SMA Treatment Access and Clinical Trials Webinar

February 15, 2018

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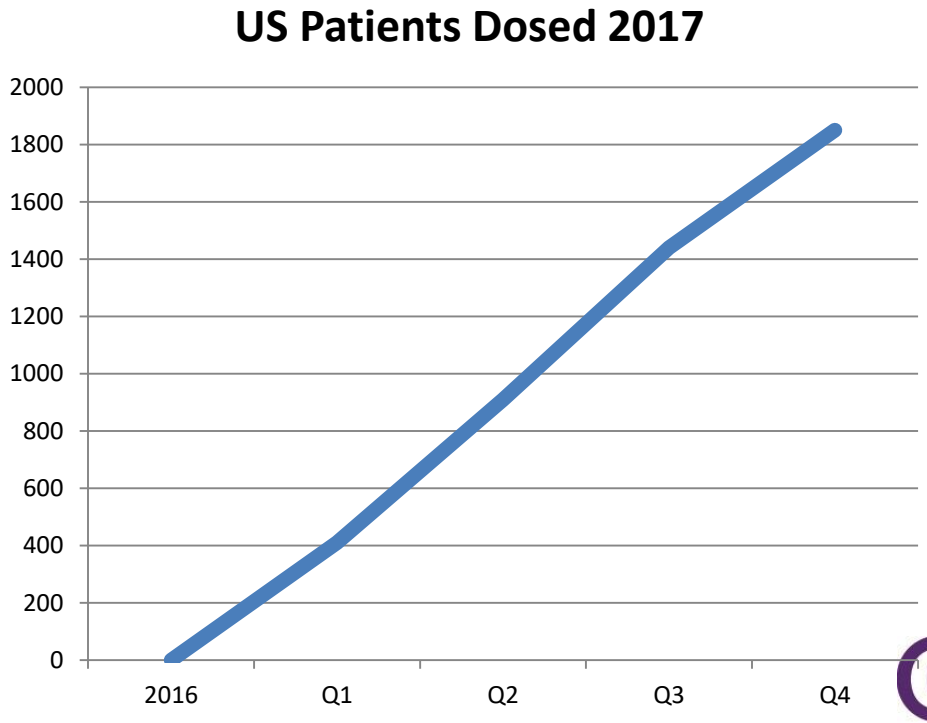
Make today a breakthrough.

Treatment Access Update

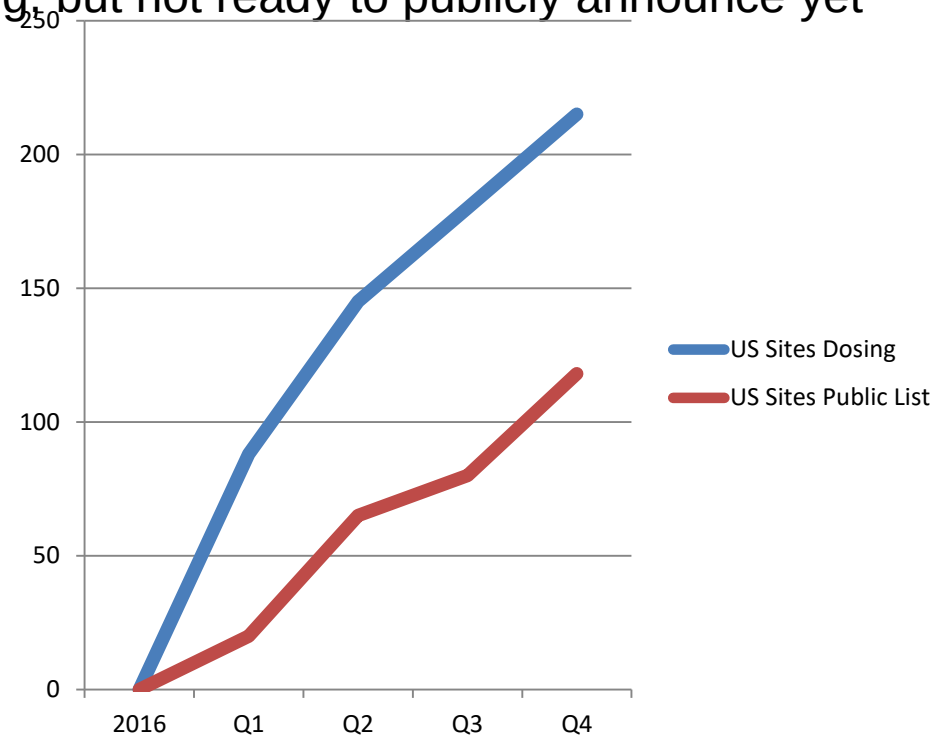
Current Dosing Metrics

- December 2017:
  - **~1,900 patients been dosed in US**
    - Including those in extension trials and support programs
  - Around 20% to 30% of all in US
- **215 sites have dosed** at least one patient
- Average of 9 per site:
  - Mix of:
  - some very high
  - most very low
- 275 sites interested



Cure SMA List – New Sites

- Progress in first year:
  - **118 sites on list confirmed.** 35 states plus DC with at least one site
  - About 100 sites are dosing, but not ready to publicly announce yet



- **Need 250-300 sites**:
  - Need to increase numbers of patients seen at each
  - Funding to Support Treatment Access
    - Increase number of SMA patients seen, treated, and followed at major sites. One year of funding for $50,000 for 14 sites.
  - Training and Support for New Sites:
    - Bring into our community – Clinical Conference

Payer	Type 0	Type I	Type II	Type III	Type IV	1 SMN2	2 SMN2	3 SMN2	4 SMN2	Pediatric	Adult	Trach	Non-Invasive	Proportion
Commercial														
Aetna	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	77%
Anthem	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Uncertain	Yes	Yes	85%
Cigna	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	85%
HCSC (BCBS	No	Yes	Yes	Yes	No	Uncertain	Yes	Yes	Yes	Yes	No	Yes	Yes	77%
Humana	Yes	Yes	Uncertain	No	No	Yes	Yes	Yes	No	Yes	Uncertain	Yes	Yes	77%
UnitedHealth	No	Yes	Yes	Yes	Uncertain	No	Yes	Yes	Yes	Yes	Yes	No	Yes	77%
Medicaid														
Arizona	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	No	No	62%
California	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	85%
Connecticut	Uncertain	Yes	Yes	Yes	Uncertain	No	Yes	Yes	Yes	Yes	Yes	No	No	77%
Delaware	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Uncertain	Yes	Yes	Yes	Yes	85%
Florida	No	Yes	Yes	Uncertain	No	No	Yes	Yes	No	Yes	Yes	No	Yes	62%
Georgia	No	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	No	No	54%
Illinois	No	Yes	No	No	No	Yes	Yes	No	No	Yes	No	No	No	31%
Indiana	No	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	No	No	54%
Iowa	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100%
Kansas	Uncertain	Yes	Yes	Yes	Uncertain	Uncertain	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100%
Kentucky	No	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	No	No	54%
Maryland	No	Yes	No	No	No	No	Yes	Yes	Yes	Yes	Yes	No	No	46%
Michigan	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Uncertain	No	Yes	69%
Minnesota	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100%
Missouri	No	Yes	Yes	Yes	Uncertain	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	85%
Montana	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	85%
Nebraska	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	Yes	Yes	69%
Nevada	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100%
New Hampshi	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	85%
North Carolin	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Uncertain	Yes	Yes	100%
Ohio	No	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	No	No	54%
Oklahoma	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	77%
Oregon	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	92%
Pennsylvania	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	85%
South Dakota	No	Yes	Yes	Yes	No	Yes	Yes	No	No	Yes	Uncertain	No	No	54%
Texas	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Uncertain	Yes	Yes	92%
Vermont	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	No	No	62%
Washington	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100%
West Virginia	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	100%
Wisconsin	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	No	No	54%
Proportion	33%	100%	94%	89%	31%	61%	100%	94%	78%	100%	86%	56%	69%	

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Coverage

- Close to 90% for:
  - Types I, II, III
  - 2 and 3 copies SMN2
  - Pediatric
- Right direction for:
  - 1 and 4 copies SMN2
  - Adult
  - Trach and Non-Invasive
- Restrictive for:
  - Types 0 and IV
- Restrictive States:
  - IL, MD, GA, IN, KY, OH, SD, WI

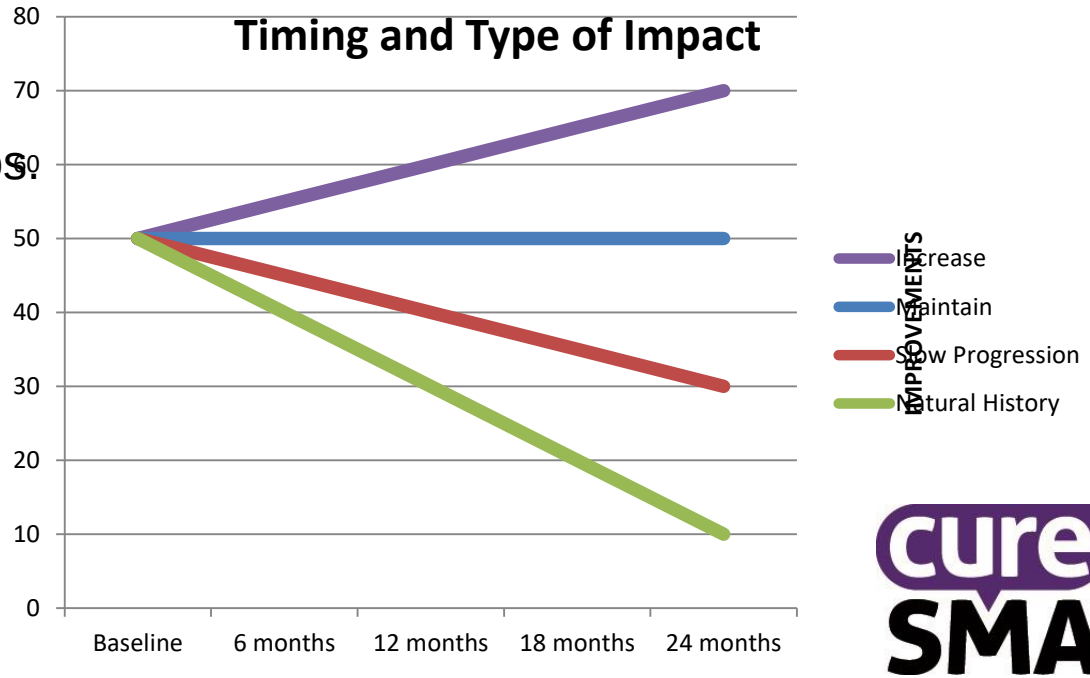
- More data needed:
  - Publications on existing data
  - Untested areas – need to collect data
  - Adult and fusion/devices

Medicare Advocacy

- Medicare's process for new drugs, like Spinraza, is different from Medicaid's approach.
  - Medicaid issues a policy up front that guides whether individual claims are approved or denied.
  - In Medicare, the process begins with individual claims being reviewed on a case-by-case basis until a consensus emerges. Once that happens, local policies are issued, potentially followed by a national policy.

Renewals Reauthorizations

- Drug is given enough time to work.
  - by building up the muscle over time
  - taking place over a year or two rather than months.
- The measurements of impact are being made as a comparison against what would have happened without the drug.
  - In SMA, patients decline and go downhill in their function over time
  - An impact from a drug is anything better than this.
  - Which could be improving (now going up) or maintaining (staying stable and keeping functions) or even a decline but at a slower than normal/usual/expected rate.
- Keep your own records – notes and videos.
- Annual membership update
- Ongoing proof:
  - 6 months to annually to longer
  - Real world data

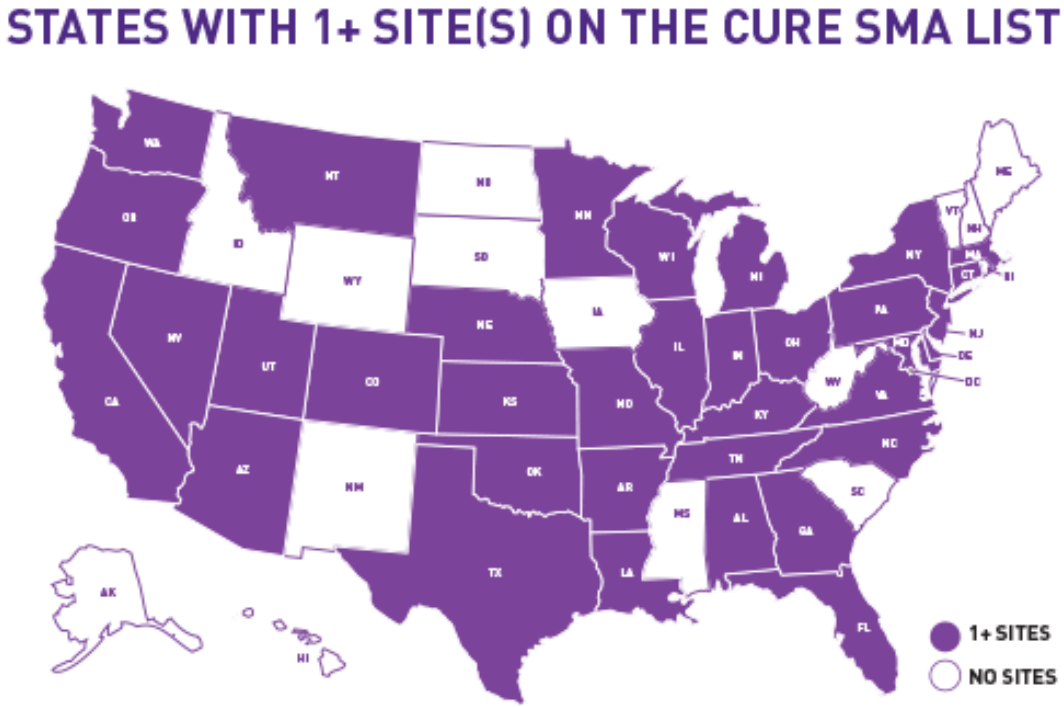


Cure SMA Resources

Cure SMA Spinraza Site List

118 confirmed sites

- Searchable by:
  - State
  - Pediatric/adult



www.cureSMA.org/spinraza/sites

Information on Specific Programs

- Resources for all drug programs that have reached the pivotal trial stage, or have been approved by the FDA. Includes:
  - Information about the treatment and how it works.
  - Current clinical trial information (for pivotal stage programs).
  - Dosing sites and access updates (for approved treatments).
  - Links to past announcements on the program.
  - Etc.

Information on Specific Programs

- Spinraza (Biogen)
  - **www.cureSMA.org/spinraza**
- AVXS-101 (AveXis)
  - **www.cureSMA.org/avxs101**
- RG7916/RO7034067 (Genentech/Roche)
  - **www.cureSMA.org/rg7916**

Insurance Coverage Resources

- Current policies for Spinraza:
  - Visit: **www.cureSMA.org/spinraza**
  - Find: Resources → Insurance Policies
- *Choice and Connection to Care: A Health Insurance Roadmap for People Living with Spinal Muscular Atrophy (SMA) and Their Caregivers*
  - A Cure SMA care series booklet on navigating commercial and government health insurance options.
  - Visit: **www.cureSMA.org/support-care/care-publications**
- Know Your Resources: How Congressional Caseworkers Can Help You Obtain Insurance Coverage for New Therapies
  - Visit: **www.curesma.org/news/congressional-caseworkers-help.html**

Other Resources

- List of currently recruiting trials:
  - **www.cureSMA.org/currenttrials**
- Resources on care and medical issues, for you and your doctor:
  - **www.cureSMA.org/support-care**

Current and Upcoming Clinical Trials

Current US Trials

A Study of CK-2127107 in Patients With Spinal Muscular Atrophy (Clinicaltrials.gov Identifier: NCT02644668)

- General Criteria*: Teens & adults 12 years of age or older (ambulatory and non-ambulatory) with SMA type II, III or IV.
- Phase: Phase 2, with 16 US sites

A Study to Investigate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics and Efficacy of RO7034067 in Infants with Type 1 Spinal Muscular Atrophy (Clinicaltrials.gov Identifier: NCT02913482)

- Also Known By: FIREFISH
- General Criteria*: Infants age 1-7 months with SMA type I.
- Phase: Phase 3 with three US sites in Palo Alto, Boston, and New York City.

A Study to Investigate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics and Efficacy of RO7034067 in Type 2 and 3 Spinal Muscular Atrophy Participants (Clinicaltrials.gov Identifier: NCT02908685)

- Also Known By: SUNFISH
- General Criteria*: Children, teens and adults age 2-25 with SMA type II or III.
- Phase: Phase 2, with no US site currently

A Study of RO7034067 in Adult and Pediatric Participants with Spinal Muscular Atrophy (Clinicaltrials.gov Identifier: NCT03032172)

- Also Known By: JEWELFISH
- General Criteria*: Children, teens and adults age 12-60 who have previously been exposed to an SMN2-targeting therapy.
- Phase: Phase 2, with site in New York City.

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Current US Trials

Gene Replacement Therapy Clinical Trial for Patients With Spinal Muscular Atrophy Type 1 (STR1VE) (Clinicaltrials.gov Identifier: NCT03306277)

- General Criteria: 1 or 2 copies of SMN2, < 6 months (< 180 days) of age
- Patients must have a swallowing evaluation test performed prior to administration of gene replacement therapy
- Phase: Phase 3, for 15 patients at 16 sites in the US

Study of Intrathecal Administration of AVXS-101 for Spinal Muscular Atrophy (STRONG) (Clinicaltrials.gov Identifier: NCT03381729)

- Up to 60 months of age and three copies of SMN2 and symptoms < 12 months of age
- Sit independently and not standing or walking independently
- Phase: Phase for 27 subjects at 11 sites in the US

Planned Studies, Not Yet Open

Scholar Rock

- SRK-015 (myostatin inhibitor) to improve muscle strength
- Safety trial on health volunteers by Q2 2018
- Proposed patient trials for SMA patients who are on therapies to up-regulating SMN levels and as monotherapy in certain populations.

sTR1VE EU

- AVXS gene therapy
- European version of current US pivotal trial that is currently enrolling

SPRINT (pre-symptomatic trial)

- AVXS gene therapy with one-time IV infusion
- Multi-national trial by Q2 2018 in pre-symptomatic patients with SMA Types 1, 2, 3
- 44 patients with 2, 3, and 4 copies of SMN2, less than six weeks of age and pre-symptomatic

REACH (broad enrollment)

- AVXS gene therapy with one-time IT injection.
- Multi-national trial expected in late 2018 or early 2019 in SMA Types 1, 2 and 3
- 50 patients with SMA Types 1, 2 and 3, between six months and 18 years of age

Considerations to be Discussed with Neurologist on Approved Treatment vs. Trials

- Evaluate available safety and efficacy data
- Evaluate possibility of placebo
  - Small molecule versus other drug modality
  - Type I enrollment versus other SMA types
- Evaluate route and timing of administration
- Understand inclusion and exclusion criteria
- Determine whether previous drug exposure allowed and when
  - *Most trials today will prohibit co-utilization with Spinraza*
  - Particularly if another SMN enhancer
  - Increased motor function must be detected for approval and much harder when on another SMN enhancer

Considerations to be Discussed with Neurologist on Approved Treatment vs. Trials

- **Recommended not to wait for future trials to open, if other options available now**
  - Delays in opening trials are common and can't be predicated
  - Changes in inclusion and exclusion are common until formally announced
  - Earliest possible administration of SMN enhancing drugs yield best results

Timing is one of biggest factor in degree of response to SMN!

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Combination Therapies: Strategic Goal at Cure SMA

- Develop combination therapies for maximally effective treatments for all types and stages of SMA
  - Identify non-SMN drug targets for combination therapies
  - Test efficacy of combinations
  - SMN2 splicing, SMN promoter, SMN stability, SMN replacement, muscle strength, motor neuron function
- Optimizing SMN enhancing therapies: second in class drugs
  - Identify tissues for SMN up-regulation (neuronal versus non-neuronal)
  - Determine how SMN levels are controlled to exploit for 2nd generation drugs
  - Determine the window of benefit for SMN in different SMA types
- **Current RFPs in basic & translational research geared to these goals**

Considerations for Combination Therapies: Combinations Must be Chosen Carefully

- **General**
  - Are they safe when used together?
  - Does the benefit of using together outweigh the risk?
  - Do they result in additive clinical benefit?
  - Does one reduce efficacy or drug availability of other?
  - Can they readily be co-administered?
- **Combining Two SMN Enhancers**
  - Are SMN levels increased together over either drug alone?
  - Do they work by different biological mechanisms?
  - Do they target different tissues, resulting in SMN enhancement in a broader distribution of cell types together than either alone?
  - Do they provide longer duration of effect together than alone?
  - If not yes to one, utility of the particular combination is unlikely.
  - Readouts in trials with two combination therapies more challenging.

Importance of Clinical Care

Clinical Care

- Continue care basics
  - Optimize respiratory care and support
    - Do not stop what has worked
  - Optimize nutrition and weight
    - Some centers are reporting a need for more protein intake with Spinraza therapy.
      - Please work with your dietician
- Pursue physical and occupational therapy
  - Goals:
    - Optimize impact of new treatments
    - Optimize function
    - Optimize independence

Clinical Care

- Illness Considerations
  - Avoid others who are ill
  - Good handwashing
  - Get influenza vaccine every year
    - Keep routine immunizations up to date
  - Have an illness plan with your doctor
    - Optimize secretion clearance and coughing
    - Optimize fluid intake

Q & A

For More Information

- A copy of this slide deck will be sent out after webinar
  - This email also includes a survey
- Slide deck and recording posted in our news section during the next week (**www.cureSMA.org/news**)
- Email **info@curesma.org**
- Call 800.886.1762