Trevena®

INNOVATING FOR PATIENTS

TRV027 Proof-of-Concept Data Presentation | Nasdaq: TRVN | September 2021

Forward-Looking Statements

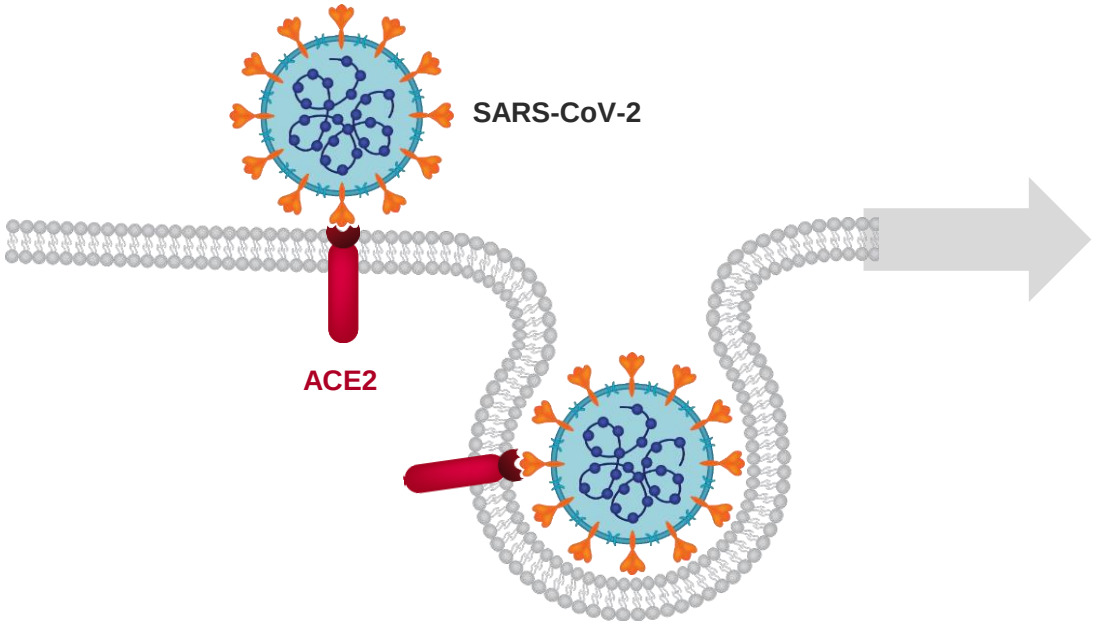
To the extent that statements contained in this presentation are not descriptions of historical facts regarding Trevena, Inc. (the “Company” or “we”), they are forward-looking statements reflecting management’s current beliefs and expectations. Forward-looking statements are subject to known and unknown risks, uncertainties, and other factors that may cause our or our industry’s actual results, levels of activity, performance, or achievements to be materially different from those anticipated by such statements. You can identify forward-looking statements by terminology such as “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “might,” “plan,” “objective,” “predict,” “project,” “suggest,” “target,” “potential,” “will,” “would,” “could,” “should,” “continue,” “ongoing,” or the negative of these terms or similar expressions. Forward-looking statements contained in this presentation include, but are not limited to, (i) statements regarding the timing of anticipated clinical trials for our product candidates; (ii) the timing of receipt of clinical data for our product candidates; (iii) our expectations regarding the potential safety, efficacy, or clinical utility of our product candidates; (iv) the size of patient populations targeted by our product candidates and market adoption of our potential drugs by physicians and patients; (v) the timing or likelihood of regulatory filings and approvals; and (vi) our cash needs.

Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: the commercialization of any approved drug product, the status, timing, costs, results and interpretation of our clinical trials or any future trials of any of our investigational drug candidates; the uncertainties inherent in conducting clinical trials; expectations for regulatory interactions, submissions and approvals, including our assessment of the discussions with the FDA or other regulatory agencies about any and all of our programs; uncertainties related to the commercialization of OLINVYK; available funding; uncertainties related to our intellectual property; uncertainties related to the ongoing COVID-19 pandemic, other matters that could affect the availability or commercial potential of our therapeutic candidates; and other factors discussed in the Risk Factors set forth in our Annual Report on Form 10-K and Quarterly Reports on Form 10-Q filed with the Securities and Exchange Commission (SEC) and in other filings we make with the SEC from time to time. In addition, the forward-looking statements included in this presentation represent our views only as of the date hereof. We anticipate that subsequent events and developments may cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we specifically disclaim any obligation to do so, except as may be required by law.

Multi-Organ Damage From Coronavirus

Elimination of ACE2 protein leads to critical hormonal imbalances

Coronavirus binds to and eliminates ACE2[1]

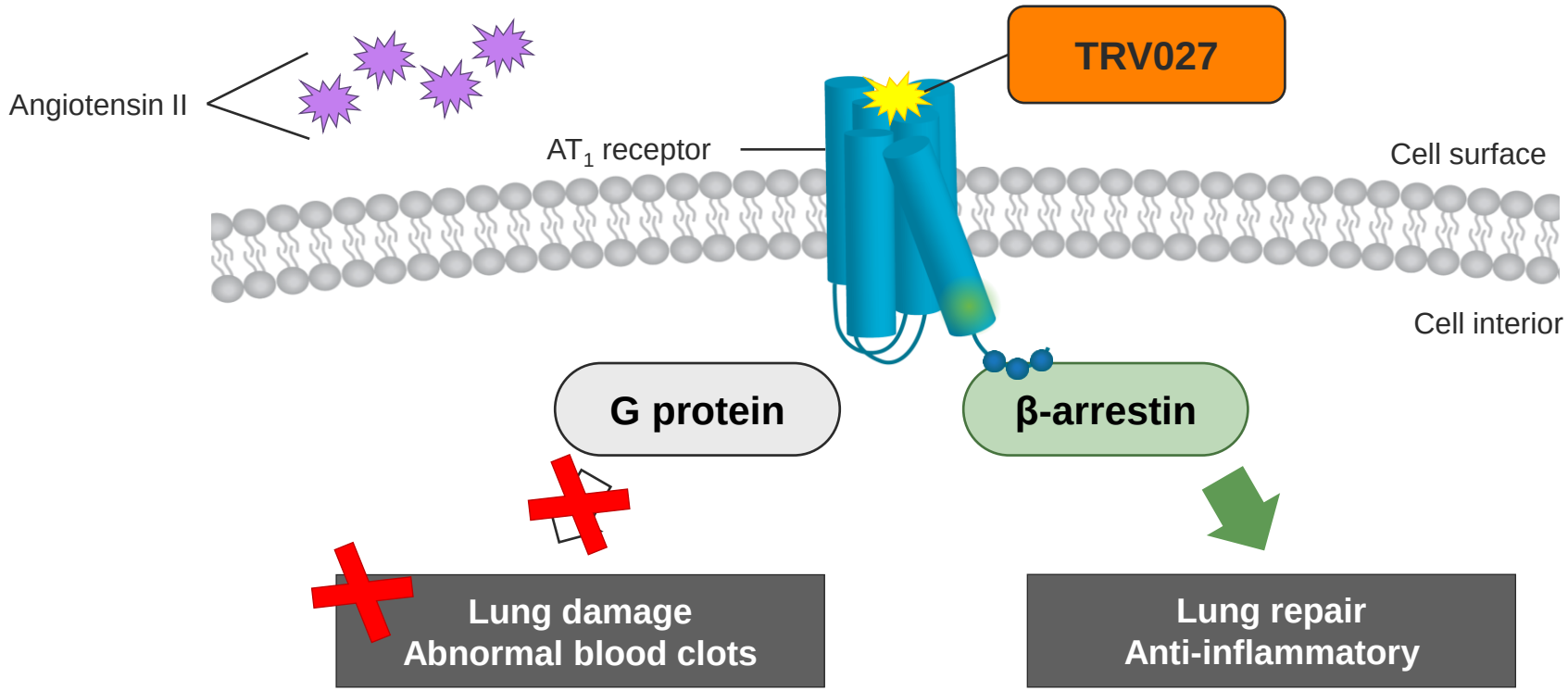


- Leads to accumulation of angiotensin II:
  - Acute lung injury and abnormal blood clots
  - Can lead to ARDS / pulmonary embolism / stroke
- 66% - 94% mortality rate for COVID-19 related ARDS[2*]
- ~1/3 of hospitalized COVID-19 patients develop clotting complications[3]

ARDS = Acute Respiratory Distress Syndrome. 1) Kuba K et al., Nat Med, 2005. 2) Gibson PG et al, Med J Aust, 2020. *In patients requiring ventilation. 3) Klok FA et al, Thromb Res, 2020.

TRV027: New MOA for COVID-19

Mechanism targeted to improve lung function and prevent abnormal clotting



TRV027 is the only selective AT_1 receptor agonist

Safety / tolerability data in ~700 patients

TRV027 COVID-19 Study - Imperial College London

- Randomized, double-blind, placebo-controlled proof-of-concept study

- N = 30 COVID-19 patients enrolled
  - Hospitalized, non-ventilated
  - ≥18 years old

Imperial College London

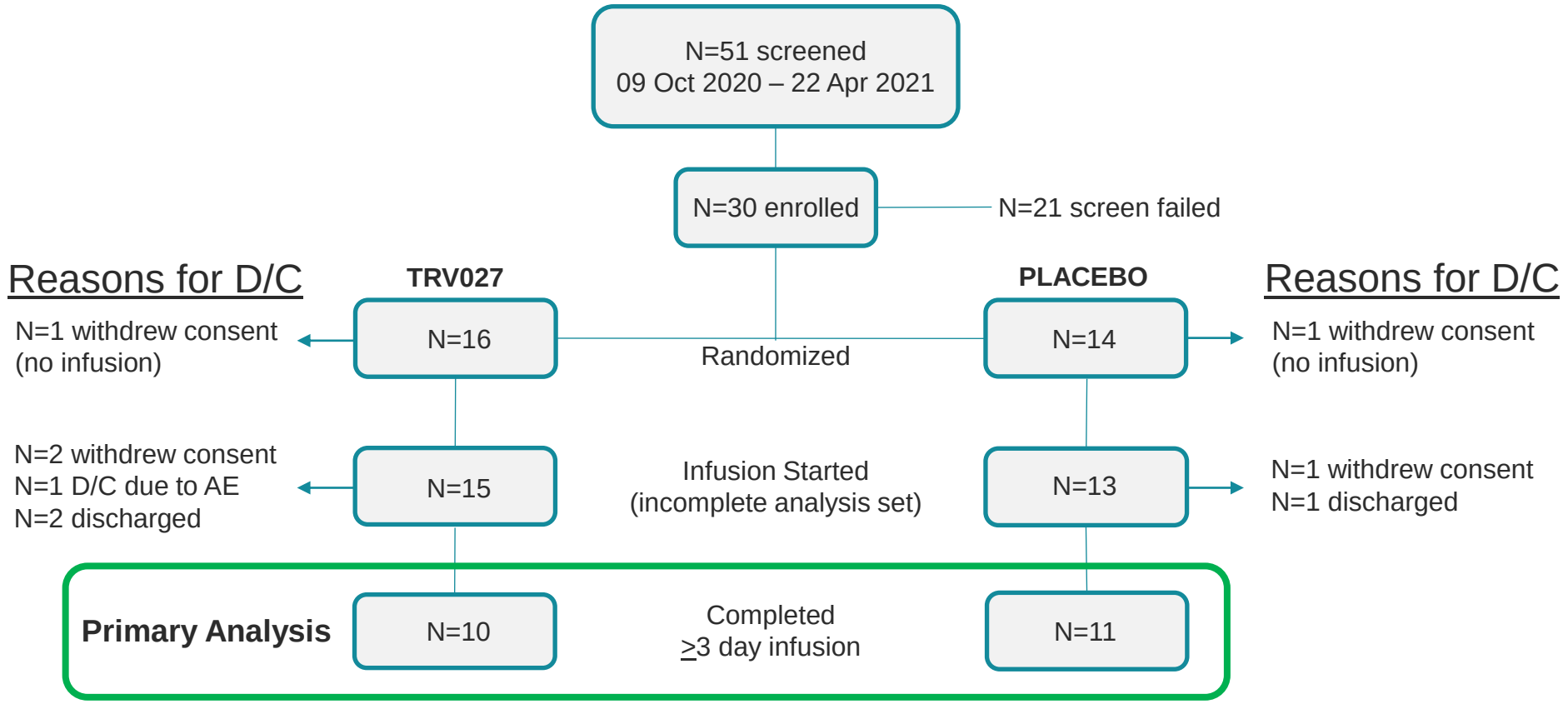
- IV infusion of placebo or TRV027 for 7 days (12 mg/hr)

- **Primary endpoint:** mean change from baseline D-dimer levels at three days
  - Biomarker used to monitor the risk of abnormal clotting throughout the vascular system
  - Elevated D-dimer associated with higher incidence of critical illness, thrombotic events, acute kidney injury and death[1]
  - Following DMSC interim review, study enrollment closed prior to reaching the full study population number necessary to detect statistically significant treatment differences

Trevena®

1) Berger J et al. Arterioscler Thromb Vasc Biol. 2020.
DMSC = Data Safety and Monitoring Committee. https://clinicaltrials.gov/ct2/show/record/NCT04419610.

Patient Disposition



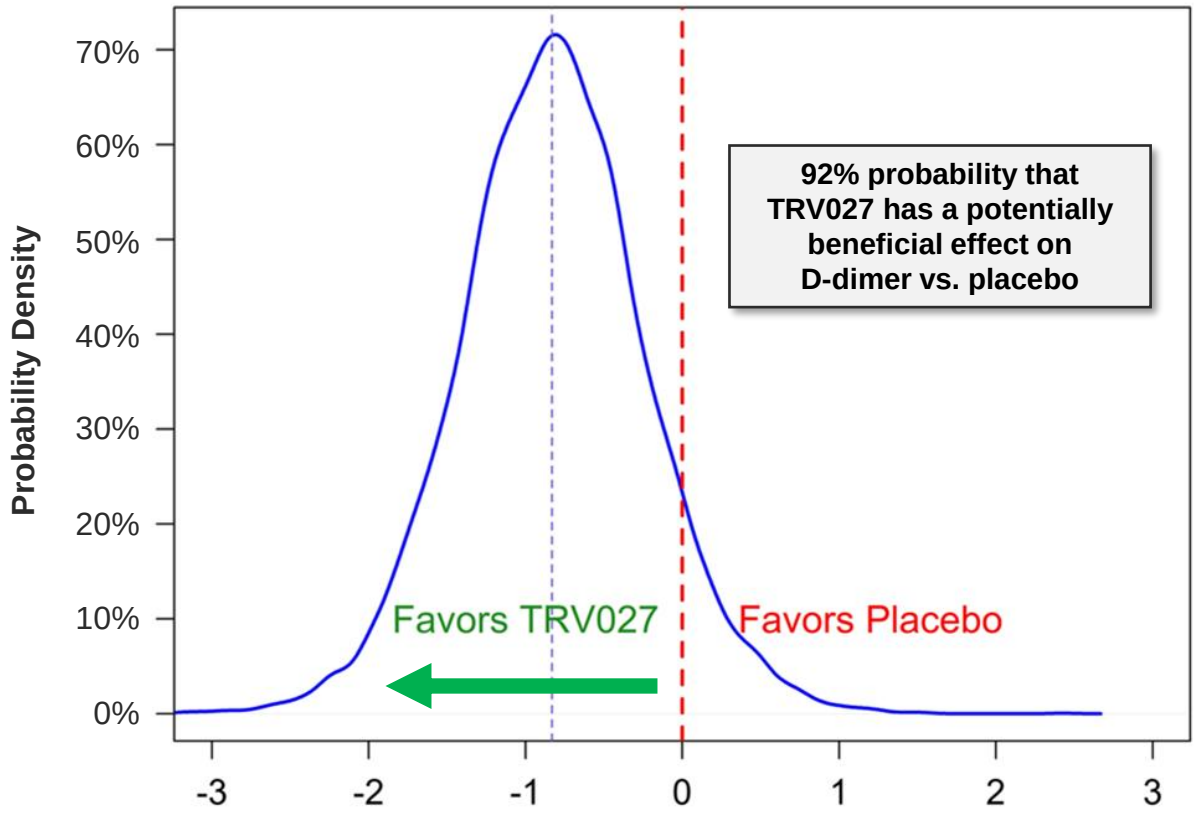
At 30 day follow-up:

24 patients survived (N=12 TRV027 / N=12 Placebo)
3 patients died (N=2 TRV027 / N=1 Placebo)[1]
1 TRV027 patient was lost to follow-up

1) All SAEs were assessed by the study clinician to be unrelated to study drug assignment or study procedures.

Primary Endpoint (D-Dimer Reduction) – Bayesian Results

TRV027 Probability of Effect on D-dimer
(adjusted for age)



D-dimer biomarker:
Recognized predictor of disease progression and mortality in COVID-19 infection

1) Percentage change from baseline D-dimer per year of age.

Time to Initial Hospital Discharge (Length of Hospital Stay)

Full Analysis Set (excludes deaths)	TRV027 (N=7)*	Placebo (N=10)	Difference
Mean (days)	11.4	23.3	**11.9 days**
Median	8	12	**4 days**
Range	5, 32	5, 86	

NOTE: Post-hoc analysis of differences in LOS not dependent upon baseline D-dimer level or SOFA score

A post-hoc analysis indicated that patients receiving TRV027 experienced ~12-day reduction in average length of hospital stay compared to placebo (11.4 vs. 23.3 days), with a median reduction of 4 days (8 vs. 12). LOS = Length of Stay, SOFA = Sequential Organ Failure Assessment
*1 patient with missing discharge date but alive at Day 30 follow-up.

Preliminary Conclusions

TRV027 was well-tolerated in hospitalized COVID-19 patients

Primary endpoint:

- **Bayesian modeling predicted 92% probability for TRV027 having a potentially beneficial impact on D-dimer levels**
- TRV027 patients experienced 70% reduction in circulating D-dimer, vs. 27% of placebo patients through 3 days of infusion

Post-hoc analysis:

- **TRV027 patients experienced a 12-day reduction in average length of hospital stay compared to placebo**[1]
- Reduction in time to hospital discharge not dependent on indices of disease severity prior to treatment

These preliminary data show that TRV027 provided initial evidence of improvement on biomarker and clinical endpoints associated with COVID-19 disease severity and progression

Trevena®

1) A post-hoc analysis indicated that patients receiving TRV027 experienced ~12-day reduction in average length of hospital stay compared to placebo (11.4 vs. 23.3 days), with a median reduction of 4 days (8 vs. 12).

Two Global Multi-Arm Platform Trials Evaluating TRV027

TRV027 data expected in ~600 patients

NIH ACTIV-4* (US)

National Institutes of Health

VANDERBILT UNIVERSITY MEDICAL CENTER

Primary outcome:

Supplemental O_2-free days
(28 days post-randomization)

Additional outcomes: in-hospital mortality, ventilator-free days, clinical status

REMAP-CAP (UK)

Primary outcomes:

In-hospital mortality
+
Organ failure support in ICU
(21 days post-randomization)

Additional outcomes: ICU / hospital length of stay, ventilator-free days, organ failure-free days

Trevena®

*ACTIV = Accelerating COVID-19 Therapeutic Interventions and Vaccines