Investor update: RSV older adults and maternal vaccine candidates

Data presented at ID Week 2020
22 October 2020
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All expectations and targets regarding future performance and the dividend should be read together with “Assumptions related to 2020 guidance and 2016-2020 outlook” on page 68 of our second quarter 2020 earnings release.
Agenda

R&D approach and RSV burden of disease
Dr Hal Barron
Chief Scientific Officer and President R&D

Vaccines R&D and RSV vaccines data
Dr. Emmanuel Hanon
Senior Vice President, Vaccines R&D

RSV opportunity
Roger Connor
President, Global Vaccines

Presentation
25 mins

Q&A
25 mins

RSV, respiratory syncytial virus
Strengthening our R&D pipeline through a focus on science related to the immune system, the use of human genetics, and advanced technologies
### Our focus on immunology is resulting in a world class Infectious Diseases portfolio

**First time in human (Phase 1)**
- 3856275* (CCL17 inhibitor) OA pain
- 3745417 (STING agonist) cancer
- 3168689* (CRK-12 inhibitor) visceral leishmaniasis
- 3511294* (LA anti-IL5 antagonist) asthma
- 3810109* (broadly neutralizing antibody) HIV
- 3957142* (NYESO1 ImmTAC) cancer
- 3439171* (H-PGDS inhibitor) DMD
- 3368716* (Type 1 PRMT inhibitor) cancer
- 3174998* (OX40 agonist) cancer
- 2798745* (TRPV4) DME
- 6097608* (CD96) cancer
- C. difficile*
- SAM (rabies model)
- S. aureus*
- COVID-19 (Clover Biopharmaceuticals)**
- COVID-19 (Medicago)**
- COVID-19 (Sanofi)**

**Proof of concept (Phase 1b/2)**
- 3640254 (maturation inhibitor) HIV
- 3228836* (HBV ASO) HBV
- 3772847* (IL33r antagonist) asthma
- Lete-cel* (3377794 NY-ESO-1 TCR) cancer
- 2330811 (OSM antagonist) systemic sclerosis
- 2330672 (linerixibat, IBATi) cholestatic pruritus in PBC
- cabotegravir** LA + rilpivirine* LA HIV
- dolutegravir** (once daily) HIV
- belantamab mafodotin* (BCMA ADC) multiple myeloma
- Zejula* (PARP inhibitor) ovarian cancer**
- dostarlimab* (PD-1 antagonist) dMMR/MSI-H EC
- otilimab* (3196165) RA, COVID-19*
- geopotidacin* (2140944) uUTI and GC
- 2330811 (OSM antagonist) systemic sclerosis
- 2330672 (linerixibat, IBATi) cholestatic pruritus in PBC
- TSR-033* (LAG3 antagonist) cancer
- Mveneo liquid
- RSV paediatric
- RSV maternal*
- RSV older adults**
- Therapeutic HBV**
- Malaria* (fractional dose)
- Shigella*

**Pivotal (Phase 2/3)**
- Benlysta* + Rituxan SLE**
- cabotegravir** LA + rilpivirine* LA HIV
- daprodustat (HIF-PHI) anaemia
- Nucala COPD/HES/nasal polyps
- belantamab mafodotin* (BCMA ADC) multiple myeloma
- Zejula* (PARP inhibitor) ovarian cancer**
- dostarlimab* (PD-1 antagonist) dMMR/MSI-H EC
- otilimab* (3196165) RA, COVID-19*
- geopotidacin* (2140944) uUTI and GC
- 3358699* (ICOS receptor agonist) HNSCC**
- GSK4182136* SARS-CoV2 antibody
- Shingrix immuno-compromised*
- Bexsero infants (US)
- MMR (US)
- Menveo

**Marketed**
- Shingrix
- Bexsero
- Menevo
- Fluarix
- Priorix / Priorix Tetra / Varilix
- Infanrix / Pediarrison / Boostrix
- Syntofrix
- Hepatitis vaccines
- Rotarix
- Cervarix
- Rukobia
- Dovato
- Juluca
- Trivicay
- Trumeq
- Epzicom / Kivexa
- Selzentry
- Zinnat
- Zeffix
- Viread
- Augmentin

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*Note: Only the most advanced indications are shown for each asset*

*In-license or other alliance relationship with third party; **Additional indications also under investigation

1. In Phase 1/2 study; 4. Otilimab in COVID-19 in Phase proof of concept, under investigation for inflammatory complications of coronavirus infection
2. In Phase 1 study; 3. Cabotegravir in COVID-19 in Phase 2b proof of concept
3. Oti/opanib in COVID-19 in Phase 2a proof of concept, under investigation for inflammatory complications of coronavirus infection
4. Oti/opanib in COVID-19 in Phase 2a proof of concept, under investigation for inflammatory complications of coronavirus infection

TB: tuberculosis; uUTI: uncomplicated urinary tract infection; GC: gonorrhoea
RSV vaccine opportunity: high unmet need
Burden most significant in infants and older adults

About RSV
• Common respiratory virus that can be serious, especially for infants and older adults
• Most common cause of bronchiolitis and pneumonia in children <1 year of age in US
• Significant cause of respiratory illness in older adults
• Morbidity and mortality comparable (and more severe some seasons) to influenza
• No vaccine currently available

Disease Burden

<table>
<thead>
<tr>
<th>Children under 5</th>
<th>Older Adults</th>
</tr>
</thead>
</table>
| 3 million hospitalisations globally per year
Leading cause of hospitalisation in infants <1 year in the US | 177,000 hospitalisations, 14,000 deaths per year in the US alone |

RSV-associated hospitalisation burden in the USA

4. CDC - [https://www.cdc.gov/features/rsv/](https://www.cdc.gov/features/rsv/) 5. 1997 – 2009 data. Figure adapted from Matias G et al. BMC Public Health 2017;17:271

Healthy young adults
RSV infection is generally associated with common cold-like symptoms
Vaccines R&D approach

Dr. Emmanuel Hanon
Senior Vice President and Head of R&D, GSK Vaccines
Our R&D approach for vaccines

Science

X

Technology

X

Culture

Design and deliver ground-breaking vaccines
- Shingrix and MenABCWY (lifecycle management)
- Key priority assets: RSV older adults, maternal, paediatric
- Therapeutic (Chronic HepB)
- Antimicrobial resistance (C. Difficile, S. Aureus)

Leverage disruptive technologies
- Address unmet needs and improve vaccine efficacy
- Make manufacturing simpler and faster
- Speed up product development timelines

Evolve vaccines R&D
- Focus on science and resourcing to accelerate development
- Attract and retain leading scientists and best talent
- Smart risk-taking and single point of accountability
Vaccines innovation approach built on platform technologies

Adjuvant systems | Bioconjugation
---|---
Adenoviral vectors | mRNA

Improve efficacy
Faster, simpler and more efficient development & manufacturing
1 In-license or other alliance relationship with third party
2 Menveo booster also in development
3 Porcine circovirus free formulation
† GSK is contributing pandemic adjuvant to COVID-19 vaccines collaborations

Note: Candidates using adjuvants are designated
GSK approach to RSV vaccines
Pre F protein structure gives greater chance of success

Limited success with post fusion RSV F protein which hides critical neutralising sites

New generation pre fusion RSV F protein exposes multiple essential neutralising sites

RSV vaccine candidates
Target protection against RSV across 3 key target populations

3 RSV vaccine candidates - All with FDA fast track designation

- **maternal** passive immunisation
  - Features pre-fusion antigen
  - Stabilised formulation designed to optimize rise in neutralising antibodies
  - Polyclonal maternal antibodies to confer protection for first 6 months
  - Phase 3 start expected Q4 2020

- **paediatric** active immunisation
  - Immunological priming to confer protection from 3 months to 2 years
  - Using adenoviral vector-based technology, a potent platform to induce an immunological memory
  - In Phase 2 development

- **+ older adults** active immunisation
  - Features pre-fusion antigen combined with AS01 adjuvant
  - Proven adjuvant to stimulate greater immune response in older adult population (as in Shingrix)
  - Phase 3 start expected Q1 2021
Key data on immunogenicity and tolerability for Maternal Vaccine Candidate (RSVPreF3) Administered to Non-pregnant Women

Data first presented at ID Week 2020
21 October 2020
Study designed to evaluate multiple doses in non-pregnant women

Study summary

- Phase I/II, randomised, observer-blind, placebo controlled, multicentre study to evaluate the safety, reactogenicity and immunogenicity of different dose levels
- 502 healthy non-pregnant women age 18-49 years enrolled
- Received 1 intramuscular doses of either 30, 60, 120 μg of RSVPreF3 vaccine or placebo
- Solicited adverse events (AEs) for 7 days post vaccination; unsolicited AEs for 30 days post vaccination; serious adverse events (SAEs) collected for 181 days post vaccination
- Immune responses collected for 91 days post vaccination
One dose is highly immunogenic and persistent at all dose levels

8-14 fold increase in RSV-A and RSV-B neutralising antibodies titers at Day 8.

Persistent immune response of 5-6 fold antibodies increase was maintained at day 91.
All doses well tolerated

Safety summary

- One dose administered all dose levels was well-tolerated
- The most frequently reported solicited adverse events were pain at injection site and headache
- Low reporting of Grade 3 solicited and unsolicited AEs
- No clinically significant changes in laboratory parameters occurred
- 3 SAEs were reported; none was related to vaccination

AEs = adverse events
SAEs = serious adverse events
Key data on immunogenicity and tolerability for Older Adults Vaccine Candidate

Data first presented at ID Week 2020
21 October 2020
Study designed to evaluate antigen and adjuvant vaccine doses in target population

Study summary

- Phase 1 / 2, placebo-controlled, multi-country trial
- Evaluation of low, medium, high doses of RSVPreF3 antigen with and without adjuvants
- 2 doses administered 2 months apart
- Results include antibody and T-cell immune responses up to 1 month post-dose 1
- Results of safety/reactogenicity up to 1 month post-dose 1

Part A – Young Adults
Ages 18-40 years randomized to 4 groups (N = 48)

30 µg (n = 12)

60 µg (n = 12)

120 µg (n = 12)

Placebo (n = 12)

Part B – Older Adults
Ages 60-80 years randomized to 10 groups (N= 1000)

30 µg (n = 100)

30 µg (n = 100)

30 µg (n = 100)

AS01E

60 µg (n = 100)

60 µg (n = 100)

60 µg (n = 100)

AS01E

120 µg (n = 100)

120 µg (n = 100)

120 µg (n = 100)

AS01E

Placebo (n = 100)
Results in older adults showed strong induction of antibody and T-cell response

**Antibody Response**
Pre-specified phase 1 / 2 success criteria: **at least 6-fold increase** in RSV-A neutralising antibodies

<table>
<thead>
<tr>
<th>Dose</th>
<th>RSVPref3 Plain</th>
<th>AS01E</th>
<th>AS01B</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 µg</td>
<td>5.6</td>
<td>5.6</td>
<td>6.2</td>
</tr>
<tr>
<td>60 µg</td>
<td>6.6</td>
<td>6.7</td>
<td>6.6</td>
</tr>
<tr>
<td>120 µg</td>
<td>9.9</td>
<td>9.5</td>
<td>8.0</td>
</tr>
</tbody>
</table>

Geometric mean of fold increase in RSV-A NAb titer 30 days post vaccination compared to pre vaccination

**T-cell Response**
Pre-specified phase 1 / 2 success criteria: **statistically demonstrated superiority of AS01 adjuvanted** over plain formulations

Increase in the frequency of RSVPref3 specific-CD4+ T cells expressing ≥2 markers** 30 days post vaccination compared to pre vaccination

NAb = neutralising antibody
** at least 2 markers among IL-2, CD40L, TNFα, IFNγ
p-values computed by comparing the Geometric Mean Frequency (GMF) adjusted for covariates (Ancova model). (AS01B vs Plain, AS01E vs Plain)
Compelling neutralising antibody response and T-cell restoration

Meaningful boosting of neutralising antibodies response in older adults

Before vaccination: Deficiency of RSVPreF₃ specific-CD4+ T-cells in older adults before vaccination

1 month post vaccination: Restored RSVPreF₃ CD4+ T-cell frequencies in older adults close to young adult level using adjuvanted formulations

Results 1 month post vaccination captured D31 (day 31 post vaccination)
GMs = geometric means; GMTs = geometric mean titers; GMFs = geometric mean frequencies; CI = confidence intervals; NAb = neutralising antibody
** expressing at least 2 markers among IL-2, CD40L, TNFa, IFNg
Well tolerated in older adults

Safety summary

- First dose was well tolerated
- Most frequently reported AEs were pain at injection site, fatigue and headache.
- AE rates tended to be higher after AS01ₐ-adjuvanted formulations compared to other vaccine formulations in OA; grade 3 AE rates were generally low
- No safety concerns for laboratory parameters nor AEs or SAEs were identified
- Low reporting of SAEs; no related or fatal SAEs
- No vaccine-related safety concerns were raised

AEs = adverse events
SAEs = serious adverse events
RSV opportunity

Roger Connor
President, GSK Vaccines
RSV older adults represents major opportunity

<table>
<thead>
<tr>
<th>Significant, widespread health burden</th>
<th>Vaccination offers likely best solution</th>
<th>First-in-class potential</th>
</tr>
</thead>
<tbody>
<tr>
<td>• ~70m(^1) age 60+ (target US population)</td>
<td>• Older adults are at greater risk than young adults for serious complications from RSV because immune systems weaken with age(^2)</td>
<td>• Data supports adjuvanted approach for boosting neutralizing antibodies response and achieving T-cell restoration</td>
</tr>
<tr>
<td>• Infection can lead to pneumonia</td>
<td>• Symptoms, burden and seasonality similar to influenza</td>
<td>• Phase 3 programme on track to commence Q1 2021</td>
</tr>
<tr>
<td>• No specific treatment or prevention for RSV infection in older adults(^2)</td>
<td>• Opportunity to improve health outcomes and reduce healthcare costs</td>
<td></td>
</tr>
</tbody>
</table>

US disease burden (per year)

- 177,000 hospitalisations\(^2\)
- 14,000 deaths\(^2\)

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2. CDC: [https://www.cdc.gov/rsv/high-risk/older-adults.html](https://www.cdc.gov/rsv/high-risk/older-adults.html)
Maternal vaccination offers potential for broad protection from birth to 6 months

Burden most significant in young infants

- ~4m annual birth cohort in the US\(^1\)
- Leading cause of hospitalisation in infants <1 year in the US\(^2\)
- Nearly half of paediatric hospitalizations and deaths occur in infants <6 months of age\(^3\)

Opportunity to protect infants from birth

- Protect infants from birth up to 6 months of life through transfer of maternal antibodies
- Potential to protect mothers and reduce transmission from mother to child
- Possible co-administration with other recommended vaccines for pregnant women (pertussis and/or flu)
- Induction of polyclonal antibody response could help reduce the risk of escape mutant viruses
- Phase 3 start on track for Q4 2020
- Data in pregnant women to be presented in 2021

Integrated maternal and paediatric programmes target protection where burden most significant


Figure adapted from PharmacoEconomics, Economic Impact of Respiratory Syncytial Virus-Related Illness in the US, Vol. 22, 2004, 275–284. Paramore LC et al. © Adis Data Information BV with permission of Springer; RSV, respiratory syncytial virus
Our RSV assets offer a compelling opportunity for GSK

**Opportunity is significant**

- Potential first-in-class with differentiated adjuvant
- 70m adults age 60+ in the US\(^1\); >300m in developed regions\(^2\)
- \(~2/3\) of older adults in US receive flu or pneumococcal vaccines\(^2\)
- Protect infants from birth up to 6 months of life
- Potential to expand portfolio of other recommended vaccines for pregnant women
- 4m birth cohort in US\(^3\); globally >130m\(^4\)
- \(~50\%\) of pregnant women in US receive flu and/or pertussis vaccines\(^5\)

**Data support move to pivotal studies**

- Compelling neutralising antibodies response and T-cell restoration in older adults; well tolerated
- Phase 3 start on track for Q1 2021; initial data expected in H2 2022* 
- Immunogenic response; good safety profile
- Data in pregnant women in-house and supportive of advancement
- Maternal phase 3 to start Q4 2020; initial data expected in H2 2022*

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\(^2\) CDC: [https://www.cdc.gov/nchs/products/databriefs/db281.htm](https://www.cdc.gov/nchs/products/databriefs/db281.htm)
\(^3\) CDC: [https://www.cdc.gov/nchs/nvss/births.htm](https://www.cdc.gov/nchs/nvss/births.htm)
\(^4\) United Nations World Population Prospects 2019
\(^5\) CDC: [https://www.cdc.gov/vitalsigns/maternal-vaccines/index.html](https://www.cdc.gov/vitalsigns/maternal-vaccines/index.html)

*Timing dependent on RSV infection circulation during pandemic lockdowns.*