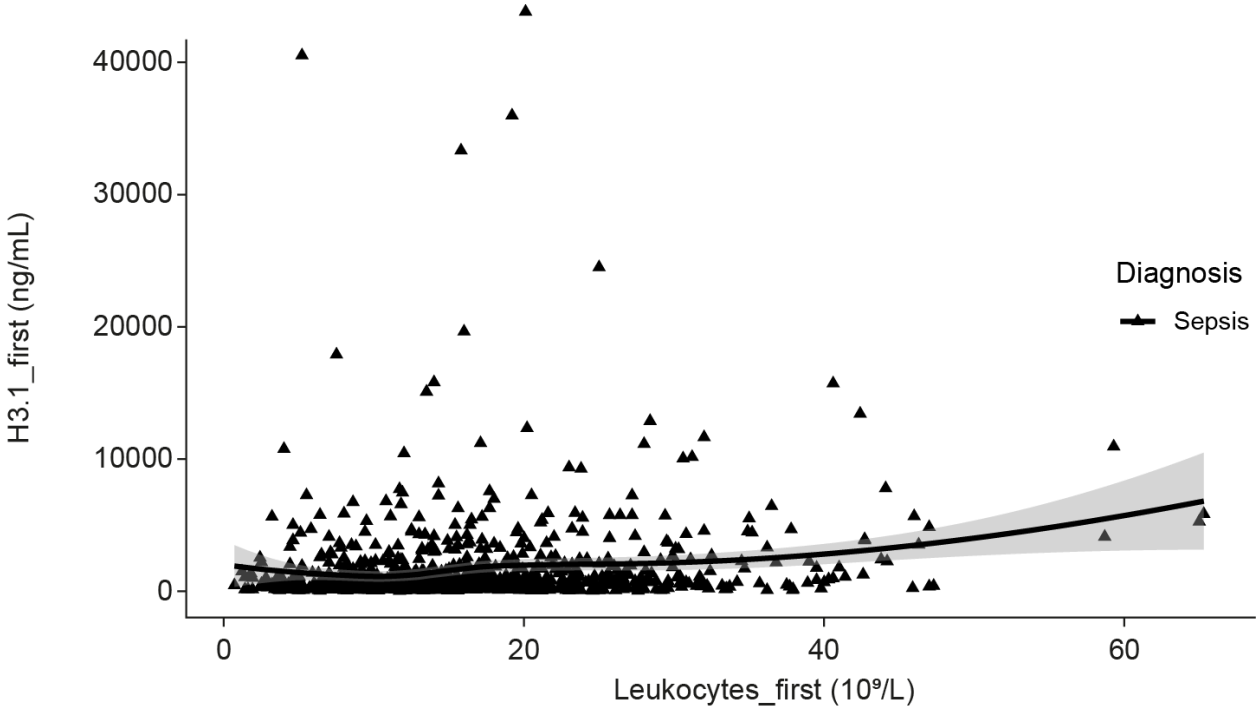
Prognostic value of admission H3.1 nucleosome levels in sepsis-associated acute kidney injury: a secondary analysis of the SISPCT randomised clinical trial

Caroline Neumann et al

This is the first publication of a large independent cohort of Intensive Care patients. We analysed H3.1 nucleosome levels in 971 patients with sepsis and septic shock.

- The key take home message is that H3.1 nucleosomes are a promising novel biomarker for early mortality and organ dysfunction in sepsis, with significantly higher levels found in septic shock than sepsis patients and a clear dose-response relationship with acute kidney injury severity.
- The findings establish H3.1 nucleosomes as an independent predictor of 28-day mortality and need for renal replacement therapy.
- The paper demonstrates that Nu.Q® H3.1 provides **ADDITIONAL** information to the clinician and suggests its potential clinical utility for risk stratification and early intervention in critically ill patients presenting with sepsis.

Correlation between admission H3.1 nucleosome levels and white cell count



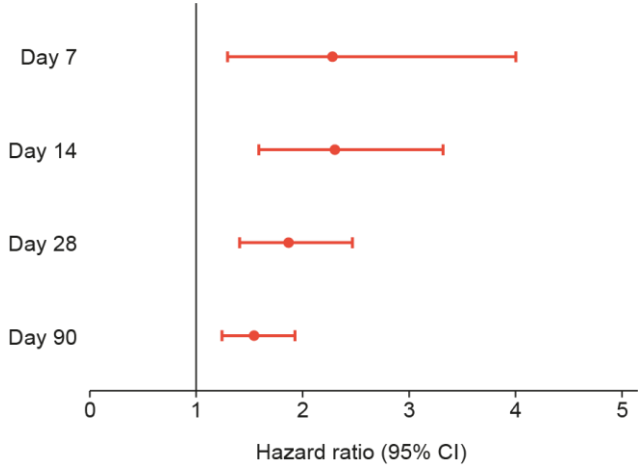
1. Neumann et al, under review

Mortality risk for different levels of H3.1 on admission

14 day mortality	Survivor			
Initial H3.1 (ng/mL)	**Yes**	**No**	**Total**	**Risk**
>20,000	0	5	5	100%
10,000-20,000	12	4	16	25%
1,000-10,000	264	36	300	12%
<1,000	508	40	548	7%
Total	**784**	**85**	**869**	**10%**

1. Neumann et al, under review

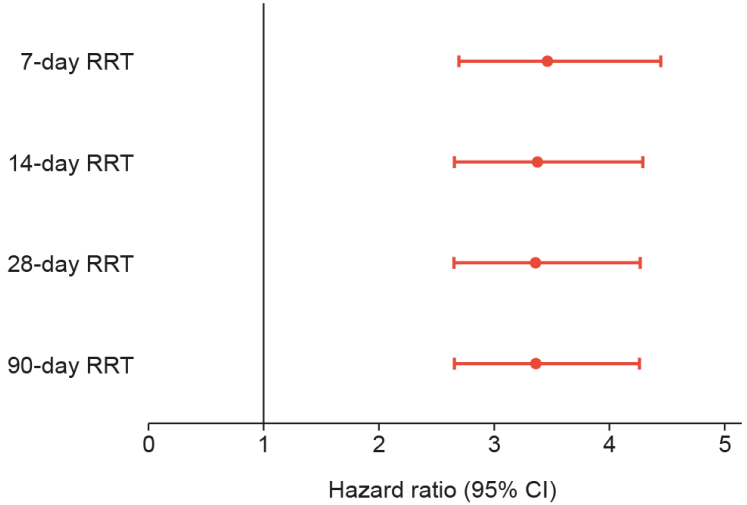
Association between log-transformed H3.1 nucleosome levels at admission and mortality risk over time in sepsis patients



Forest plot demonstrating the hazard ratios (HRs) with 95% confidence intervals (CIs) for mortality at days 7, 14, 28 and 90 in relation to admission H3.1 nucleosome levels (log-10 transformed) in sepsis and septic shock patients. The analysis shows the strongest association between H3.1 levels and early mortality (day 7: HR 2.28, 95% CI 1.30–4.01; day 14: HR 2.30, 95% CI 1.59–3.32), with a gradual attenuation over time (day 28: HR 1.86, 95% CI 1.41–2.47; day 90: HR 1.54, 95% CI 1.24–1.93). All associations remained statistically significant ($p<0.05$) throughout the 90-day follow-up period. The raw data are shown in Supplemental Table 3.

1. Neumann et al, under review

Forest plots of hazard ratios for RRT outcomes



Forest plot showing adjusted hazard ratios with 95% confidence intervals (CIs) for renal replacement therapy (RRT) outcomes at different time points after admission in sepsis and septic shock patients (n=831). The analysis demonstrates consistent hazard ratios of approximately 3.5–4.0 across all time periods (7, 14, 28 and 90 days), indicating that elevated admission H3.1 nucleosome levels (>2500 ng/mL) are associated with increased risk of requiring RRT. The sustained elevation in hazard ratios suggests that admission H3.1 levels may have prognostic value for predicting RRT requirements throughout the critical care stay. The raw data are shown in Supplemental Table 7.

1. Neumann et al, under review

Plasma H3.1 nucleosomes as biomarkers of sepsis and organ failure

Daan F.L. Filippini et al

It is our largest study yet; 1713 patients with 4283 samples analyzed from a well characterized cohort and a highly respected consortium.

- The key take home message is that organ failure and inflammation in sepsis are closely associated with NETosis, measured through our Nu.Q® H3.1 nucleosome levels.
- Patients with acute kidney injury (AKI), disseminated intravascular coagulation (DIC), and acute respiratory distress syndrome (ARDS) exhibit significantly higher H3.1 levels compared to those without these conditions.
- Additionally, H3.1 levels show promise in differentiating hyper- and hypo-inflammatory endotypes.
- Like Neumann et al, the paper demonstrates that Nu.Q® H3.1 provides ADDITIONAL information to the clinician and suggests its potential clinical utility for risk stratification and early intervention in critically ill patients presenting with sepsis.
- The differentiation between hyper- and hypo-inflammatory endotypes is particularly interesting in that H3.1 could potentially help “personalise” sepsis care and treatment.

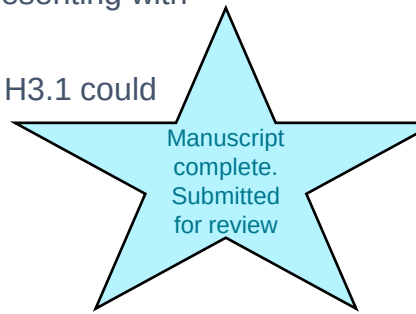


Table 2. Baseline H3.1 nucleosomes and mortality

	All		*Hypoinflammatory*		*Hyperinflammatory*	
	n = 1638		**n = 1099**		**n = 538**	
	OR (95% CI) per log10 increase	***P* value**	**OR (95% CI) per log10 increase**	***P* value**	**OR (95% CI) per log10 increase**	***P* value**
30-day mortality	1.65 (1.4-1.95)	< 0.001	1.23 (0.97-1.55)	0.093	1.58 (1.22-2.06)	0.001
90-day mortality	1.6 (1.37-1.87)	< 0.001	1.23 (0.99-1.53)	0.057	1.47 (1.14-1.91)	0.003

Values are presented as odds ratio (OR) per log10 increase of baseline H3.1 nucleosome concentration, along with the 95% confidence interval (CI). Values are derived by a logistic regression.

Plasma H3.1 nucleosomes as biomarkers of sepsis and organ failure, Daan F.L. Filippini et al. Data on File. Manuscript submitted

Summary

- We have shared a taster of clinical data and scientific evidence to support the use of our proprietary Nu.Q® NETs H3.1 assay

- We believe the data supports the fact that H3.1 will become an integral biomarker in the management of sepsis; it is both a marker of badness and a cause of consequence (as histones contribute to organ injury) which in turn means H3.1 could not only be aid to diagnosis but also be a therapeutic target.

Summary

Licensing Portfolio: Platform stable, reproducible

Application	Proof of Concept	Viability study	Final Validation study	Licensed
Animal				
Canine Cancer Screening				✓ Launched
Canine Cancer Monitoring				✓
Feline Cancer				✓
Automated test				In negotiation
Human			Regulatory/Adoption study	
Sepsis				Data room available
Cancer				Data room
Lung Cancer Screening				Data room
Minimal Residual Disease & Disease Management				Data room
Multi-Cancer Early Detection				Data room
Capture-PCR™				Data room

Investment Summary: NYSE:VNRX

- Listed NYSE, commercial stage diagnostics company — developing **low-cost, early detection and treatment monitoring diagnostics** in human and animal health
  - Disease areas – global killers: Cancer, Sepsis; significant market opportunities, >$10's Billion
  - $23 million in vet milestone payments banked
  - Early 2025 revenue targeting:
- **Nu.Q® Vet (8 licensing deals already selling)**
- **Nu.Q® Discover**
- **Nu.Q® NETs / Nu.Q® Cancer direct/indirect sales of CE-Marked human clinical product(s) in Europe**

2025 Focus: closing large human licencing deals, in cancer and sepsis

Question & Answer Session

Lou Batchelor

Thank you for your interest in Volition.

For more details, please visit www.volition.com