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Please note that unless otherwise stated, the share prices used in this presentation is taken at the close of business for the most recent practical day.
Pick best performing exhibiting stock over next year

Winner to be announced next year

Details available on competition entry form

*Terms and conditions apply
Juvenescence: Investing in the Age of Longevity

Market Overview

Summary
U.S. & Trump

• Trump a Keynesian Laffer curve man
• Substantial borrowing for infrastructure
• Higher interest rates coming
• Offshore USD repatriation amnesty a possibility
• Markets priced to perfection
Cyclically Adjusted PE Ratio

- Excluding dot com exuberance, CAPE is approaching all time high.
- Ten-year forward average returns fall monotonically as CAPE at entry increase.
- BEWARE of the “this time is different” pundits – fundamental valuation ALWAYS matters.

Source: Bloomberg
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Number of listed companies</td>
<td>4,796</td>
<td>7,322</td>
<td>3,671</td>
</tr>
<tr>
<td>Market cap USD billions (2016)</td>
<td>$2,975</td>
<td>$12,322</td>
<td>$25,303</td>
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<tr>
<td>GDP billions (2016)</td>
<td>$6,325</td>
<td>$11,769</td>
<td>$18,565</td>
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<tr>
<td>Market cap as % GDP</td>
<td>47.0%</td>
<td>104.7%</td>
<td>136.3%</td>
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<tr>
<td>Individual direct ownership</td>
<td>50.0%</td>
<td>27.2%</td>
<td>21.5%</td>
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<tr>
<td>Number of ETFs (US domestic)</td>
<td>0</td>
<td>2</td>
<td>658</td>
</tr>
<tr>
<td>NYSE annual share volume</td>
<td>5,360</td>
<td>104,636</td>
<td>316,495</td>
</tr>
<tr>
<td>Equity options traded (contracts in millions)</td>
<td>32</td>
<td>199</td>
<td>3,626</td>
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</table>

<table>
<thead>
<tr>
<th></th>
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<tr>
<td>Mutual funds</td>
<td>$40</td>
<td>$1,725</td>
<td>$3,725</td>
</tr>
<tr>
<td>Index funds</td>
<td>&lt;$1</td>
<td>$85</td>
<td>$1,990</td>
</tr>
<tr>
<td>Hedge funds – long/short equity</td>
<td>&lt;$1</td>
<td>$130</td>
<td>$850</td>
</tr>
<tr>
<td>Venture capital</td>
<td>$4</td>
<td>$48</td>
<td>$333</td>
</tr>
<tr>
<td>Buyout</td>
<td>&lt;$1</td>
<td>$80</td>
<td>$827</td>
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</table>
SIDESHOW

STATE FAIR FREAKZ PRESENTS

The BIG CIRCUS

SIDE SHOW

THE STRANGEST SHOW ON EARTH !!!

MAIN ENTRANCE
The Brexit Side Show

• Brexit likely to become a side show due to major imbalances within the EU:
  – Unsustainable debt levels in periphery
  – Highly vulnerable banking system
  – Germany export dependent – TARGET 2
  – Election cycle – France & Germany
UK’s EU Budget Contributions

• UK’s payments to the EU budget since 1973 approx. £500b

• UK’s rebates reduces this figure to £380b which is still nearly £9b p.a.

What could £380b buy you?
The conditions of admission and the adjustments to the Treaties on which the Union is founded, which such admission entails, shall be the subject of an agreement between the Member States and the applicant State. This agreement shall be submitted for ratification by all the contracting States in accordance with their respective constitutional requirements.

Article 50

1. Any Member State may decide to withdraw from the Union in accordance with its own constitutional requirements.

2. A Member State which decides to withdraw shall notify the European Council of its intention. In the light of the guidelines provided by the European Council, the Union shall negotiate and conclude an agreement with that State, setting out the arrangements for its withdrawal, taking account of the framework for its future relationship with the Union. That agreement shall be negotiated in accordance with Article 218(3) of the Treaty on the Functioning of the European Union. It shall be concluded on behalf of the Union by the Council, acting by a qualified majority.
Europe

• Europe continues to move from crisis to crisis
• Elections loom in Germany and France
• Populism makes further integration unlikely
• Fully expect EU to lose further member in the next 3 years
Target2 Balances

Source: European Central Bank
Euro Area 10 Year Spread Over Bunds

Source: Bloomberg
Emerging Markets

• Strong USD a negative for EMs
• China significant non-performing loans
• Significant debt problems elsewhere
• Still commodity dependent
Macro Summary

- Central bank derived capital misallocation
- China slowdown
- Imbalances within the EU remain
- Strong USD
- Equity and bond markets priced to perfection
THE NEXT BIG THING
Global Financial Crisis

3D printing

Battery technology

Human redundancy

BREXIT

Eurozone crisis

Fracking

Artificial intelligence

Robotics

Unsustainable Chinese growth

Prime London real estate

Gold bull market

Depreciating yen

Uranium bull market

Biotech bull market

Internet of things

Age of automation

Renewable energy boom
“I don’t have a vision of the future. I have a vision of now.”

King Gillette - Founder Gillette Safety Razor Company
INVESTING IN THE AGE OF LONGEVITY
What is Ageing?
Is Ageing Pre-Programmed?
Bridge to Longevity
Actuarial Escape Velocity
AGEING IS VERY COMPLEX
Four million years produced an 11-year increase from 20 to 31.

115 years produced a 41 year increase.
WHAT IS AGEING?

*When wear and tear out runs repair.*
Correlation between Ageing & Disease

- **Global Cumulative DALYs (thousands)**
  - 0-27 days
  - 1-59 months
  - 5-14 years
  - 15-29 years
  - 30-49 years
  - 50-59 years
  - 60-69 years
  - 70+ years

- **Respiratory infections**
- **Neonatal conditions**
- **Nutritional deficiencies**
- **Malignant neoplasms**
- **Diabetes mellitus**
- **Endocrine, blood, immune disorders**
- **Mental and behavioral disorders**
- **Neurological conditions**
- **Sense organ diseases**
- **Cardiovascular diseases**

Source: World Health Organisation – DALY – Disability Adjusted Life Year
IS AGEING PRE-PROGRAMMED?
MODELS OF AGEING

Yeast - Saccharomyces cerevisiae
Mouse - Mus musculus
Earth worm - Caenorhabditis elegans
Fruit fly - Drosophila melanogaster
Historically high infant mortality rate

Extended period of healthy life

Steep decline reduces burden on healthcare system

**Life Expectancy**

<table>
<thead>
<tr>
<th>Year</th>
<th>% of deaths</th>
<th>Year</th>
<th>% of deaths</th>
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<tbody>
<tr>
<td>1900</td>
<td>12%</td>
<td>2015</td>
<td>23%</td>
</tr>
<tr>
<td>Influenza and pneumonia</td>
<td>12%</td>
<td>Heart disease</td>
<td>23%</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>11%</td>
<td>Cancer</td>
<td>23%</td>
</tr>
<tr>
<td>Diarrheal disease</td>
<td>8%</td>
<td>COPD</td>
<td>6%</td>
</tr>
<tr>
<td>Heart disease</td>
<td>8%</td>
<td>Accidents</td>
<td>5%</td>
</tr>
<tr>
<td>Stroke</td>
<td>6%</td>
<td>Stroke</td>
<td>5%</td>
</tr>
<tr>
<td>Kidney disease</td>
<td>5%</td>
<td>Alzheimer's disease</td>
<td>4%</td>
</tr>
<tr>
<td>Accidents</td>
<td>4%</td>
<td>Diabetes mellitus</td>
<td>3%</td>
</tr>
<tr>
<td>Cancer</td>
<td>4%</td>
<td>Influenza and pneumonia</td>
<td>2%</td>
</tr>
<tr>
<td>Senility</td>
<td>3%</td>
<td>Kidney disease</td>
<td>2%</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>2%</td>
<td>Suicide</td>
<td>2%</td>
</tr>
</tbody>
</table>

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At present, more than one year of research is required for each additional year of expected life. Longevity escape velocity occurs when this ratio reverses, so that life expectancy increases faster than one year per one year of research, as long as that rate of advance is sustainable.
Usual Suspects:
• Stop smoking
• Stay active
• Lose excess fat
• Eat a balanced diet
• Get enough sleep
• Exercise your brain

Experimental Options:
• Metformin
• Resveratrol/pterostilbene
• Nicotinamide (NR/NMN)
• Rapamycin/rapalogs
• Bromocriptine
• Organ replacement
• Gene therapy
• Bio-printing – tissue and organ
**Sirtuins**

- Sirtuins are a family of proteins
- Intimate connection between sirtuins and NAD⁺ (Nicotinamide adenine dinucleotide)
- NAD⁺ availability decreases over age
- Mechanistically regulate energy and metabolism
- NAD⁺ & sirtuins crucial in ageing/longevity control
DRUGS/TARGETS & PATHWAYS OF AGEING

Rapamycin

Metformin

mTOR PATHWAY

TOR = target gene of rapamycin, antibiotic soil organism

GROW FACTORS

NUTRIENTS

CELLULAR STRESS

mTOR PROTEIN (FRAP1 Gene)

mTOR inhibitors
Rapamycin*, resveratrol
*Srccinus FDA-approved drug

Transcription Initiation Factor
PROTEIN MAKING

Cell Growth & Multiplication
Digestion of Cellular Debris
New Blood Vessel Formation (Angiogenesis)
Cell Metabolism

CELL SURVIVAL

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Phenomenon by which normal cells cease to divide

Not solely caused by ageing – more generally due to DNA damage in response to endogenous and exogenous environment

Leonard Hayflick observed replicative senescence whereby fibroblasts reach a maximum of 50 divisions then become senescent – the Hayflick Limit

Senescent cells don’t die, remain metabolically active and often promote inflammation
Conventional education model broken

Work longer and have multiple careers

When to have children?

Where does it stop 100, 200 ... 500 years old?

War, famine and plagues become determinants of life span
IMPLICATIONS OF INCREASING LONGEVITY

18 - World Population
- in Billions
- Data from UN

15 - 1800-2015 estimates

12 -

9 -

6 -

3 -

0 -

1800 1900 2000 2100

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DEFUNCT
KEY OPINION LEADERS

- **Professor David Sinclair**
  - Department of Genetics Harvard Medical School
- **Aubrey de Grey**
  - Chief Scientific Officer, SENS Research Foundation
- **Dr Walter Bortz**
  - Professor of Medicine, Stanford University School of Medicine
- **Cynthia Kenyon**
  - Vice President Ageing Research, Calico
- **Dr Nir Barzilai**
  - Founding Director, Institute for Aging Research
- **Dr Alex Zhavoronkov**
  - Chief Executive Officer, Insilico Medicine
- **Nathanial David**
  - President, Unity Biotechnology
- **Professor Linda Partridge**
  - Max Planck Institute for Biology of Ageing
- **Laura Deming**
  - Partner, The Longevity Fund
- **Elizabeth Parish**
  - Chief Executive Officer – Bioviva
- **Patrick Cox**
  - Maudlin Economics
- **John Mauldin**
  - Founder, Maudlin Economics
- **Dr Peter Attia**
  - The Eating Academy
- **Professor Alastair Buchan**
  - Dean of Medical School, Oxford University
- **Dr Matthew Freeman**
  - Head, Sir William Dunn School of Pathology, Oxford U
<table>
<thead>
<tr>
<th></th>
<th>Longevity Companies</th>
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<tbody>
<tr>
<td>1.</td>
<td>Alkahest</td>
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<td>2.</td>
<td>BioTime</td>
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<td>3.</td>
<td>Bioviva Science</td>
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<td>4.</td>
<td>Bluebird Bio</td>
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<td>5.</td>
<td>Calico</td>
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<td>Chronos Therapeutics</td>
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<td>7.</td>
<td>CohBar</td>
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<td>8.</td>
<td>Dignity</td>
</tr>
<tr>
<td>9.</td>
<td>Editas Medicine, Inc</td>
</tr>
<tr>
<td>10.</td>
<td>Elysium Health Inc</td>
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<tr>
<td>11.</td>
<td>Freenome</td>
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<td>12.</td>
<td>Genescient</td>
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<td>13.</td>
<td>Gero</td>
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<td>14.</td>
<td>Grail</td>
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<td>15.</td>
<td>Human Longevity Inc</td>
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<td>16.</td>
<td>Hydra Life Sciences</td>
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<td>17.</td>
<td>Insilico Medicine, Inc</td>
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<td>18.</td>
<td>Intellia Therapeutics, Inc</td>
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<td>19.</td>
<td>KITE Pharma</td>
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<td>20.</td>
<td>L-Nutra</td>
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<td>21.</td>
<td>Metrobiotech</td>
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<td>22.</td>
<td>Navitor Pharmaceuticals</td>
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<td>Oisin Biotechnologies</td>
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<td>24.</td>
<td>Omnity</td>
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<td>25.</td>
<td>Organovo Holdings, Inc</td>
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<td>26.</td>
<td>Proteostasis Therapeutics</td>
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<td>27.</td>
<td>Regeneron</td>
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<td>28.</td>
<td>Samumed</td>
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<td>29.</td>
<td>Sangamo BioSciences, Inc</td>
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<td>30.</td>
<td>SENS</td>
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<tr>
<td>31.</td>
<td>The Methuselah Foundation.</td>
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<tr>
<td>32.</td>
<td>Service Corporation</td>
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<td>33.</td>
<td>Sibelius Natural Products</td>
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<tr>
<td>34.</td>
<td>SIWA Therapeutics</td>
</tr>
<tr>
<td>35.</td>
<td>Unity Biotech</td>
</tr>
</tbody>
</table>
Macro Ideas

- Gold
- Silver
- KOPSI – Korean equity ind.
- Malaysian Ringgit (vs. USD)
- Mexican Peso (vs. USD)
- **Short** French bonds
- **Short** Italian bonds
<table>
<thead>
<tr>
<th>Long</th>
<th>US Market Cap</th>
<th>Dividend Yield</th>
<th>P/E Ratio</th>
<th>EV / EBITDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amarin Corp PLC</td>
<td>868</td>
<td>0.00%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Amgen Inc</td>
<td>122,281</td>
<td>2.77%</td>
<td>15.57</td>
<td>8.78</td>
</tr>
<tr>
<td>Aurora Labs Ltd</td>
<td>103</td>
<td>0.00%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Avation PLC</td>
<td>163</td>
<td>1.13%</td>
<td>7.13</td>
<td>9.87</td>
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<tr>
<td>Bristol-Myers Squibb Co</td>
<td>92,425</td>
<td>2.78%</td>
<td>20.16</td>
<td>18.08</td>
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<tr>
<td>Condor Gold PLC</td>
<td>52</td>
<td>0.00%</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Editas Medicine Inc</td>
<td>792</td>
<td>0.00%</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Gilead Sciences Inc</td>
<td>88,528</td>
<td>3.07%</td>
<td>6.40</td>
<td>4.70</td>
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<td>Reinsurance Group of America I</td>
<td>8,138</td>
<td>1.29%</td>
<td>12.07</td>
<td>-</td>
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<tr>
<td>Salvarx Group PLC</td>
<td>13</td>
<td>0.00%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Sony Corp</td>
<td>40,967</td>
<td>0.56%</td>
<td>-</td>
<td>8.72</td>
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<tr>
<td>Synergy Pharmaceuticals Inc</td>
<td>1,007</td>
<td>0.00%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Wal-Mart Stores Inc</td>
<td>214,954</td>
<td>2.92%</td>
<td>16.15</td>
<td>7.52</td>
</tr>
<tr>
<td>Zenith Minerals Ltd</td>
<td>18</td>
<td>0.00%</td>
<td>-</td>
<td>-</td>
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# Short Ideas

<table>
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<tr>
<th>Short</th>
<th>US Market Cap</th>
<th>Dividend Yield</th>
<th>P/E Ratio</th>
<th>EV / EBITDA</th>
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<tbody>
<tr>
<td>Alphabet Inc</td>
<td>572,898</td>
<td>0.00%</td>
<td>29.88</td>
<td>15.39</td>
</tr>
<tr>
<td>Amazon.com Inc</td>
<td>405,164</td>
<td>0.00%</td>
<td>172.47</td>
<td>28.62</td>
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<tr>
<td>Deutsche Bank AG</td>
<td>26,223</td>
<td>1.22%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Facebook Inc</td>
<td>405,407</td>
<td>0.00%</td>
<td>43.01</td>
<td>20.51</td>
</tr>
</tbody>
</table>
Summary

• Macro picture is confused but Japan is best bet for gains
• The fall of American titan stocks cannot be too far away
• Longevity will be a money fountain
• It will also transform the trajectory of lives, and leads to questions about automation, education etc.
WHAT'S THE DIFFERENCE BETWEEN LIVING TO 83 VS 110?

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